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Regulatory Science: The Future of Food Safety Risk Assessment

**Paul Hepburn, Adam Wood
and Richard Cubberley**



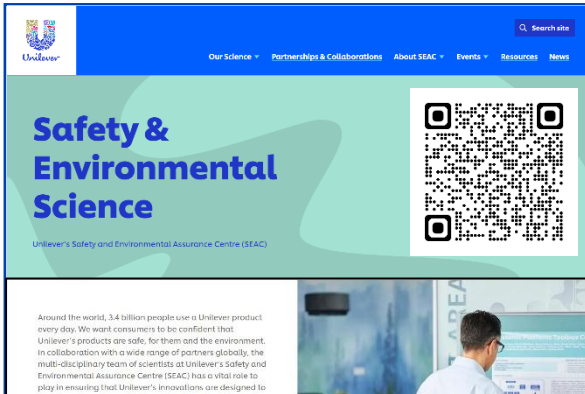
FSSAI International Training Centre, 10 Oct 2025

Please contact paul.hepburn@unilever.com or
adam.wood@unilever.com with any questions

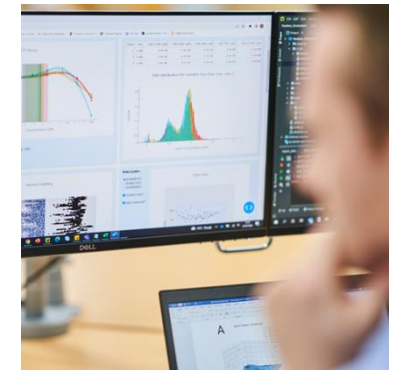


Our Purpose is to use leading-edge Science & Data to:

1 Protect People & the Environment from harm



2 Enable product Innovation, De-risking & Compliance



3 Pioneer industry & regulatory application of New Approaches, in partnership with other change leaders

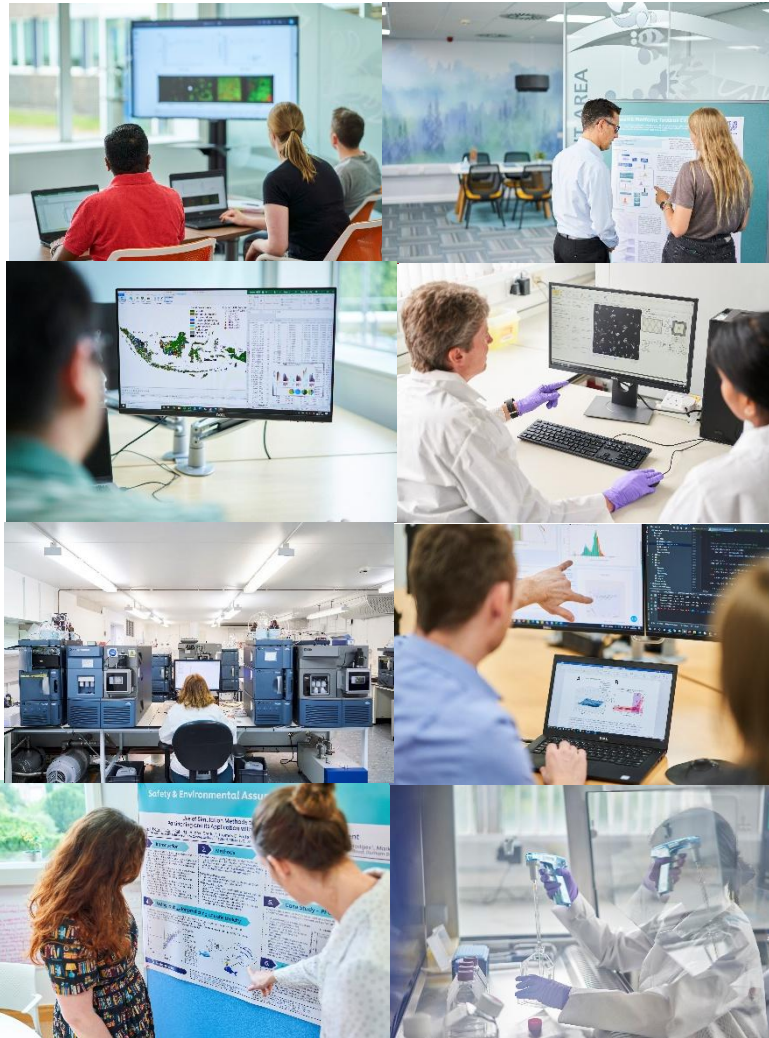


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SERS Expertise



SERS is a diverse, multi-disciplinary team of ~180 scientists covering:

- Cell & Molecular Biology
- Chemistry
- Computational Modelling
- Environmental Safety
- Environmental Sustainability
- Exposure Science
- Informatics & Data Science
- Mathematics & Statistics
- Microbiology
- Process Safety
- Regulatory Science (chemical & food safety)
- Toxicology

Collaboration:

- Academic
- Industry
- Government

20+ Nationalities

15+ Languages

9 Countries

- Deploy expertise on higher risk business projects
- Collaborate with leading external research teams to develop & apply new scientific capability
- Leverage science & global networks for consumer trust & freedom to operate

Safety Risk Assessments

- Consumers, Workers, Environment

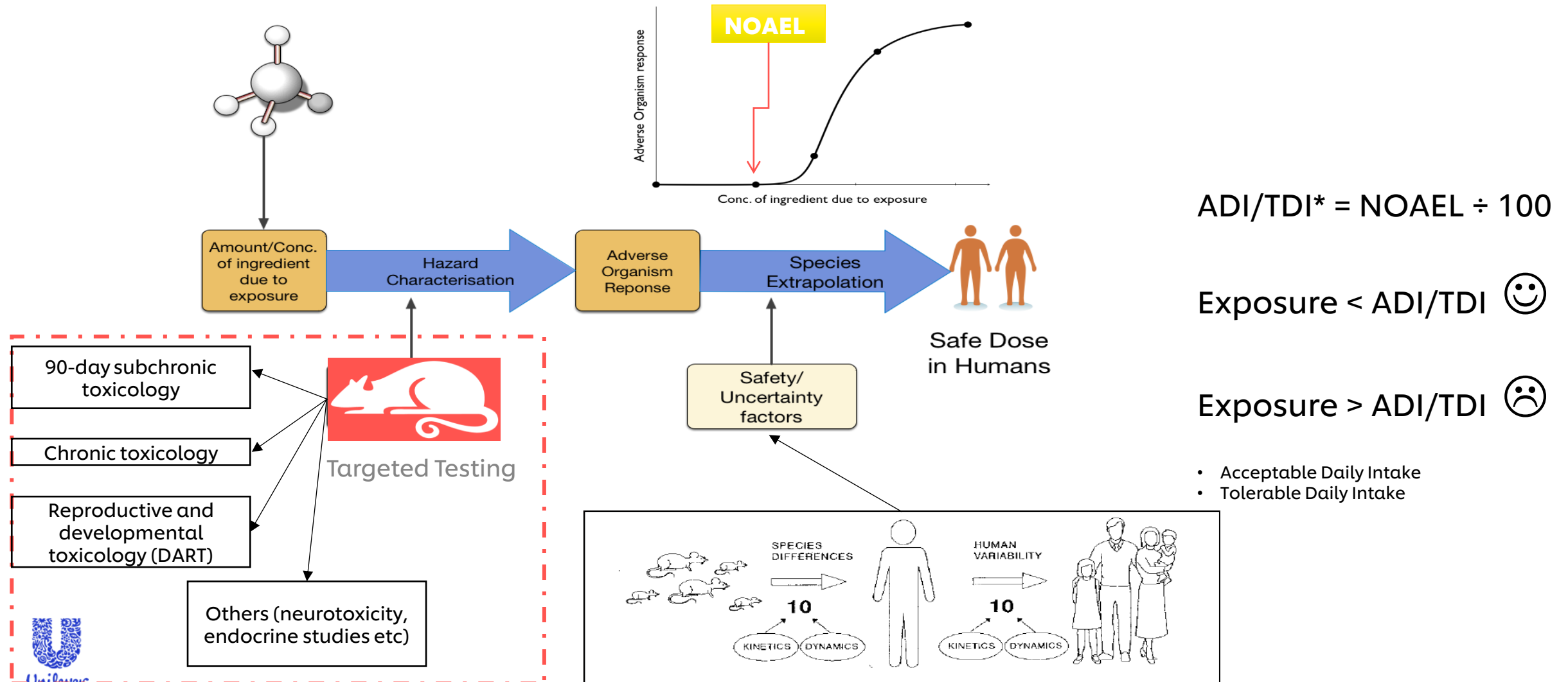
Life Cycle Assessments

- Environmental Impacts

Product Compliance

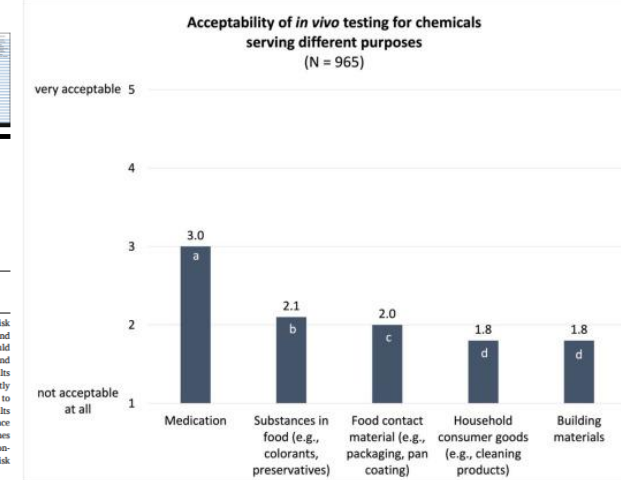
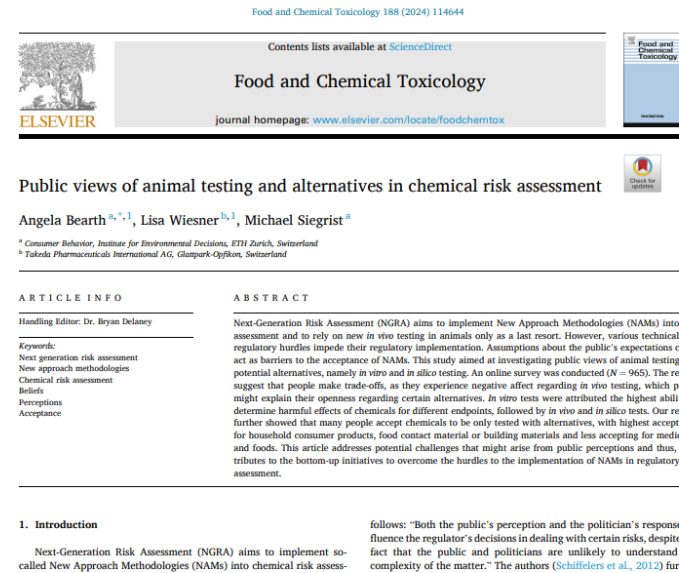
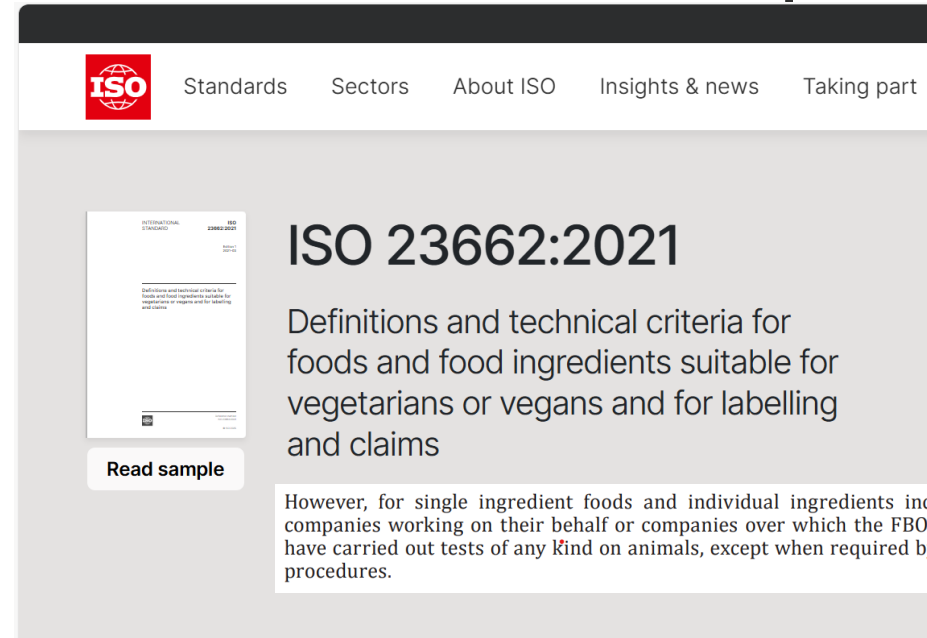
- Regulatory Data & Dossiers

Traditional Risk Assessment for Food Safety



Reasons for change...

- **Human relevance** – Various pathological findings in animals are not human-relevant – e.g. some hepatic tumours in mice (aspartame/sweetener) – consequence can be detrimental to consumer trust in food/safety and lack of approval – US Delaney clause etc
- **Mechanistic** -possibility for more informative risk assessments – sensitive populations, mixture effects etc.
- **Changing consumer attitudes** – growing consumer dissatisfaction with animal testing (no longer a cosmetics only issue!)
- **Vegan claims** – compliance relies upon consideration of animal testing (e.g. ISO)
- **Speed/resource** – dramatic uptake in novel food innovation to meet e.g. sustainability targets – traditional paradigm too lengthy

ISO Standards Sectors About ISO Insights & news Taking part

ISO 23662:2021

Definitions and technical criteria for foods and food ingredients suitable for vegetarians or vegans and for labelling and claims

Read sample

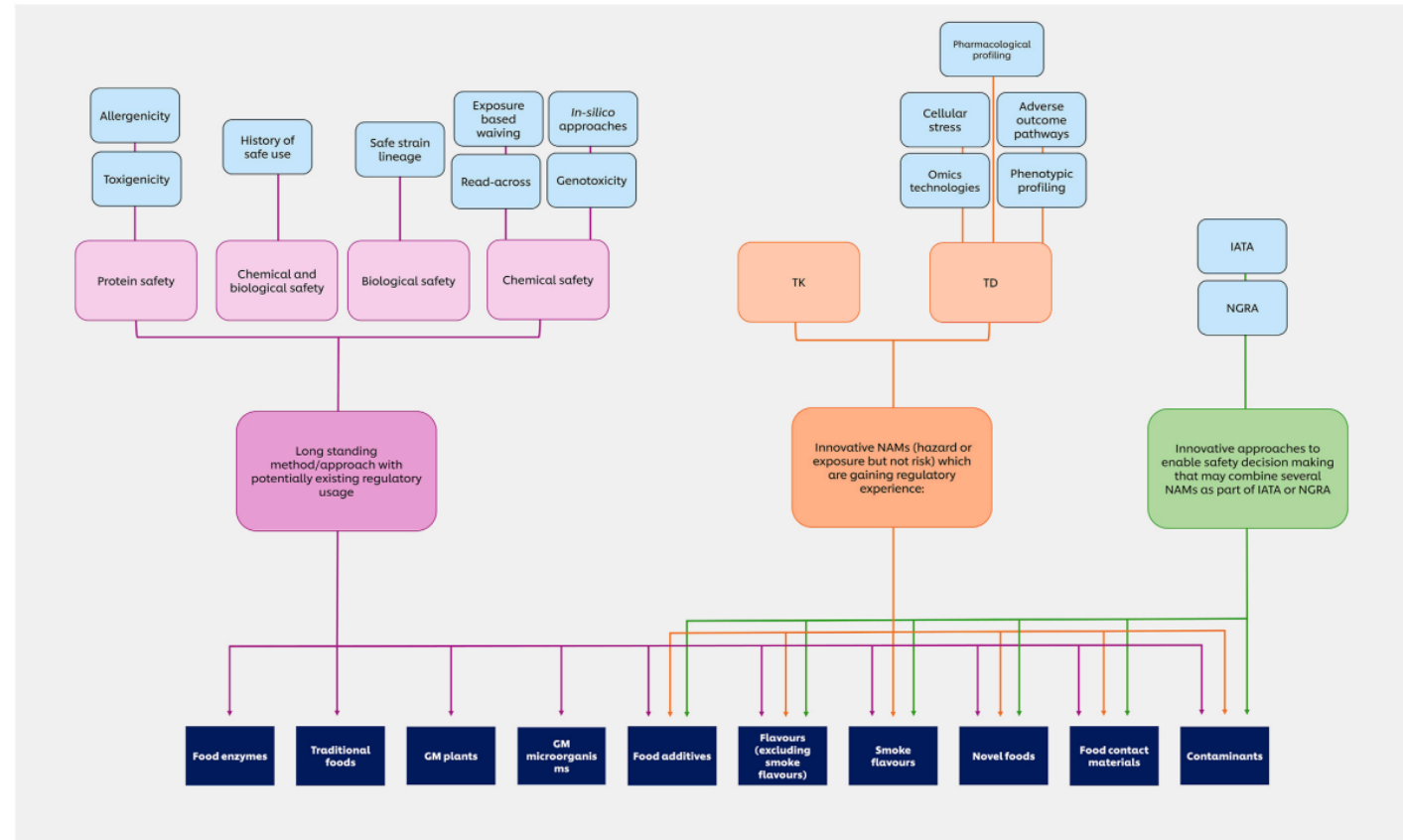
However, for single ingredient foods and individual ingredients including processing aids, FBOs, companies working on their behalf or companies over which the FBO has effective control shall not have carried out tests of any kind on animals, except when required by public authorities' regulatory procedures.

NGRA and New Approach Methodologies (NAMs)

- NAMs - Approaches that do not rely on generating new experimental animal data (though including those which use historical animal data) and comprising:
In vitro, *in silico*, *in chemico* and *ex vivo* human models
- Such approaches may be used to provide information on hazard or exposure or used in combination.
- Some NAMs are long-standing (history of use), others are more-recent (transcriptomics).

Their use in risk assessment is considered the next generation of risk assessment (NGRA)

Many NAMs of relevance to food safety exist and many could find use across multiple types of 'regulated products' (additives, flavours etc).

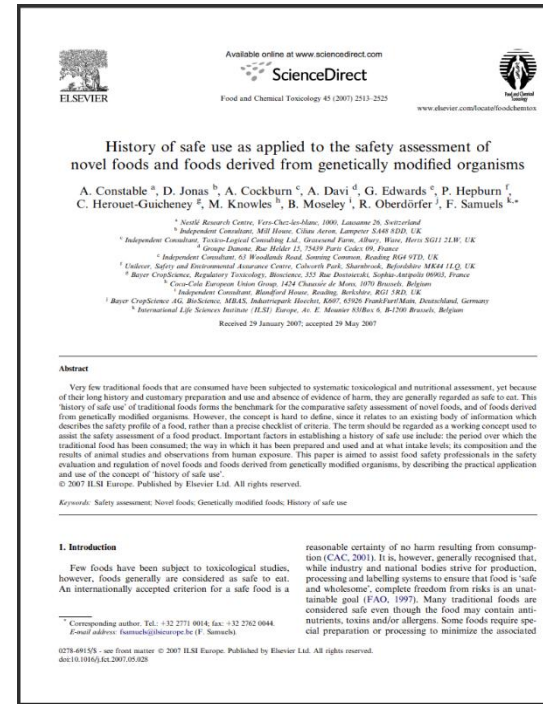


Wood et al., (2025). Regulatory Toxicology and Pharmacology, Volume 162, November 2025

CASE STUDIES

History of use

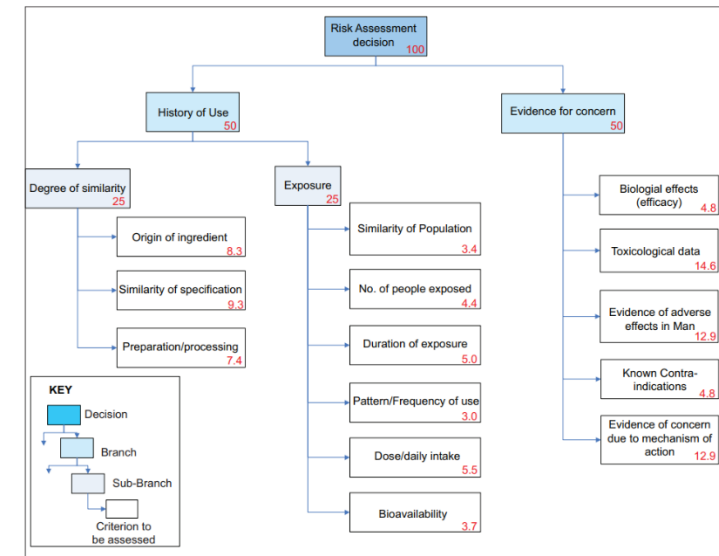
- A long-standing method (chemical and biological safety) that has played a role in numerous 'whole food' assessments, such as GM-crops and other novel foods, but also e.g. botanical extracts.
- Most often involves building an argument that a food is 'substantially equivalent' to a reference food and that reference food has a substantial and well characterised history of consumption.
- Relies on considering factors such as 1.) compositional similarity between proposed/reference food, 2.) evidence of adverse effects from reference food and 3.) data on how the comparator is prepared, consumed etc.



Constable et al., 2007, Food and Chemical Toxicology, Volume 45, Issue 12



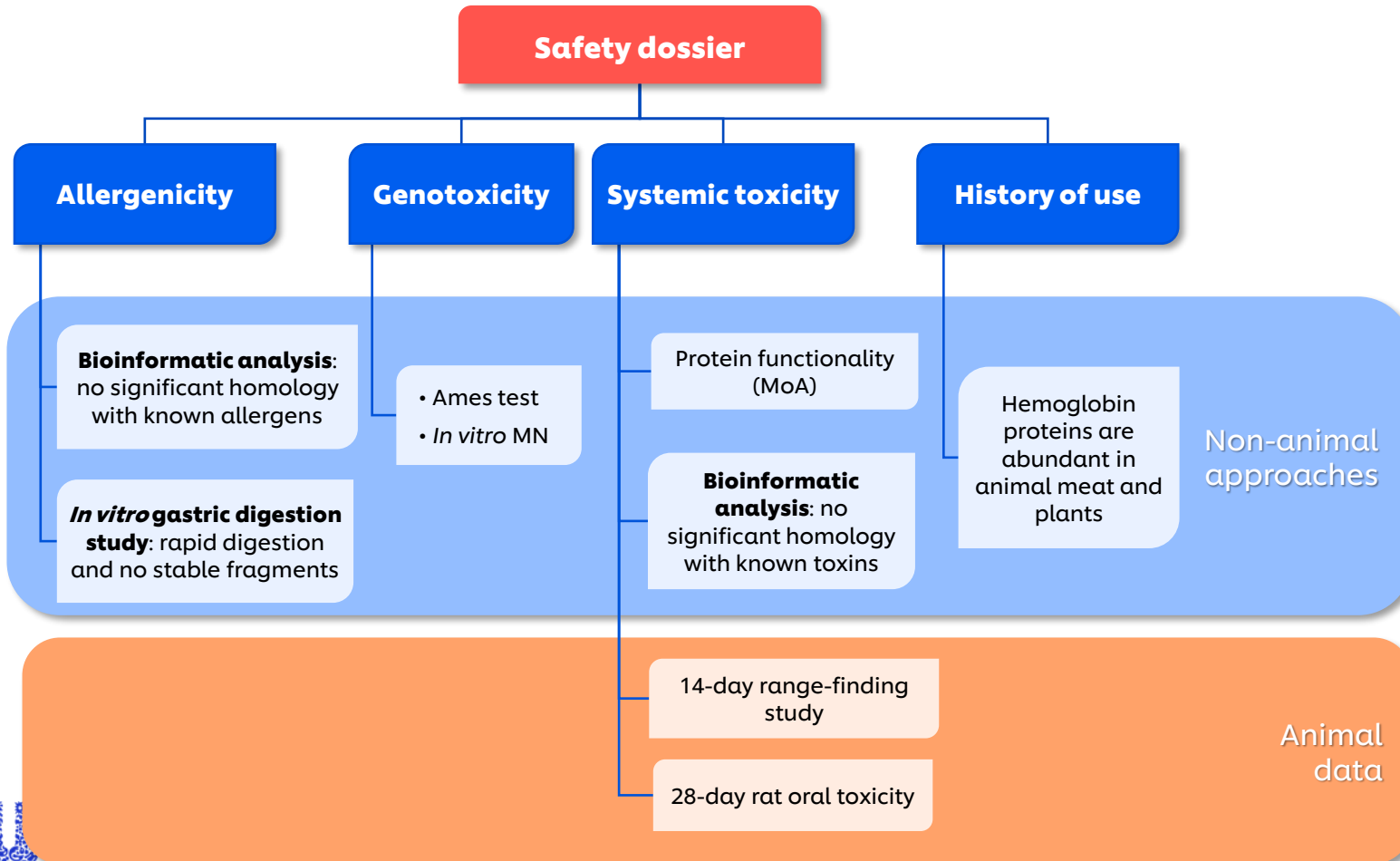
Neely et al., 2011, Toxicology International, 18 (Suppl1)



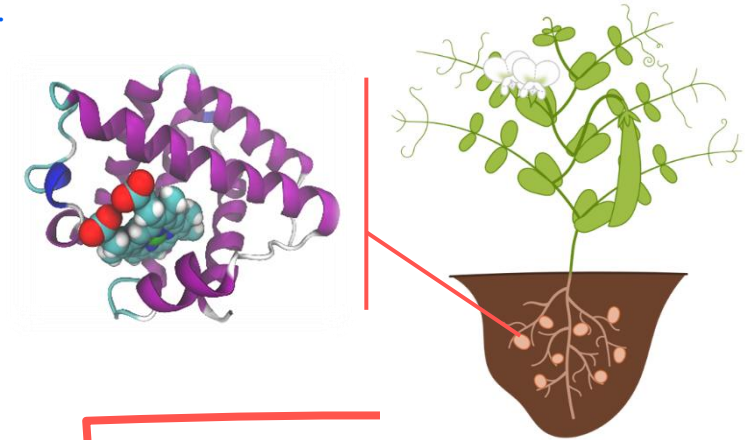
Soy leghemoglobin

- **Identity of the food:** leghemoglobin from soy (*Glycine max*) expressed in yeast (*Pichia pastoris*).
- **Proposed use:** food ingredient in meat-replacement products as iron source.

Safety dossier



GRAS Notification (2017)



Key points

- The history of consumption of hemoglobin proteins in food together with the NAM data provided clear evidence to make a determination of safety.

Conclusion could have been based on comparison with other haemoglobin/overall protein intake rather than NOAEL from in vivo tox study.

Threshold of toxicological concern (TTC)

- The ability to waive toxicological testing for a substance without data if exposure falls below a threshold under which there is no appreciable health risk.
- Vast amount of guidance and best practice available externally.
- Significant work still underway externally to further develop approach – e.g. new rules, database harmonisation, new categories etc – e.g. FDA expanded decision tree.
- Work underway to develop an internal TTC (iTTC) value that could represent a higher tier method to waive exposures for substances without data.

GUIDANCE DOCUMENT

ADOPTED: 24 April 2019
doi: 10.2903/j.efsa.2019.5708

Guidance on the use of the Threshold of Toxicological Concern approach in food safety assessment

EFSA Scientific Committee, Simon J More, Vasileios Bampidis, Diane Benford, Claude Bragard, Thorhallur I Halldorsson, Antonio F Hernández-Jerez, Susanne Hougaard Bennekou, Kostas P Koutsourakis, Kyriaki Machera, Hanspeter Naegele, Simon S Nielsen, Josef R Schlatter, Dieter Schrenk, Vittorio Silano, Dominique Turck, Magdaléna Younes, Ursula Gundert-Remy, George E N Kass, Juliane Kleiner, Anna Maria Rossi, Rositsa Serafimova, Linda Reilly and Heather M Wallace

Abstract

The Scientific Committee confirms that the Threshold of Toxicological Concern (TTC) is a pragmatic screening and prioritisation tool for use in food safety assessment. This Guidance provides clear step-by-step instructions for use of the TTC approach. The inclusion and exclusion criteria are defined and the use of the TTC decision tree is explained. The approach can be used when the chemical structure of the substance is known, there are limited chemical-specific toxicity data and the exposure can be estimated. The TTC approach should not be used for substances for which EU food/feed legislation requires the submission of toxicity data or when sufficient data are available for a risk assessment or if the substance under consideration falls into one of the exclusion categories. For substances that have the potential to be DNA-reactive mutagens and/or carcinogens based on the weight of evidence, the relevant TTC value is 0.0025 µg/kg body weight (bw) per day. For organophosphates or carbamates, the relevant TTC value is 0.3 µg/kg bw per day. All other substances are grouped according to the Cramer classification. The TTC values for Cramer Classes I, II and III are 30 µg/kg bw per day, 9 µg/kg bw per day and 1.5 µg/kg bw per day, respectively. For substances with exposures below the TTC values, the probability that they would cause adverse health effects is low. If the estimated exposure to a substance is higher than the relevant TTC value, a non-TTC approach is required to reach a conclusion on potential adverse health effects.

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Keywords: Threshold of toxicological concern, risk assessment, Cramer classification scheme

Requestor: European Food Safety Authority
Question number: EFSA-Q-2017-00468
Correspondence: sc.secretariat@efsa.europa.eu

frontiers in toxicology

Internal Threshold of Toxicological Concern (iTTC): Where We Are Today and What Is Possible in the Near Future

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¹The Procter and Gamble Company, Cincinnati, OH, United States; ²Research Institute for Fragrance Materials, Woodcliff Lake, NJ, United States; ³American Chemistry Council, Washington, DC, United States; ⁴Solvation, Limited Liability Company (LLC), Durham, NC, United States; ⁵Coactiva Europe, Brussels, Belgium; ⁶Bioscience Resource, Germany

OPEN ACCESS

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Specialty section: This article was submitted to Computational Toxicology and Informatics, a section of the journal Frontiers in Toxicology

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Keywords: Threshold of toxicological concern, iTTC, iTTC, in vitro, in vivo, MVE, physiologically based pharmacokinetic modeling, PBPK, metabolism

INTRODUCTION

Industries and regulatory agencies across the world are challenged with performing human health safety assessments, risk-based prioritizations, and evaluations of thousands of chemicals. In vitro testing in animal toxicological studies is time- and resource-intensive, impractical for thousands of substances, and biased for cosmetics ingredients. Therefore, there has been a concerted effort within the scientific and regulatory communities toward the development and utilization of alternative approaches [European Union (EU) Cosmetic Regulation (Regulation 1223/2009), US NRC, US National Research Council, 2017]. The Threshold of Toxicological Concern (TTC)

https://www.fda.gov/food/food-chemical-safety/expanded-decision-tree-fdas-food-chemical-toxicity-screening-tool

An official website of the United States government Here's how you know

FDA U.S. FOOD & DRUG ADMINISTRATION

Home / Food / Food Ingredients & Packaging / Food Chemical Safety / Expanded Decision Tree: FDA's Food Chemical Toxicity Screening Tool

Expanded Decision Tree: FDA's Food Chemical Toxicity Screening Tool

Food Chemical Safety

List of Select Chemicals in the Food Supply Under FDA Review

Chemical Compound

Input Data

Expanded Decision Tree
Data from 1,000's of Compounds

Output Data

EDT Tiers

VI
or
V
or
IV
or
III
or
II

Examples

Adopted: 21 March 2024
DOI: 10.2903/j.efsa.2024.6709

SCIENTIFIC OPINION

Flavouring group evaluation 419 (FGE.419): 2-methyl-1-(2-(5-(p-tolyl)-1H-imidazol-2-yl)piperidin-1-yl)butan-1-one

EFSA Panel on Food Additives and Flavourings (FAF) | Maged Younes | Gabriele Aquilina | Laurence Castle | Gisela Degen | Karl-Heinz Engel | Paul J. Fowler | Maria Jose Frutos Fernandez | Peter Fürst | Ursula Gundert-Remy | Rainer Gürtler | Trine Husøy | Melania Marco | Peter Moldovea | Sabina Passamonti | Romina Shah | Ine Waalkens-Berendsen | Matthew Wright | Romualdo Benigni | Claudia Bolognesi | Kevin Chipman | Eugenia Cordelli | Karin Norby | Camilla Svendsen | Maria Carli | Gabriele Gagliardi | Carla Martino | Salvatore Multari | Wim Mennes

Correspondence: fip@efsa.europa.eu

Abstract
The EFSA Panel on Food Additives and Flavourings (FAF) was requested to evaluate the safety of 2-methyl-1-(2-(5-(p-tolyl)-1H-imidazol-2-yl)piperidin-1-yl)butan-1-one (FL-no: 16.134) as a new flavouring substance, in accordance with Regulation (EC) No 1331/2008. The substance has not been reported to occur naturally and is chemically synthesised. In food, it is intended to be used as a flavouring substance only in chewing gum. The chronic dietary exposure to FL-no: 16.134 was estimated to be 45 µg/person per day for a 60-kg adult and 28.4 µg/person per day for a 15-kg 3-year-old child. FL-no: 16.134 did not show genotoxicity in a bacterial reverse mutation test and an in vitro mammalian cell micronucleus assay. Based on the submitted toxicokinetic and metabolism data, it can be predicted that the flavouring substance is metabolised to innocuous products only. The Panel derived a lower confidence limit of the benchmark dose (BMDL) of 0.71 mg/kg bw per day for a 20% increase in the relative thyroid (including parathyroid) weight observed in a 90-day toxicity study in rats. Based on the BMDL, adequate margins of exposure of 887 and 374 could be calculated for adults and children, respectively. The Panel concluded that there is no safety concern for FL-no: 16.134 when used as a flavouring substance at the estimated level of dietary exposure, based on the intended use and use levels as specified in Appendix B. The Panel further concluded that the combined exposure to FL-no: 16.134 from its use as a food flavouring substance and from its presence in toothpaste and mouthwash is also not of safety concern.

KEYWORDS
2-methyl-1-(2-(5-(p-tolyl)-1H-imidazol-2-yl)piperidin-1-yl)butan-1-one, FGE.419, FL-no: 16.134

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EFSA Journal 2024;22(3):6709
<https://doi.org/10.2903/j.efsa.2024.6709> efsa.onlinelibrary.wiley.com/doi/10.2903/j.efsa.2024.6709 | 1 of 18

Example 1: 2-methyl-1-(2-(5-(ptolyl)-1H-imidazol-2-yl)piperidin-1-yl)butan-1-on (substance A)

- Cramer Class III (90µg/person per day)
- Dietary exposure estimates of 45 and 28.4 µg/day for adults and children, respectively
- Exposure less than TTC – no animal data needed
- Applicant did perform a 90-day study (BMDL = 0.71 mg/kg – MoE 887 and 374 respectively).
- **Animal testing unnecessary**

Example 2: 2-(4-methylphenoxy)-N-(1H-pyrazol-3-yl)-N-(thiophen-2-ylmethyl)acetamide (substance B)

- Cramer Class III (90µg/person per day)
- Dietary exposure: 225 µg/day (adults) and 142 µg/day (children).
- Exposures were hence ~2-fold above TTC and animal studies performed (90-day and developmental toxicity study). No effects in either study (up to 100 mg/kg) and MoE (min) was 10,500
- **In the future, possibly an internal TTC could be used to address safety for cases like this.**

ADOPTED: 12 September 2018
doi: 10.2903/j.efsa.2018.5421

SCIENTIFIC OPINION

Scientific Opinion of Flavouring Group Evaluation 411 (FGE.411): 2-(4-methylphenoxy)-N-(1H-pyrazol-3-yl)-N-(thiophen-2-ylmethyl)acetamide from chemical group 30 (miscellaneous substances)

EFSA Panel on Food Additives and Flavourings (FAF), Maged Younes, Gabriele Aquilina, Laurence Castle, Karl-Heinz Engel, Paul Fowler, Maria Jose Frutos Fernandez, Peter Fürst, Ursula Gundert-Remy, Rainer Gürtler, Trine Husøy, Peter Moldovea, Agneta Oskanson, Sandra Rastner, Romina Shah, Ine Waalkens-Berendsen, Detlef Wölfl, Romualdo Benigni, Mona-Lise Birkedal, Claudia Bolognesi, Leon Brimer, Kevin Chipman, Francesca Mancini, Daniel Marzouk, Pasquale Moscone, Gerard Mulder, Camilla Svendsen, Jan van Bennekom, Maria Anastasiadou, Maria Carli and Wim Mennes

Abstract
EFSA was requested to deliver a scientific opinion on the implications for human health of the flavouring substance 2-(4-methylphenoxy)-N-(1H-pyrazol-3-yl)-N-(thiophen-2-ylmethyl)acetamide (FL-no: 16.133), in the Flavouring Group Evaluation 411 (FGE.411), according to Regulation (EC) No 1331/2008 of the European Parliament and of the Council. The substance has not been reported to occur in natural source materials of botanical or animal origin. It is intended to be used as a flavouring substance in specific categories of food but not intended to be used in beverages, except for milk and dairy based beverages that are opaque. The chronic dietary exposure to the substance estimated using the added portion exposure technique (APET), is calculated to be 225 µg/person per day for a 60-kg adult and 142 µg/person per day for a 15-kg 3-year-old child. A 90-day oral gavage study in rats showed no adverse effects at doses up to 100 mg/kg body weight (bw) per day, providing an adequate margin of safety. Developmental toxicity was not observed in a study with rats at the dose levels up to 1,000 mg/kg bw per day. The Panel concluded that there is no safety concern for FL-no: 16.133, when used as a flavouring substance at the estimated level of dietary exposure calculated using the APET approach and based on the recommended use and use levels as specified in Appendix S. This conclusion does not apply for use in beverages where the substance can be subject to phototransformation.

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Keywords: Flavouring, 2-(4-methylphenoxy)-N-(1H-pyrazol-3-yl)-N-(thiophen-2-ylmethyl)acetamide, FGE.411, FL-no: 16.133

Requestor: European Commission
Question number: EFSA-Q-2015-02820
Correspondence: FIP@efsa.europa.eu

www.efsa.europa.eu/efsaopinion EFSA Journal 2018;16(12):5421

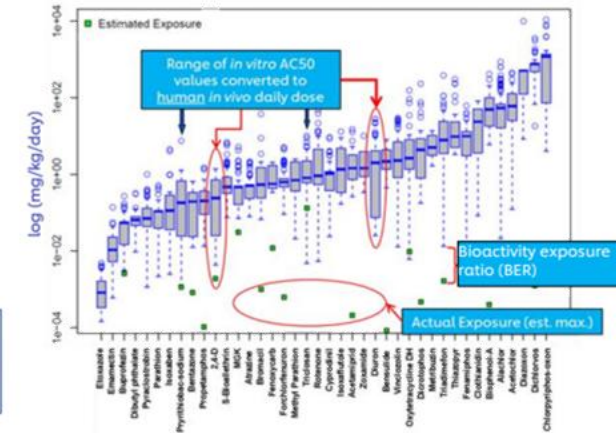
The need for innovative NAMs

Until recently, for, ingredients used at levels >TTC or ingredients where a history of use cannot be established...

Demonstrating safety without animal testing was challenging. However, in recent years, tremendous progress made in areas such as...

- High-throughput screening
- Computational sciences – bioinformatics, pharmacokinetic modelling, statistics etc

These scientific advancements have opened new possibilities that have collectively shifted the dial in terms of our ability to demonstrate safety using non-animal methods



Graph from Rusty Thomas EPA, with thanks, Rotroff et al (2010) Toxicological Sciences, 117, 348-358

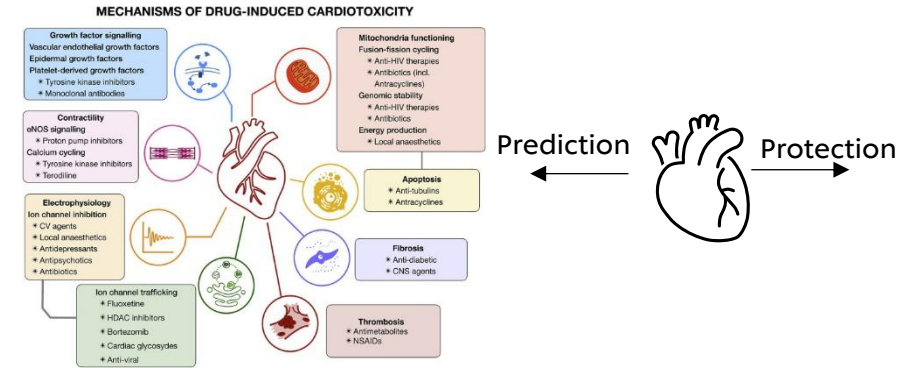
$$BER = \frac{\text{Lowest bioactivity POD}}{\text{Internal in vivo exposure (Cmax)}} (\mu\text{M})$$

NAM development – protection vs prediction

Rapid development of NAMs for use in risk assessment. Two alternate philosophies:

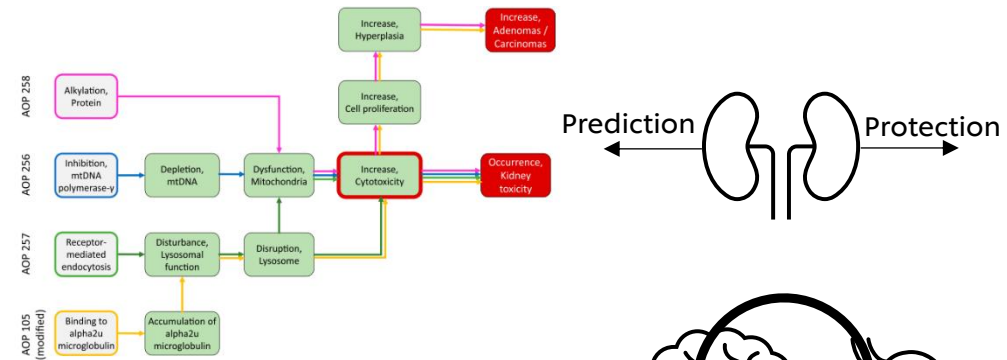
- 1.) NAMs developed to **predict** (possibly quantitatively) adverse effects
- 2.) NAMs developed to measure bioactivity (quantitatively) without classification as adversity or not.

Both have a place in **future** risk assessment. **Unilever have invested significant resource into protective NAMs**



Manoshina et al., (2021). Cell Reports Medicine. 2:3 100216

NAMs capturing early biological changes protective of apical effects



Mally and Jarzina (2022). Frontiers in Toxicology

There are 78 major human organs; let's say there are five different ways in which chemicals could be toxic to each one (an underestimate); and let's say we need five key events (including a molecular initiating event) measured across each IATA with new in vitro tests. That's around 2000 assays conducted at just one dose and at one time point for complete human AOP-driven biological coverage.

Carmichael et al., (2022). Altex, 39:3

Limited coverage approaches

Cell based/reporter assays

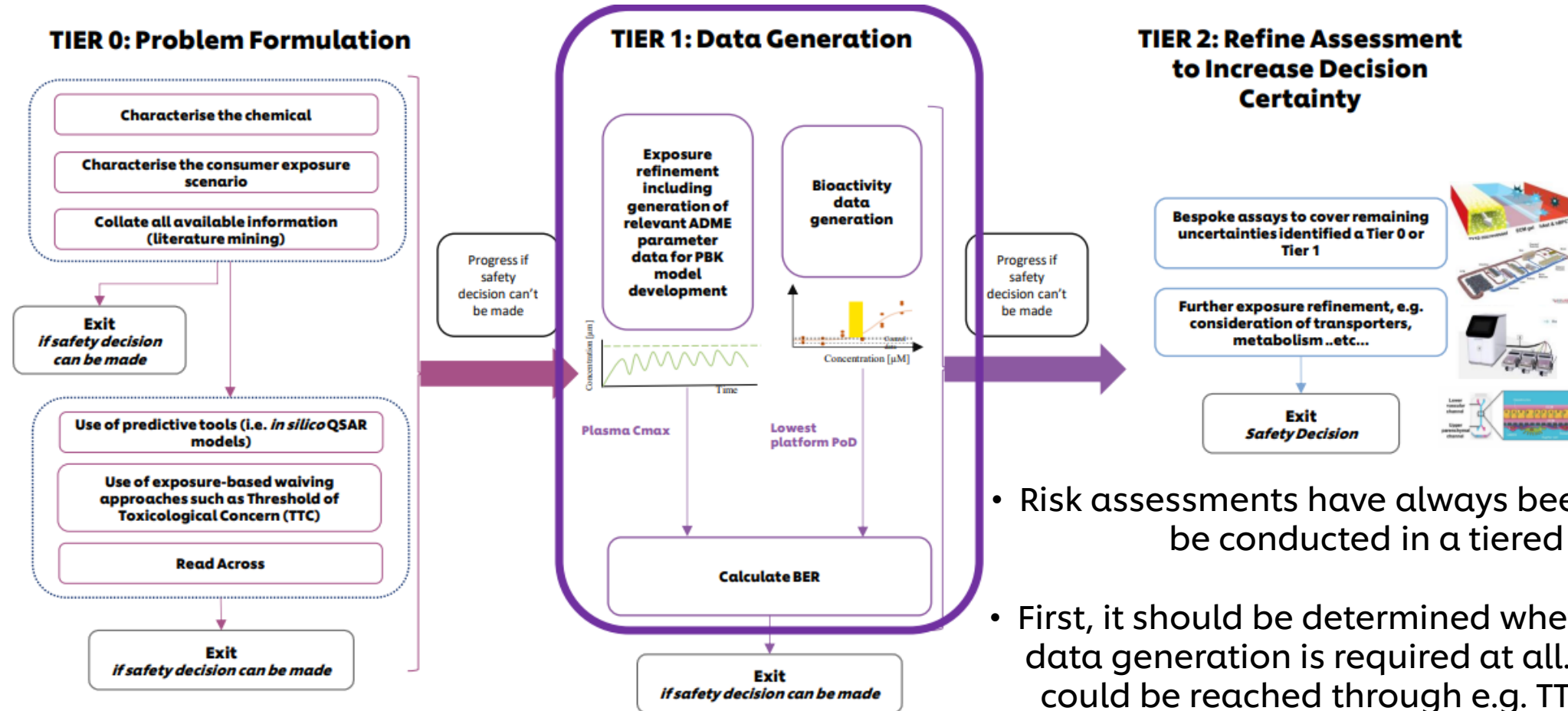
Data rich approaches

Transcriptomics

Cell painting

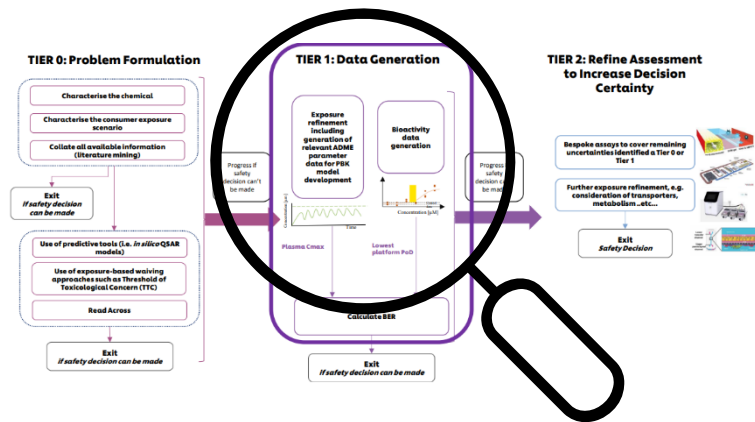
State of the art (>20-years)

Place of innovative NAMs in tiered risk assessment framework



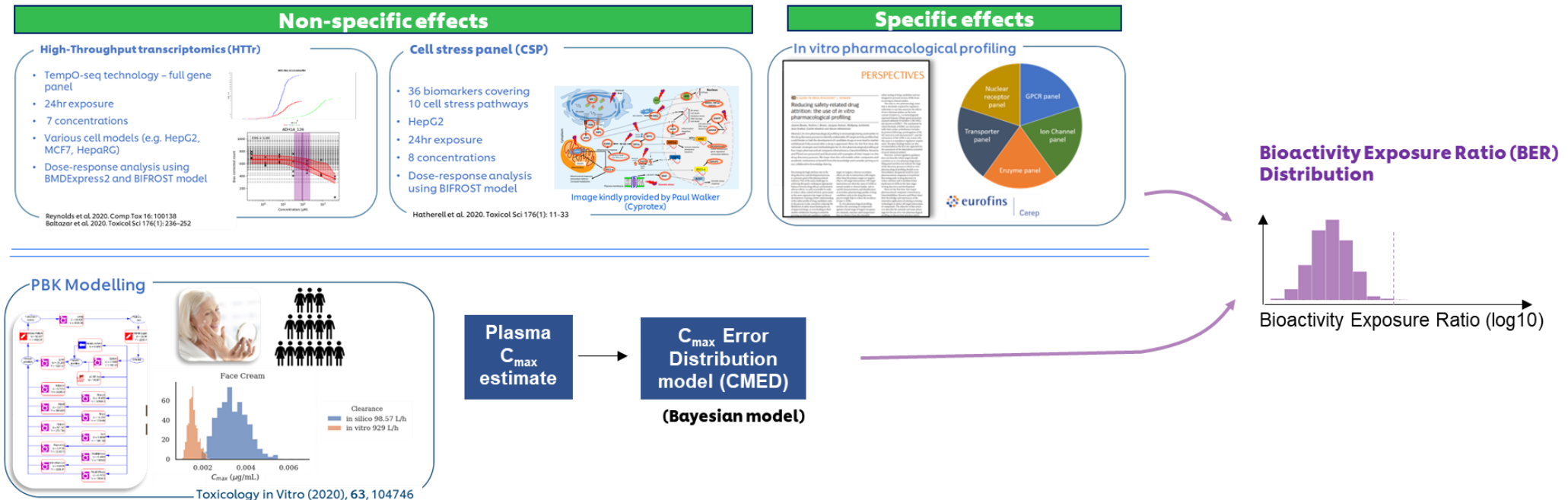
- Risk assessments have always been and will always be conducted in a tiered manner.
- First, it should be determined whether experimental data generation is required at all. A safety decision could be reached through e.g. TTC or read-across without new studies being performed.
- If data generation is needed, **NAMs are used in a tiered way, starting with broad coverage (protective) NAMs progressing to specific (predictive) NAMs as needed.**

Unilever's NAM toolbox and NGRA tiered framework approach



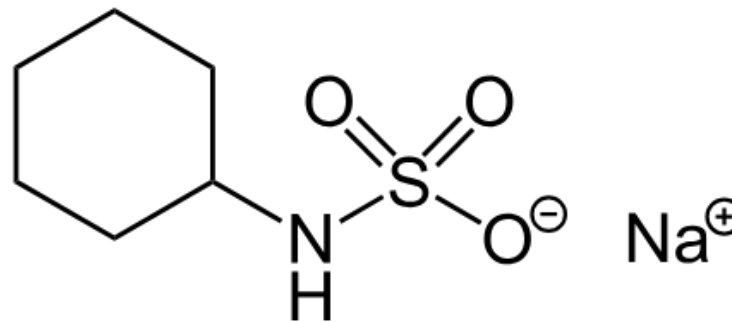
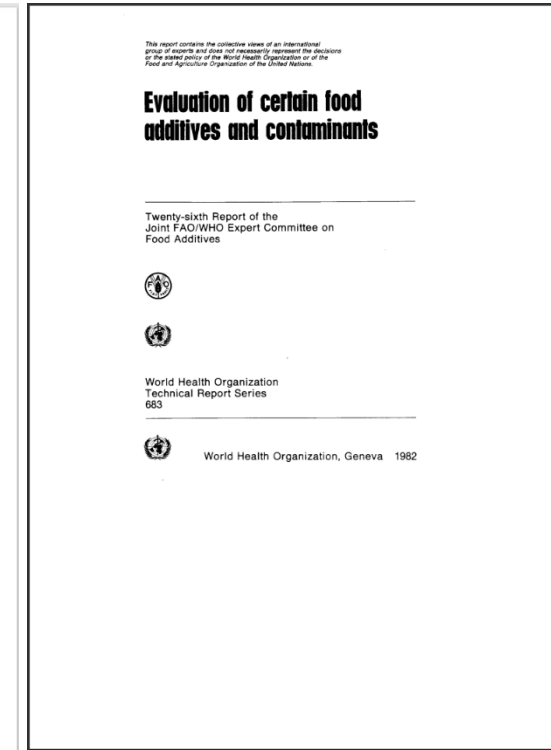
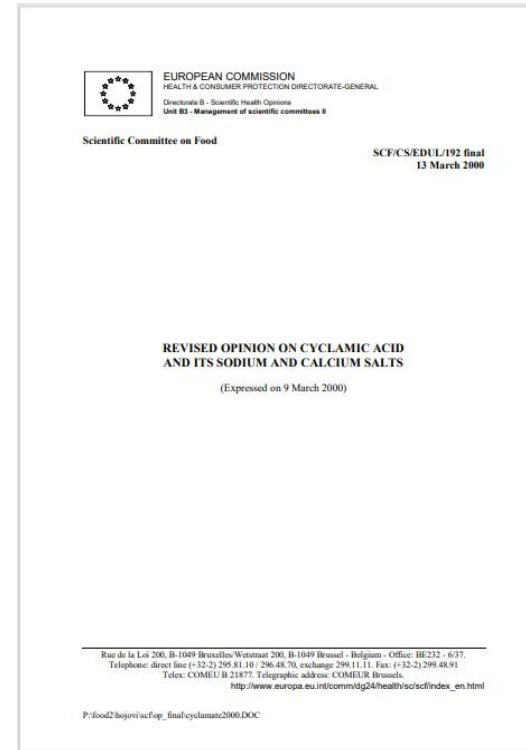
- Unilever's basic NAM toolbox uses **non-specific and specific NAMs**.
- Point of departures (PoDs) from these are compared with PBK model estimates of internal exposure to enable risk characterisation (through a **bioactivity exposure ratio/BER**).

Point of Departure (PoD) determination from Bioactivity assays



Case study - cyclamate

- Sodium cyclamate, also called E952 (ii), is used as an artificial sweetener.
- Has been reviewed by JECFA (1982) and the SCF (2000) with ADIs established as 0-11 mg/kg (JECFA) and 0-7 mg/kg (SCF). Re-evaluation currently underway by EFSA.
- ADI is based on a NOAEL of 100 mg/kg derived from a 90-day rat study where the rats were administered cyclohexylamine (CHA: the major metabolite of cyclamate).



E Number Name

E 420	Sorbitols
E 421	Mannitol
E 950	Acesulfame K
E 951	Aspartame
E 952	Cyclamates
E 953	Isomalt
E 954	Saccharins
E 955	Sucralose
E 957	Thaumatin
E 959	Neohesperidine DC
E 960a	Steviol glycosides from Stevia
E 960c	Enzymatically produced steviol glycosides
E 960d	Glucosylated steviol glycosides

EFSA's Assessment

Re-evaluation ongoing
Re-evaluation ongoing
Re-evaluation completed in 2025
Re-evaluation completed in 2013
Re-evaluation ongoing
Re-evaluation ongoing
Re-evaluation completed in 2024
Re-evaluation ongoing
Re-evaluation completed in 2021
Re-evaluation completed in 2022
First evaluated in 2010
Evaluated in 2019
Evaluated in 2022
First evaluated in 2007

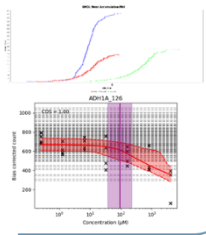
Unilever's NAM toolbox

Point of Departure (PoD) determination from Bioactivity assays

Non-specific effects

High-Throughput transcriptomics (HTTr)

- TempO-seq technology - full gene panel
- 24hr exposure
- 7 concentrations
- Various cell models (e.g. HepG2, MCF7, HepaRG)
- Dose-response analysis using BMDEExpress2 and BIFROST model



Reynolds et al. 2020, Comp Tox 16: 100138
Baltazar et al. 2020, Toxicol Sci 176(1): 236-252

Cell stress panel (CSP)

- 36 biomarkers covering 10 cell stress pathways
- HepG2
- 24hr exposure
- 8 concentrations
- Dose-response analysis using BIFROST model

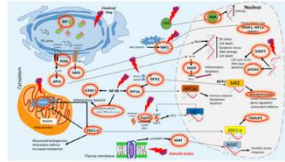
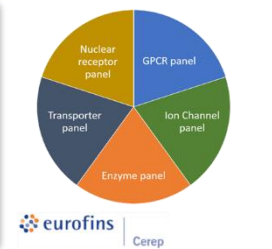


Image kindly provided by Paul Walker (Cyprotex)

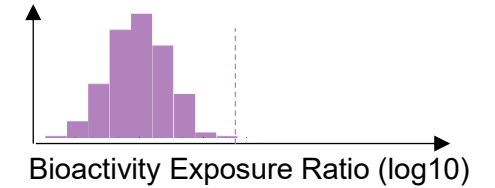
Hatherrell et al. 2020, Toxicol Sci 176(1): 11-33

Specific effects

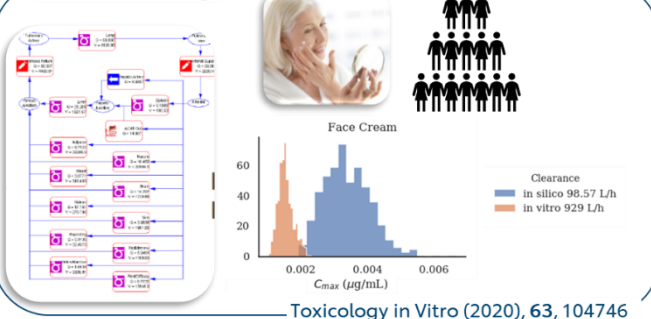
In vitro pharmacological profiling



Bioactivity Exposure Ratio (BER) Distribution



PBK Modelling



Toxicology in Vitro (2020), 63, 104746

Plasma
 C_{max}
estimate

C_{max} Error
Distribution
model (CMED)

(Bayesian model)

NGRA data - cyclamate

Exposure/PBK modelling:

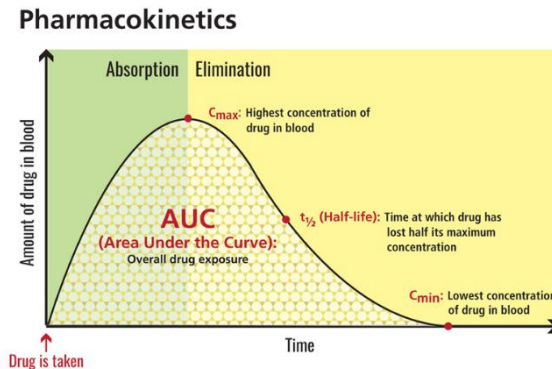
PBK models need several building blocks!

An external dose

Physical-chemical properties

Pharmacokinetic properties

The outcomes are estimates of internal exposure, such as the maximum concentration in plasma (C_{max})

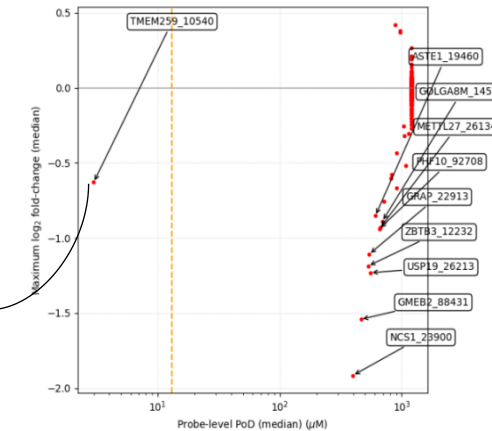
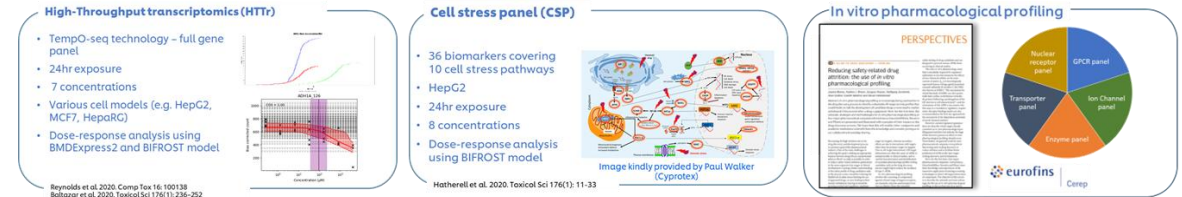


For cyclamate, our PBK modelling estimated a C_{max} of **~69 µM** after consumption of the ADI

Point of departure estimation:

Sodium cyclamate tested in the Unilever NAM toolbox

- Result is a series of PoDs across various NAMs



For cyclamate, the lowest PoD across the NAMs was from the transcriptomics study

PoD (13)

= 'Bioactivity : Exposure Ratio' (BER) (13/69 = 0.18)

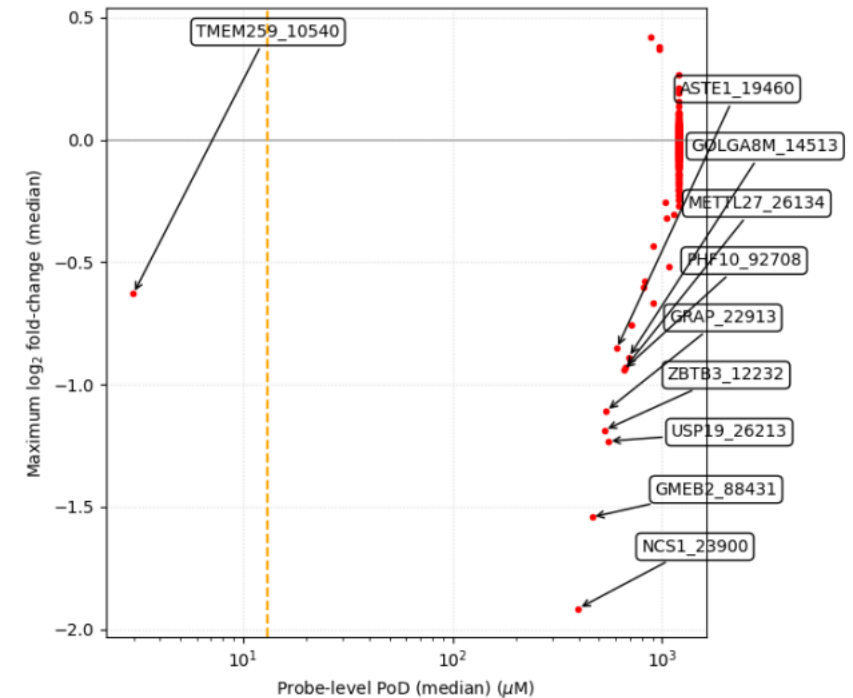
Exposure (69)

For cyclamate, bioactivity occurs at a lower exposure than dietary intake of the ADI – **higher tier models needed!**

Cyclamate - summary

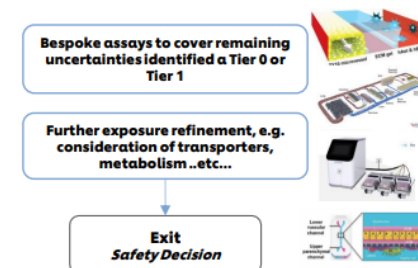
- PBK estimates of internal exposure – at the ADI, C_{max} = ~68 µM.
- Lowest PoD from the NAMs (~12 µM) came from the transcriptomics study - HepG2 cells when looking for the lowest responding genes – **highly conservative!**
- NAM PoDs less than C_{max} - further experimental data generation would be required.
- **(Next generation) risk assessments require tiering!**
- Exciting developments underway externally with higher tier *in vitro* models e.g. organ on chip, alternative data analysis methods – key characteristics, gene signatures and computational sciences – AI etc.

Call to action: Evolution of dietary intake surveys to **always** include information on the time of intake as well as the amounts of consumed will be needed to support the shift to NGRA by the food sector



Single gene level PoDs after Cyclamate treatment (HepG2 cells) – unlikely toxicological significance

TIER 2: Refine Assessment to Increase Decision Certainty



External developments

- In recent years, national and international food safety authorities have been working towards further integrating NAMs in risk assessment.
- Food industry have made positive steps towards building internal NGRA capability and working to achieve regulatory change.
- Progress is still needed to maximise the use of NAMs in food safety assessments!



Agenda

New Approach Methodologies (NAMs) in Future Food Safety Risk Assessment

a Joint Workshop by World Health Organization (WHO) and Nanyang Technological University, Singapore (NTU Singapore)

Royal Plaza on Scotts, Singapore, 18 to 20 June 2025



EFSA Strategy 2027

Science
Safe food
Sustainability

future challenges. Within its risk assessment approaches, EFSA will develop and integrate new scientific developments focusing on NAM-based methods and the minimisation of animal testing, innovations in food systems, data, and technology, and strive to meet One health policy needs.

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

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Abstract

While whole animal studies have their place in risk assessment of food and feed components, it is thought that more modern approaches such as human focused new approach methodologies (NAMs) would bring advantages including a greater focus to the human species, a focus on molecular mechanism and kinetics and the possibility of addressing susceptible populations. This report outlines the thinking from the authors and culminates in activity proposals in seven distinct but interacting scientific areas i.e. development of additional AOPs/AOP networks (AOPs), advanced cell culture models including Organ on a chip (OCs), toxicokinetic assessment with a focus on physiological based kinetic modelling (PBK), exposure, human susceptibility, data integration and new concepts in human risk assessment. Furthermore, the development of a Forum is proposed to facilitate the implementation of new approaches and concepts in risk assessment. The report was compiled by the project team, renowned experts in the various areas, and recommendations were discussed with EFSA and further refined following consultation with external experts via a dedicated workshop. The authors are convinced that if the recommendations are taken up, there will be a significant impact in the field, resulting in increasing the uptake and utilisation of these emerging technologies by all stakeholders involved.

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Key words: Next Generation Risk Assessment, New Approach Methods, implementation, AOP, IATA

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Countdown to 2027 – maximising use of NAMs in food safety assessment: closing the gap for regulatory assessments in Europe

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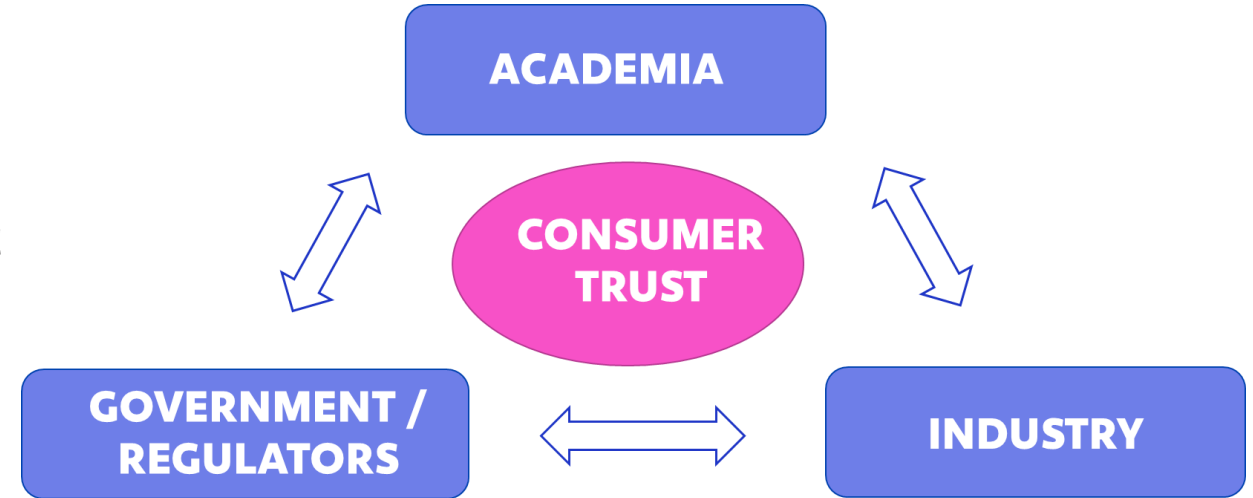
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Wrap-up

- Food safety is complex because food is complex! 'Food' comprises everything from single chemicals (flavours, additives) to complex mixtures with nutritionally relevant components.
- Multitude of different toxicological studies needed to deliver safe food given its complexity.
- The food safety ecosystem has played a key historical role in the development and application of NAMs.
- Paradigm shift is underway in risk assessment towards the use of innovative NAMs.
- **Multi-disciplinary, multi-stakeholder engagement and collaboration needed to fully achieve the vision of non-animal safety science.**



The screenshot shows the EPA website's 'News Releases' page. The header includes the EPA logo and navigation links: 'Environmental Topics', 'Laws & Regulations', 'Report a Violation', and 'About EPA'. The main content area features the title 'EPA and Unilever Announce Major Research Collaboration to Advance Non-animal Approaches for Chemical Risk Assessment' dated August 19, 2021. A 'Contact Information' section lists the EPA Press Office email as epress@epa.gov. The text of the release states that EPA and Unilever have announced a collaborative agreement to explore better ways to assess chemical risks associated with consumer products, building on prior cooperation between the two organizations regarding New Approach Methods (NAMs). It mentions that this collaboration is helping EPA implement its New Approach Methods Work Plan and is the foundation for new efforts to demonstrate that these novel approaches can help decision makers better protect consumers, workers and the environment. A quote from H. Christopher Frey, Deputy Assistant Administrator for Science Policy in EPA's Office of Research and Development, is included, along with a statement about the new collaborative effort aiming to establish a framework for the Next Generation of Risk Assessments based on NAMs.