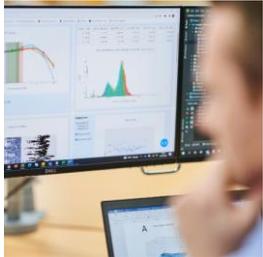


# Overview of New Approach Methodologies (新途径方法综述)

## Carl Westmoreland and Dawei Tang (汤大为)

New Approach Methodologies for Future Food Safety Risk Assessment Seminar  
Beijing, 14<sup>th</sup> October 2025

**SERS**  
Safety, Environmental & Regulatory Science



# Next Generation Risk Assessment (NGRA) New Approach (non-animal) Methodologies (NAMs)

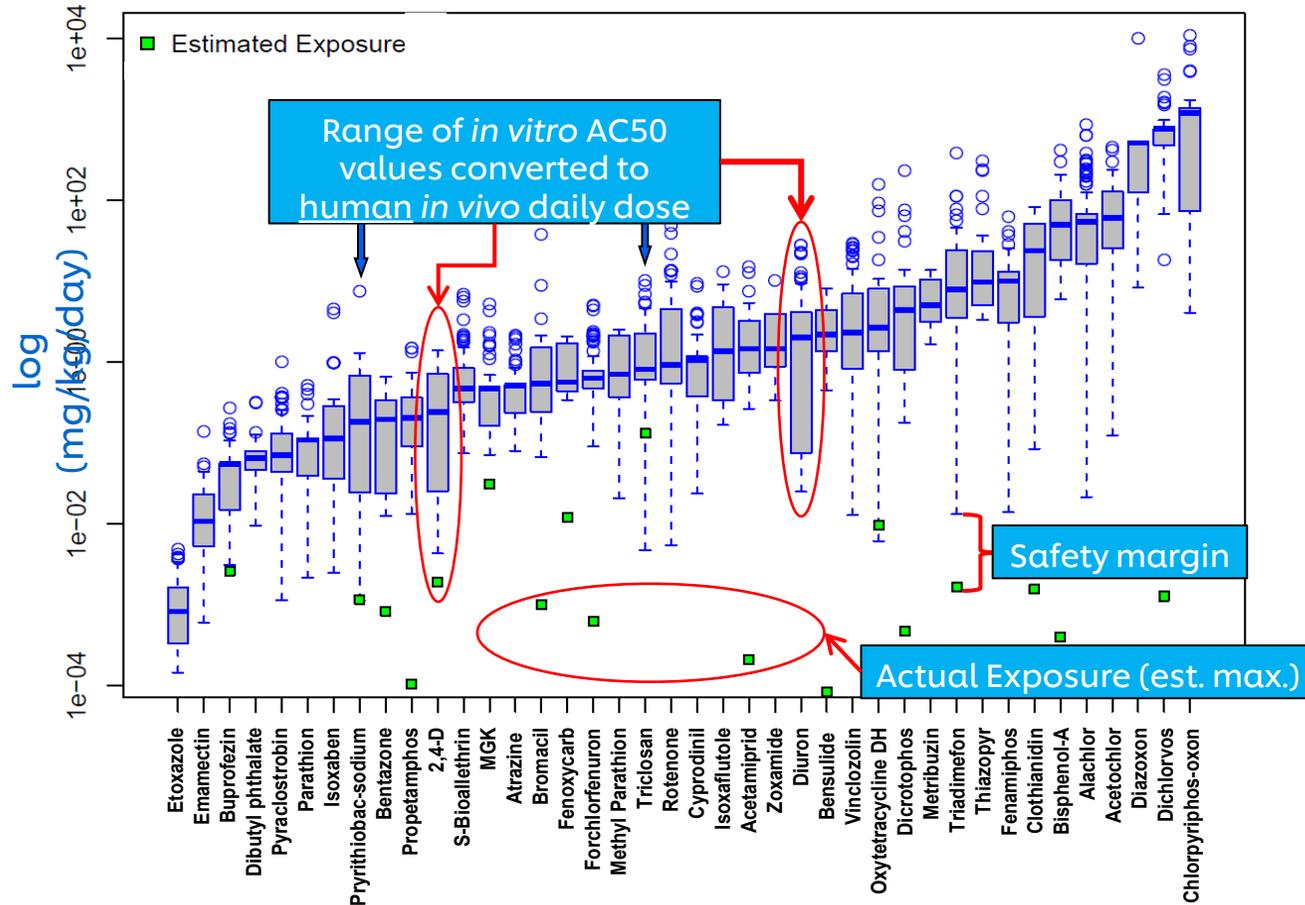
**NGRA** is an exposure-led, risk assessment approach that integrates New Approach Methodologies (NAMs) to assure (human & environmental) safety without the use of animal testing

**NAMs** are any *in vitro* or computational (*in silico*) method that enables mechanistically based chemical safety assessment and contributes to the replacement of animals

讨论争议点：下/新一代风险评估； Next/New?

# Applying the NGRA concept to Safety Assessment – PROTECTION not PREDICTION (保护而不是预测)

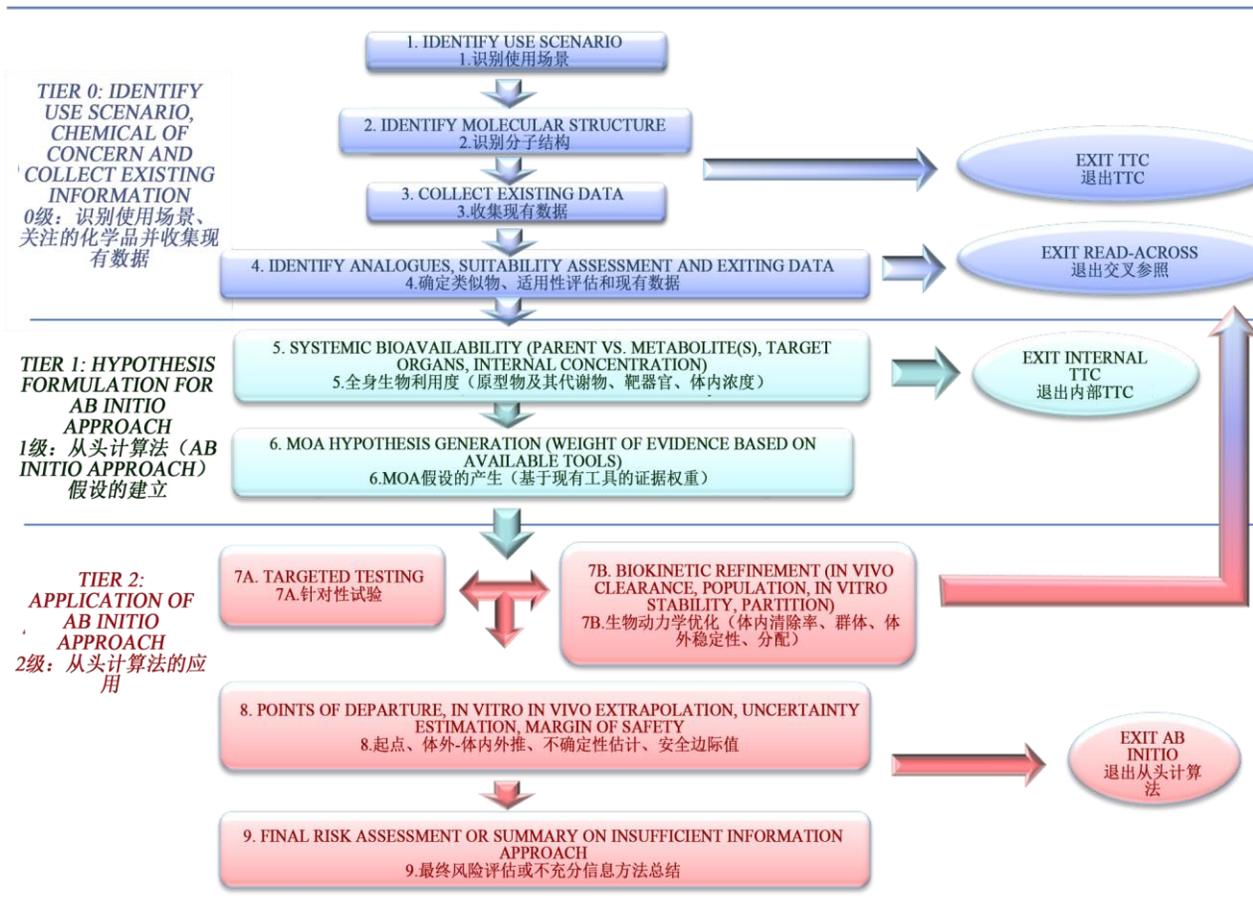
Distributions of Oral Equivalent Values and Predicted Chronic Exposures



- If no bioactivity is observed at relevant exposures, there can be no adverse effects.
- No need to predict the results of high dose toxicology studies in animals.



# 下一代风险评估框架-分层迭代



使用中  
Likely in use  
Maybe in use

- Read across 交叉参照
- Exposure-based waiving 基于暴露的豁免
- In silico tools 计算机模拟工具
- 代谢及代谢物鉴定
- 基于生理学的动力学模型
- In chemico assays 化学分析法
- 'Omics 组学
- Reporter gene assays 报告基因测定
- In vitro pharmacological profiling 体外病理学分析
- 3D culture systems 3D培养系统
- Organ-on-chip 器官芯片
- Pathways modelling 通路模型
- Human studies 人体临床研究



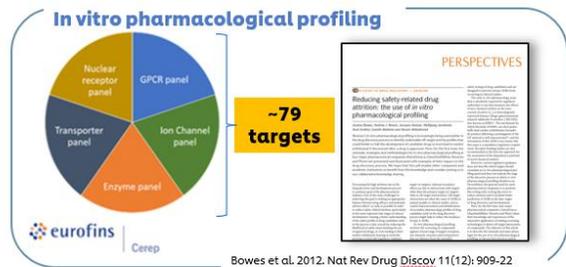
从头开始的化学安全评估：基于暴露考虑和非动物方法的工作流程

Berggren et al (2017) Computational Toxicology 4, 31-44



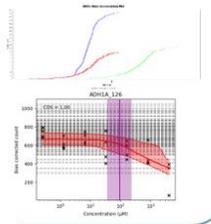
# Risk Assessment Outcome

## BIOACTIVITY (生物活性)



### High-Throughput transcriptomics (HTTr)

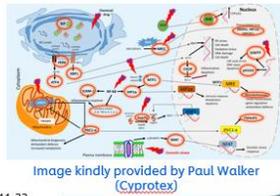
- TempO-seek technology – full gene panel
- 24hr exposure
- 7 concentrations
- Various cell models (e.g. HepG2, MCF7, HepaRG)
- Dose-response analysis using BMDExpress2 and BIFROST model



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

### Cell stress panel (CSP)

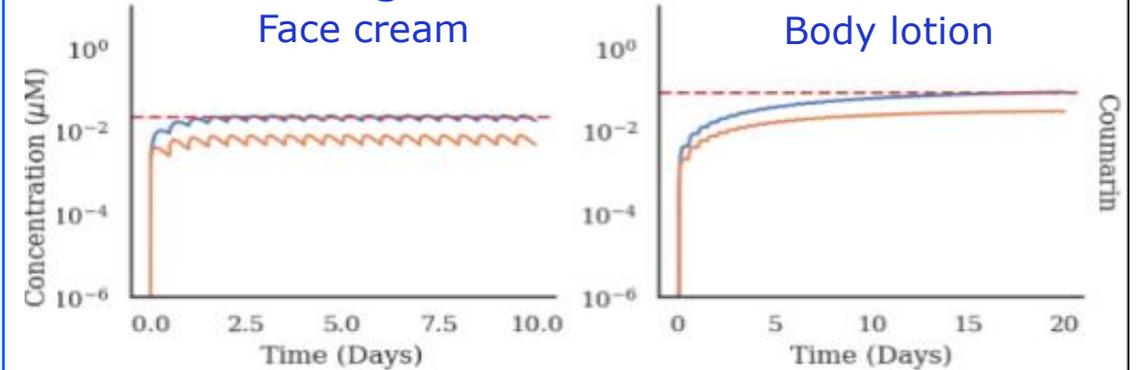
- 36 biomarkers covering 10 cell stress pathways
- HepG2
- 24hr exposure
- 8 concentrations
- Dose-response analysis using BIFROST model



Hatherell et al. 2020. *Toxicol Sci* 176(1): 11-33

## EXPOSURE (暴露量)

### Physiologically Based Kinetic Modelling (PBK)



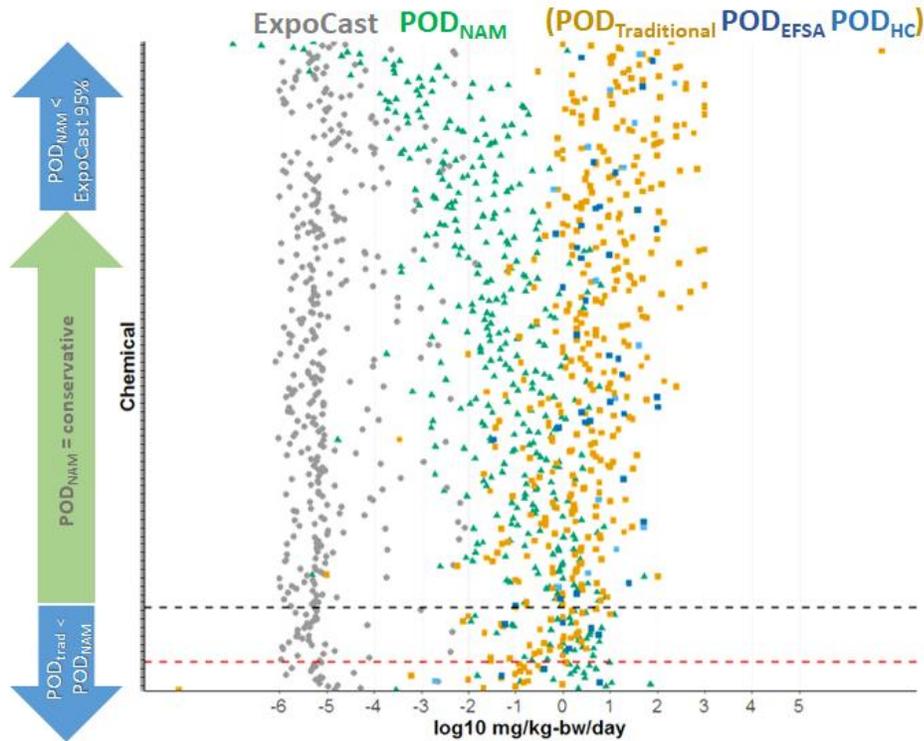
Identify lowest (most sensitive) point of departure, expressed in  $\mu\text{M}$

Identify realistic worst-case plasma exposure ( $C_{\text{max}}$ ) expressed as  $\mu\text{M}$

$$\text{BIOACTIVITY EXPOSURE RATIO} = \frac{\text{BIOACTIVITY}}{\text{EXPOSURE}}$$

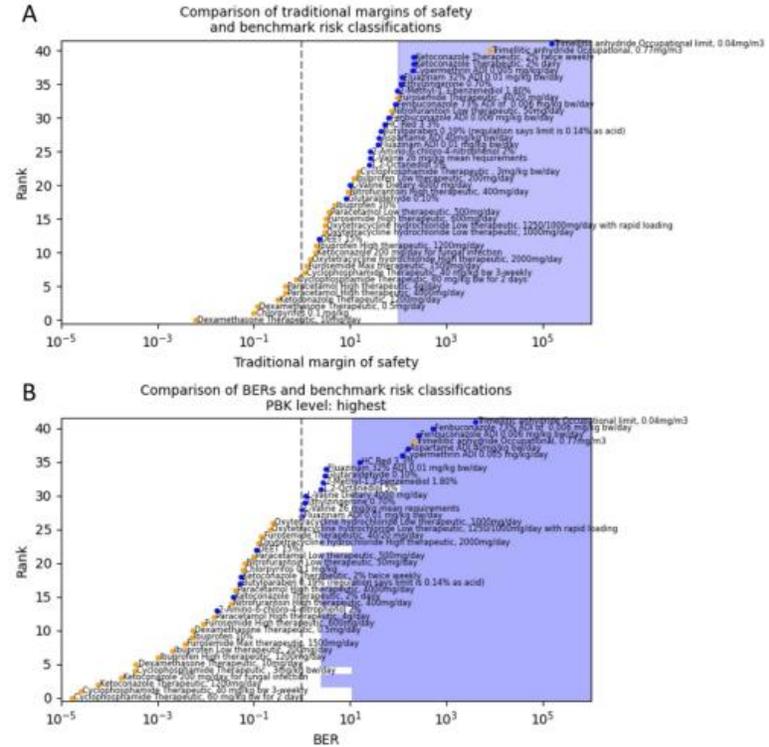
The bigger the BER, the greater the confidence that bioactivity will not occur in exposed consumers

# NGRA在“保护”上的表现



Case Studies Demonstrating Application of Bioactivity as a Protective POD

[Paul-Friedman et al., 2020](#)

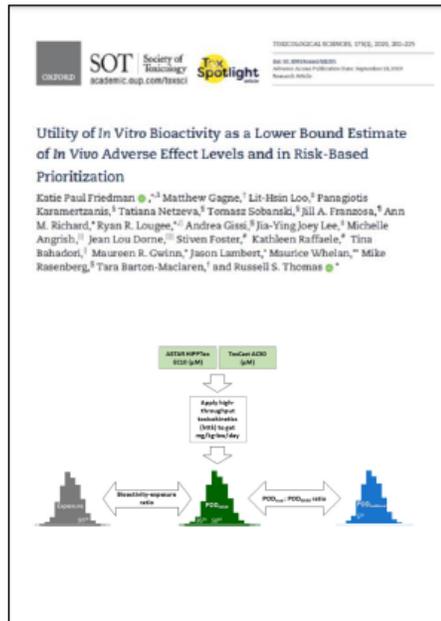
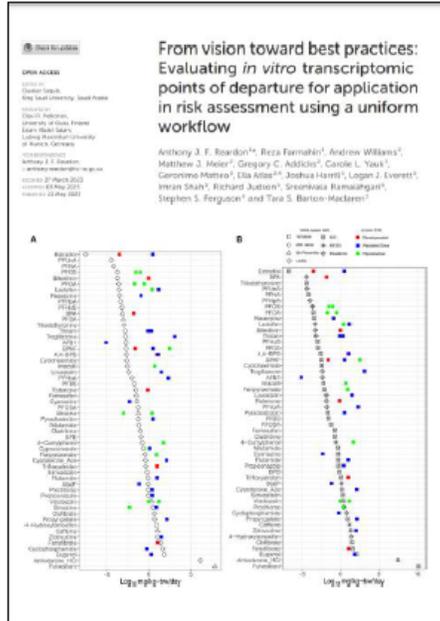


NAM-based assessments can be at least as protective as animal-based assessments

[Cable et al., 2025](#)



# 基于NAMs的NGRA案例研究：



Science Approach Document

**Bioactivity Exposure Ratio: Application in Priority Setting and Risk Assessment**

Health Canada

March 2021

<https://www.canada.ca/en/environment-climate-change/services/evaluating-existing-substances/science-approach-document-bioactivity-exposure-ratio-application-priority-setting-risk-assessment.html>

OECD  
Organisation for Economic Co-operation and Development

ENV/CBM/MONO/2021/04

Finalized English 27 October 2021

ENVIRONMENT DIRECTORATE  
CHEMICALS AND BIOTECHNOLOGY COMMITTEE

Case Study on use of an Integrated Approach for Testing and Assessment (IATA) for Systemic Toxicity of Phenoxymethyl when included at 1% in a body lotion

Series on Testing and Assessment  
No. 309

JT818793

**EUTOXRISK**  
EU-ToxRisk  
An Integrated European 'Flagship' Program  
Driving Mechanism-based Toxicity Testing and Risk Assessment for the 21<sup>st</sup> Century

Case Study 16 Reporting Template

Team: 2  
Team Members: Barira Islam, Uğur Sarıkan, Marcel Leist, Alessandra Romagnolo, Jukka Suni, Andrew White.

Compound ID: 01\_16-02  
Compound Name: (4-Hydroxy-2,2,6,6-tetramethylpiperidin-1-yl)oxalanilamide  
TEMPOL  
Structure: CC1(C)C(C(C1)O)C(=O)NCC2=CC=CC=C2

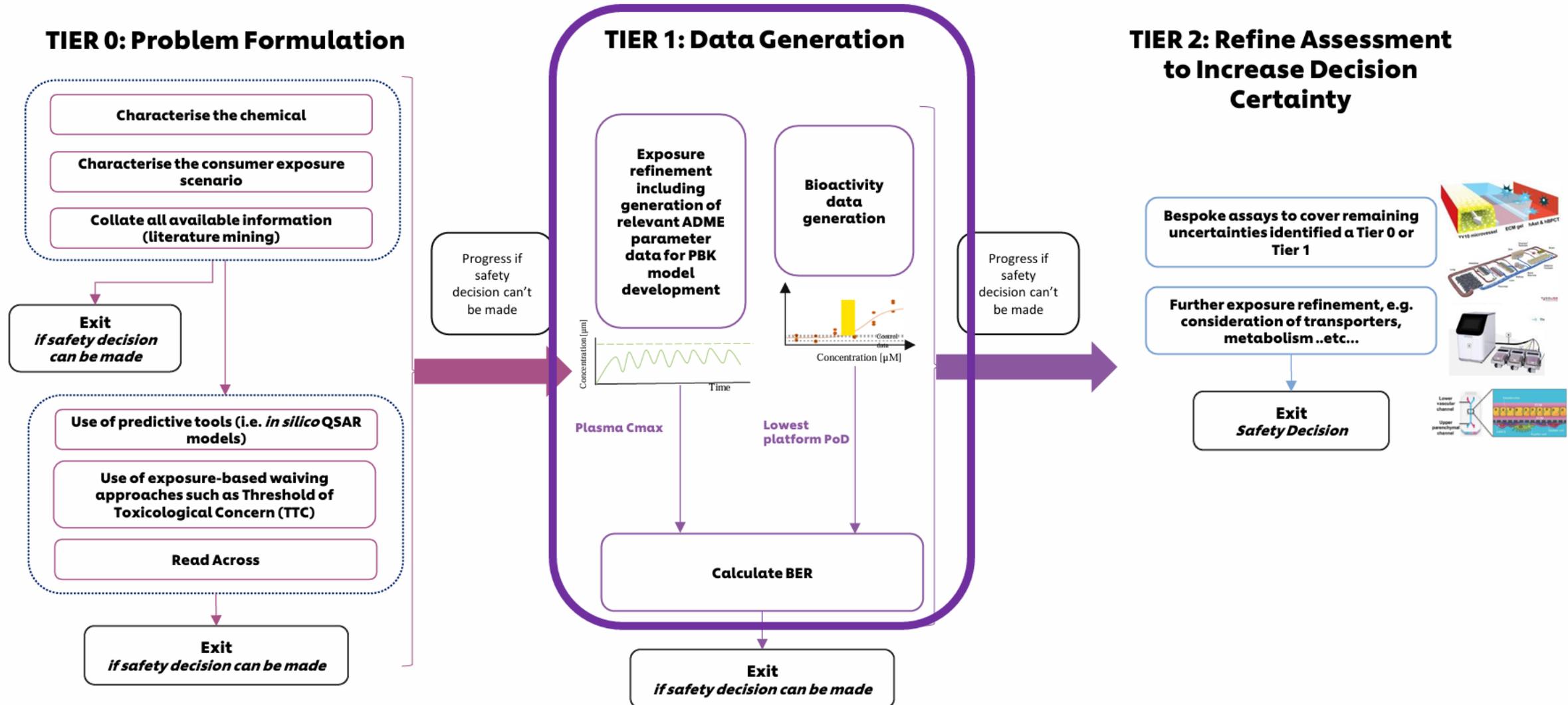
Ab Initio Case Study Objectives

Other Identifiers: CAS ID 3226-96-2; CHE



# Unilever: A NAMs/NGRA Tiered Framework Approach:

## The overall goal is a human safety risk assessment





**SOT** | Society of  
Toxicology  
academic.oup.com/toxsci

Toxicological Sciences, 2025, 204(1), 79–95

<https://doi.org/10.1093/toxsci/kfae159>

Advance Access Publication Date: December 18, 2024

Research article

# Advancing systemic toxicity risk assessment: Evaluation of a NAM-based toolbox approach

Sophie Cable\*, Maria Teresa Baltazar, Fazila Bunglawala, Paul L. Carmichael, Leonardo Contreas, Matthew Philip Dent, Jade Houghton, Predrag Kukic, Sophie Malcomber, Beate Nicol, Katarzyna R. Przybylak, Ans Punt, Georgia Reynolds, Joe Reynolds, Sharon Scott, Dawei Tang, Alistair M. Middleton 

Safety and Environmental Assurance Centre (SEAC), Unilever, Colworth Science Park, Sharnbrook MK44 1LQ, United Kingdom

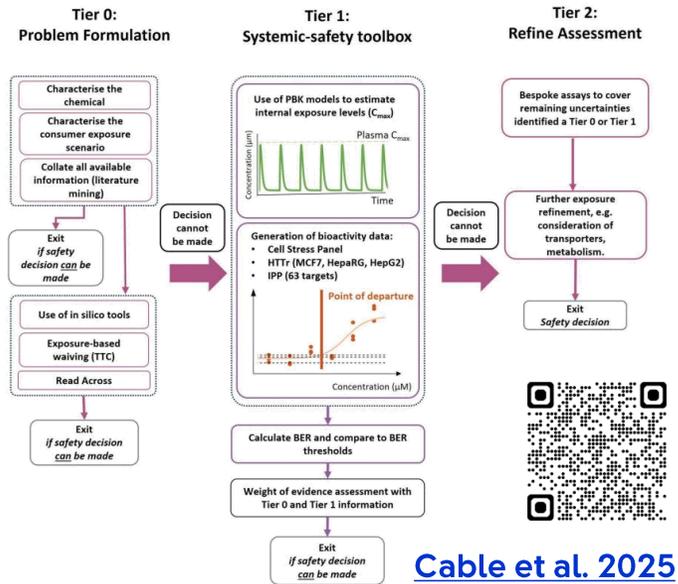
physiologically based biokinetics



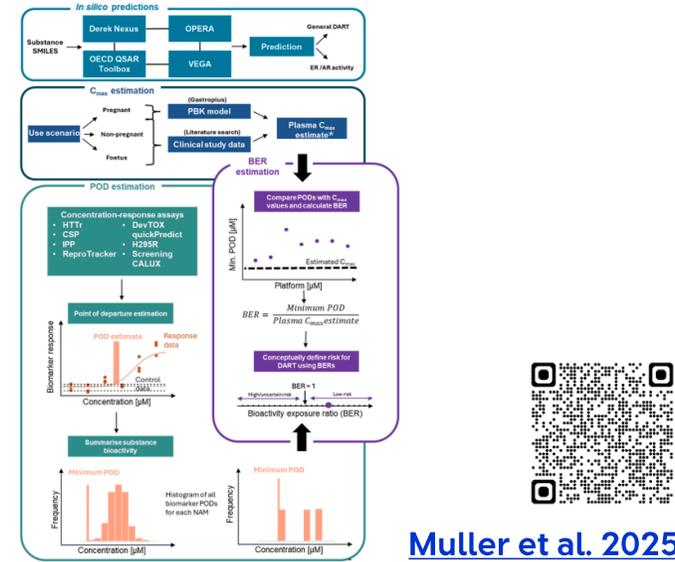
<https://youtu.be/5Z2S8MnKp7g>

# Unilever Next Generation Risk Assessment Frameworks (联合利华下一代风险评估框架)

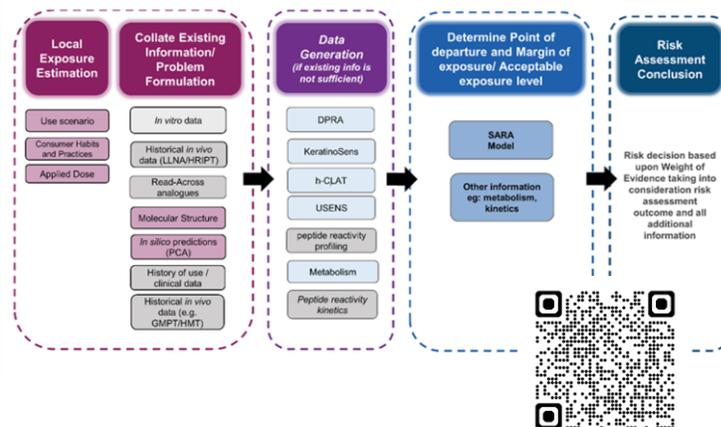
## Systemic



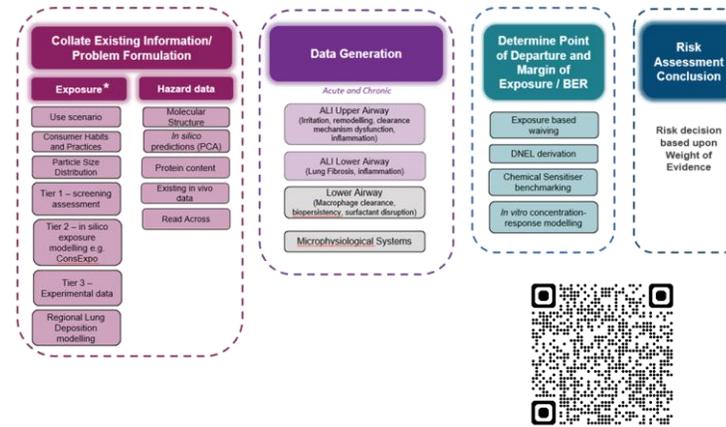
## Developmental & Reproductive



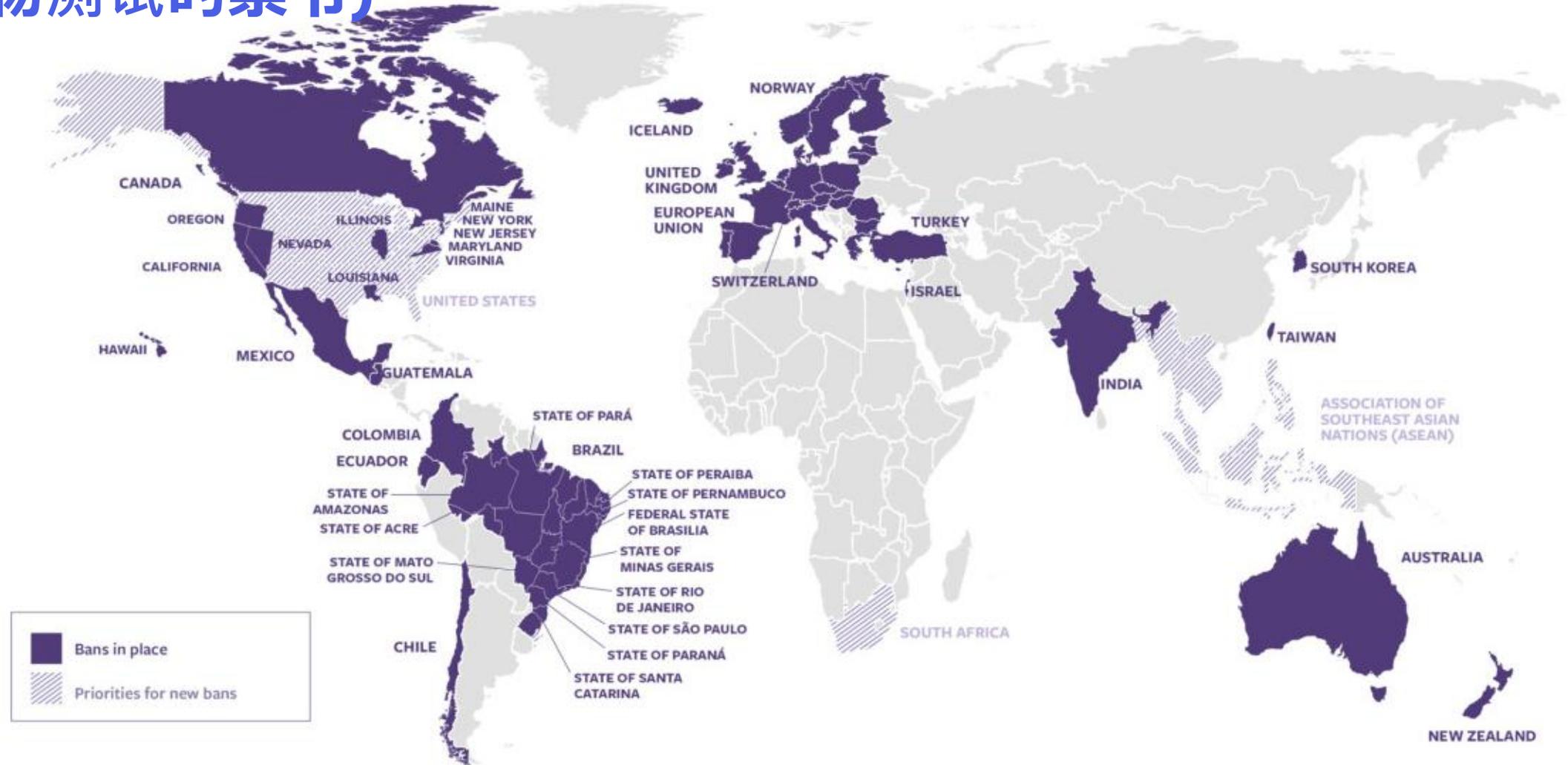
## Skin Sensitisation



## Inhalation



# Global Animal Testing Bans for Cosmetics (全球对于化妆品的动物测试的禁令)



# 国际化妆品组织共同努力：



2018

Computational Toxicology 7 (2018) 20-26

Contents lists available at ScienceDirect

Computational Toxicology

Journal homepage: www.elsevier.com/locate/comtox

**Principles underpinning the use of new methodologies in the risk assessment of cosmetic ingredients**

Matthew Dent<sup>a,\*</sup>, Renata Teixeira Amaral<sup>b</sup>, Pedro Amores Da Silva<sup>a</sup>, Jay Ansell<sup>c</sup>, Fanny Boileve<sup>d</sup>, Massimo Hatano<sup>e</sup>, Akhiko Hirose<sup>f</sup>, Yutaka Kasai<sup>g</sup>, Petra Kern<sup>h</sup>, Reinhard Krelling<sup>i</sup>, Stanley Milstien<sup>j</sup>, Beta Montemayor<sup>k</sup>, Juliemara Oliveira<sup>l</sup>, Andrea Richarz<sup>m</sup>, Rob Taalman<sup>n</sup>, Eric Vaillancourt<sup>o</sup>, Rajeshwar Verma<sup>p</sup>, Nishira Vieira O'Reilly Cabral Posada<sup>q</sup>, Craig Weiss<sup>r</sup>, Hajime Kojima<sup>s</sup>

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<sup>c</sup>US Personal Care Products Council (PCPC), 1620 L St. NW, Suite 2200, Washington, DC 20036, USA  
<sup>d</sup>Unilever R. & D. Center, Personal Care Division, Unilever Research & Innovation, 100, 20036, USA  
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<sup>g</sup>Kan Corporation, External Relations & Government Affairs 2-2-3, Benka, Saitama-shi, Tokyo 331-8501, Japan  
<sup>h</sup>Unilever R. & D. Center, Personal Care Division, Unilever Research & Innovation, 100, 20036, USA  
<sup>i</sup>German Products (GfE) GmbH, Global Toxicology and Environmental, Am Urban Park 1, 68347 Badlamb, Germany  
<sup>j</sup>US Food and Drug Administration (FDA), Office of Cosmetics and Colors (OCC), Center for Food Safety and Applied Nutrition (CFSAN), 10855 Campus Drive, College Park, MD 20740, USA  
<sup>k</sup>Cosmetics Alliance Canada, 430 Brossard Road East Suite 101, Mississauga, ON L4X 3L3, Canada  
<sup>l</sup>Healthline Health Regulatory Agency (AHVISA), Gerência de Produtos de Higiene, Perfumaria e Cosméticos, Rua Teófilo S. dos Santos, 170, 20130-000, Rio de Janeiro, RJ, Brazil  
<sup>m</sup>European Commission, Joint Research Centre (JRC), Directorate for Health, Consumers and Reference Materials, Chemical Safety and Alternative Methods Unit, Via E. Fermi 270, 21027 Segrate, VA, Italy  
<sup>n</sup>Cosmetics Europe, Avenue Hermès 40, 1140 Auderghem, Belgium  
<sup>o</sup>Health Canada (HC), Consumer Product Safety Directorate, Health, Environment and Consumer Safety Branch, 280 Laurier Ave. W., Ottawa, ON K1A 0K6, Canada  
<sup>p</sup>Indian Council of Cosmetic Manufacturers and Distributors (ICCMD), 21022 Paldi Parkway, Sector 28/13, Gurgaon, Haryana, India  
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<sup>r</sup>Unilever R. & D. Center, Personal Care Division, Unilever Research & Innovation, 100, 20036, USA  
<sup>s</sup>Unilever R. & D. Center, Personal Care Division, Unilever Research & Innovation, 100, 20036, USA

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<https://doi.org/10.1016/j.comtox.2018.06.001>

化妆品成分风险评估中新方法使用的的基本原则



2021

Regulatory Toxicology and Pharmacology 121 (2021) 105026

Contents lists available at ScienceDirect

Regulatory Toxicology and Pharmacology

Journal homepage: www.elsevier.com/locate/yrtph

**Paving the way for application of next generation risk assessment to safety decision-making for cosmetic ingredients**

M.P. Dent<sup>a,\*</sup>, E. Vaillancourt<sup>b</sup>, R.S. Thomas<sup>c</sup>, P.L. Carmichael<sup>d</sup>, G. Ouedraogo<sup>e</sup>, H. Kojima<sup>f</sup>, J. Barroso<sup>g</sup>, J. Ansell<sup>h</sup>, T.S. Burton-Maclaren<sup>i</sup>, S.H. Bennedouk<sup>j</sup>, K. Bookelbröder<sup>k</sup>, J. Ezendand<sup>l</sup>, J. Field<sup>m</sup>, S. Fitzpatrick<sup>n</sup>, M. Hatan<sup>o</sup>, R. Krelling<sup>p</sup>, M. Lorenzini<sup>q</sup>, C. Mahony<sup>r</sup>, B. Montemayor<sup>s</sup>, R. Mazarro-Costa<sup>t</sup>, J. Oliveira<sup>u</sup>, V. Rogiers<sup>v</sup>, D. Smegal<sup>w</sup>, R. Taalman<sup>x</sup>, Y. Tokura<sup>y</sup>, R. Verma<sup>z</sup>, C. Willett<sup>aa</sup>, C. Yang<sup>ab</sup>

<sup>a</sup>Unilever Safety and Environmental Assurance Centre, Sharnbrook, Bedfordshire, MK44 3LQ, UK  
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<sup>c</sup>Center for Computational Toxicology and Exposure, U.S. Environmental Protection Agency, Research Triangle Park, NC, 27711, USA  
<sup>d</sup>Unilever R. & D. Center, Personal Care Division, Unilever Research & Innovation, 100, 20036, USA  
<sup>e</sup>National Institute of Health Sciences, 1-18-1, Kamiyoga, Setagaya-ku, 108-8501, Tokyo, Japan  
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<https://doi.org/10.1016/j.yrtph.2021.105026>

为化妆品成分安全决策应用NGRA铺平道路



2025

ICCS INTERNATIONAL COLLABORATION ON COSMETICS SAFETY

**Best Practice Guidance Document**

*Skin Sensitization Assessment: Using New Approach Methods for Substances in Cosmetics and Personal Care Products*

ICCS INTERNATIONAL COLLABORATION ON COSMETICS SAFETY

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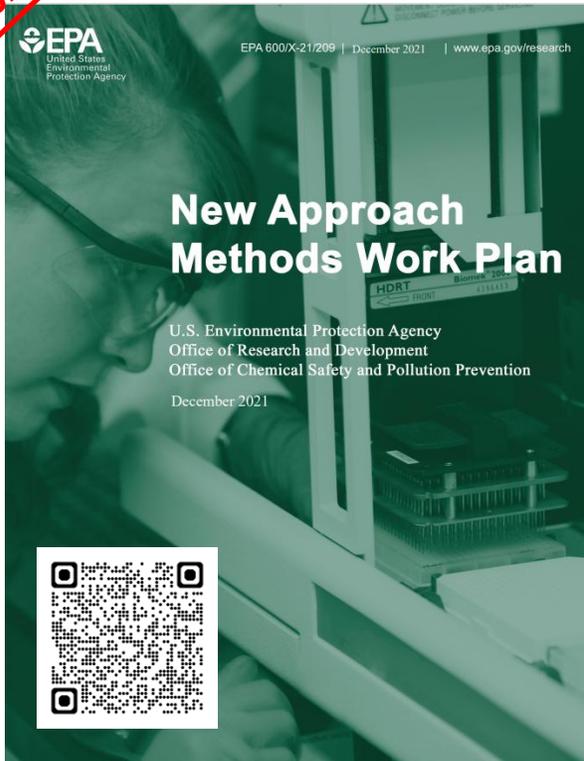
最佳实践指导文件：皮肤致敏：在化妆品成分中使用新方法



# 各监管机构在准备组织转型中，以支持NAMs/NGRA的监管使用：



2021



[New Approach Methods Work Plan \(epa.gov\)](https://www.epa.gov/new-approach-methods-work-plan)



2023



[towards-an-animal-free-regulatory-system-for-industrial-chemicals](https://echa.europa.eu/en/information/news-and-communications/reports-and-publications)



Environment and Climate Change Canada

Environnement et Changement climatique Canada



Health Canada Santé Canada

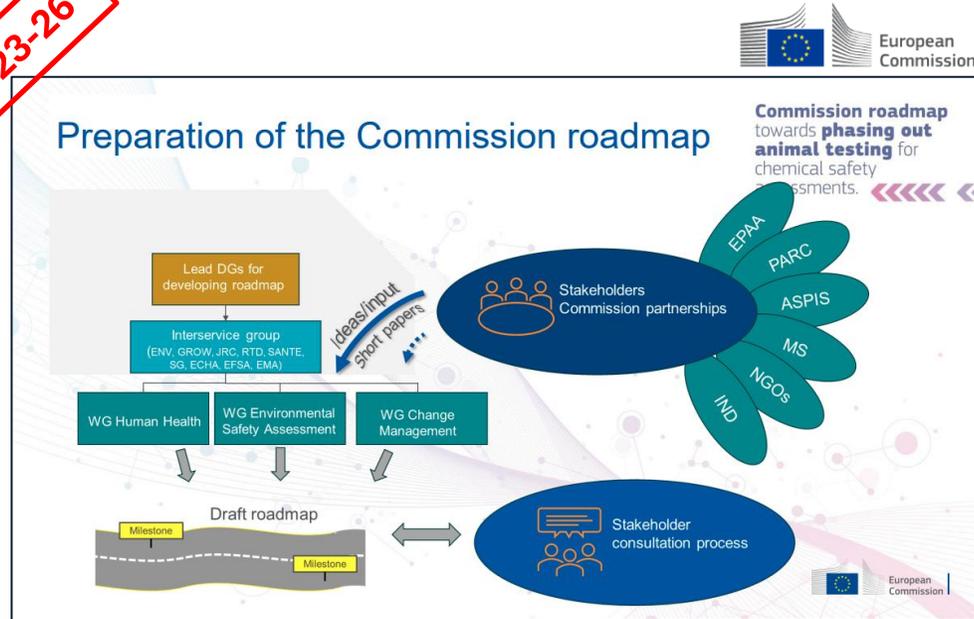
2025



[Strategy to replace, reduce or refine vertebrate animal testing under CEPA](https://www.ec.gc.ca/cepa/strategy-to-replace-reduce-or-refine-vertebrate-animal-testing-under-cepa)

# 欧盟委员会Roadmap路线图：将逐步淘汰化学品安全的动物测试，以支持欧洲向NGRA的有序过渡

2023-26



欧盟委员会Roadmap路线图将于2026年第一季度发布。

路线图提案由人类健康、环境安全与变更管理工作组开发，经过3次公开研讨会和磋商。

包括EPAA、PARC、ASPIS在内的利益相关者全程参与，帮助建立信任并促进合作。



[Roadmap towards phasing out animal testing](https://doi.org/10.1016/j.yrtph.2025.105818)

2025



<https://doi.org/10.1016/j.yrtph.2025.105818>

欧洲替代动物测试方法合作伙伴关系(EPAA,European Partnership for Alternative Approaches to Animal Testing)与欧盟委员会及其他组织合作，于2025年3月组织了一次无动物化学品安全评估会议。

[https://echa.europa.eu/documents/10162/127346428/AF-CSA\\_Conference+Report.pdf/d7994cf5-4b38-9a8a-9cbc-0c89da0dcad8?t=1749891499636](https://echa.europa.eu/documents/10162/127346428/AF-CSA_Conference+Report.pdf/d7994cf5-4b38-9a8a-9cbc-0c89da0dcad8?t=1749891499636)

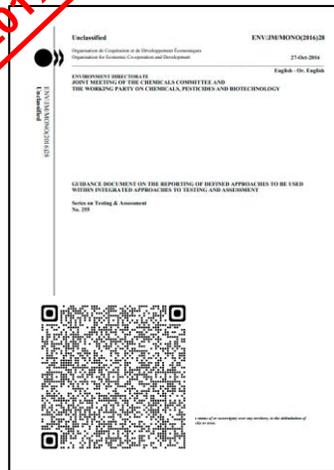


# 经合组织（OECD）综合测试与评估方法（IATA）及指导文件正在推动NGRA标准化：



IATA结合多种信息来源来得出化学品毒性结论，并且是为应对特定的监管情景或决策背景而开发的。

2017



在IATA中**确定性方法**报告的指导文件

2019



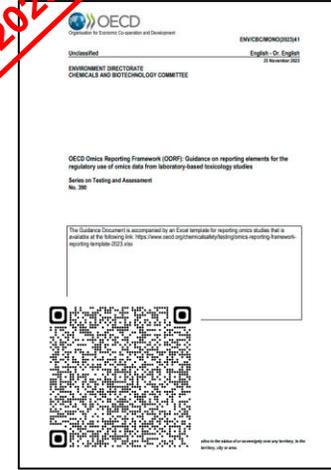
建立化学品评估**证据权重**的指导原则

2021



**生理学基础动力学 (PBK) 模型**报告指导文件

2023



**组学报告框架 (OORF)**: 组学数据报告要素指南”

2023

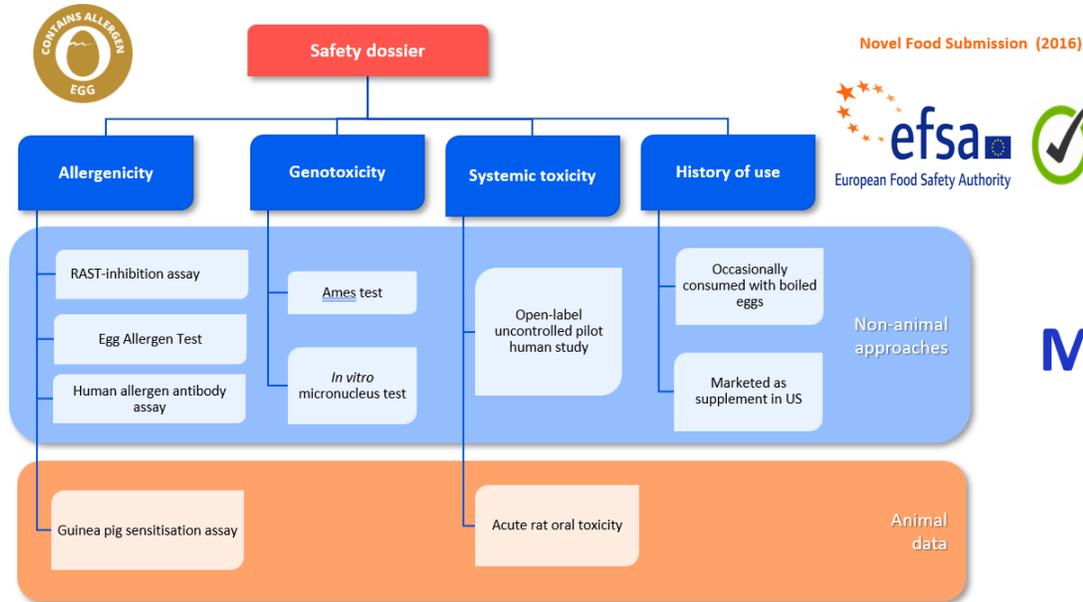


**(Q)SAR 评估框架**: 定量结构-活性关系模型和预测指南



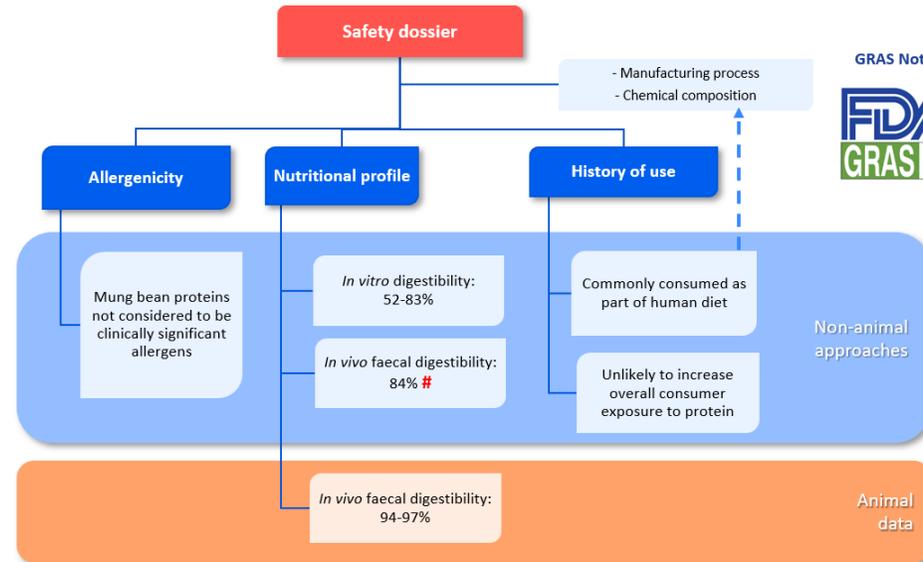
# Food Safety without Animal Testing – Regulatory Examples (食品非动物测试方法法规案例)

## Egg membrane hydrolysate 鸡蛋膜水解物



欧洲食品安全局

## Mung bean protein isolate 绿豆分离蛋白



美国食药监局

# existing *in vivo* data, not generated for the intended assessment

# NAMs and NGRA in Food Safety

Regulatory Toxicology and Pharmacology 162 (2025) 105863

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## Regulatory Toxicology and Pharmacology

journal homepage: [www.elsevier.com/locate/yrtph](https://www.elsevier.com/locate/yrtph)



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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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 Regulatory toxicology

**ABSTRACT**

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Safety assessments of regulated food products in the European Union (EU) largely rely on experimental animal studies. Currently, the European Commission is developing a roadmap to phase out animal testing for chemical safety assessment across all relevant pieces of legislation, including foods, while the ambition of the European Food Safety Authority (EFSA) is that by 2027, new scientific developments, i.e., new approach/non-animal methods (NAMs), will be integrated into assessments leading to “the minimisation of animal testing”. However, considering recent requests that have been made to conduct new animal studies for some regulated products, significant progress is required to minimise further and ultimately replace animal testing in the food safety environment. To advance this, we review several NAMs amenable for use in food safety assessment and reflect on their presence in EU food safety regulation and sectoral guidance. For many years, proposals to incorporate NAMs into food safety assessments have been made with questionable regulatory impact. Therefore, we present several amendments which could be made to the EU food regulatory system and current strategies towards phasing out animal testing which, if taken up, could lead to a tangible difference in the extent of animal testing within the food safety environment. Recognising that research may be required for some of these NAMs to enhance regulatory uptake, we propose potential follow-up projects that complement recent research & innovation (R&I) needs published by EFSA which food safety stakeholders could coordinate or participate in.

# Opportunities for increased use of NAMs in Food Safety (在食品安全中更多的使用新途径方法的机会)

A. Wood et al.

Regulatory Toxicology and Pharmacology 162 (2025) 105863

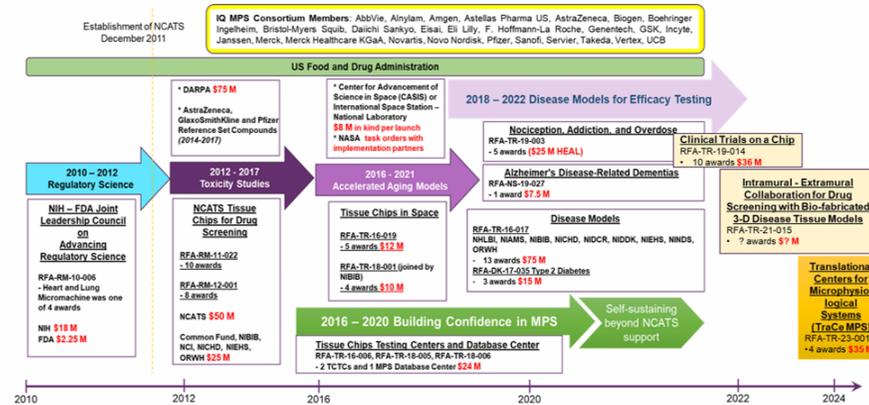
**Table 2**

Example EFSA opinions across range of regulated product types where animal testing has been conducted unnecessarily, including potential NAMs that could have been conducted to conclude safety without such studies.

Regulated product domain	Potential NAM alternatives	Substance/food	Overview	Studies conducted and results	Non-animal approach	Reference
Flavourings	EBW	2-(4-methylphenoxy)-N-(1H-pyrazol-3-yl)-N-(thiophen-2-ylmethyl)acetamide	In a 2018 evaluation following their (EFSA) flavouring evaluation procedure, exposure for the flavouring was estimated as 225 µg/person/day (adults) and 142 µg/person/day (child) which exceeded the respective TTC value (Cramer class III) of 90 µg/day by 2.5 and 1.6-fold for adults and children respectively. As a consequence a 90-day and developmental toxicity study were considered necessary.	A 90-day and developmental toxicity study were conducted and NOAELs were established at the highest tested doses of 100 and 1000 mg/kg bw/day respectively.	Possibility to demonstrate safety using the iTTC approach, where internal exposure estimates could have been obtained through use of the dietary exposure estimate and a variety of pharmacokinetic modelling approaches performed in a tiered manner, that is parameterised using <i>in silico</i> data first before proceeding to <i>in vitro</i> data if required.	<a href="#">EFSA (2018d)</a>
Flavourings	EBW	2-methyl-1-(2-(5-(p-tolyl)-1H-imidazole-2-yl)piperidin-1-yl)butan-1-one	In a 2024 evaluation following their (EFSA) flavouring evaluation procedure, exposure for the flavouring was estimated as 45 and 28.4 µg/person per day), for adults and children, respectively, which were 2 and 3.2-fold below the respective TTC (90 µg/person/day). In agreement	Although no further data was required the applicant conducted a 90-day study where a BMDL20 of 0.71 mg/kg bw/day was calculated.	TTC. As suggested in <a href="#">Table 4</a> , by integrating last-resort requirement into respective foods regulation and ensuring greater communication between applicants and EFSA during application procedure, the need for testing (or lack thereof) can be discussed prior to commissioning such tests.	<a href="#">EFSA (2024b)</a>

# NGRA and NAMs science is constantly evolving and there are still many challenges (进展和挑战)

## Opportunities with Organs-on-Chips (OoC)



The USA NIH-funded 'Tissue Chips' Landscape = >\$400m to-date

## Maximising the wealth of data in transcriptomics

## Reproducibility and Validation

**SOT** Society of Toxicology  
academic.oup.com/toxsci

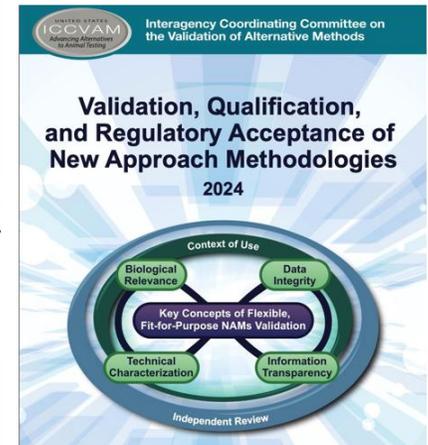
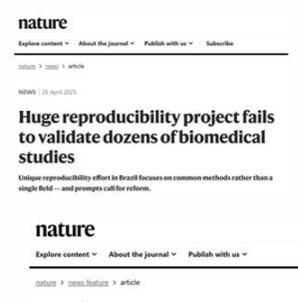
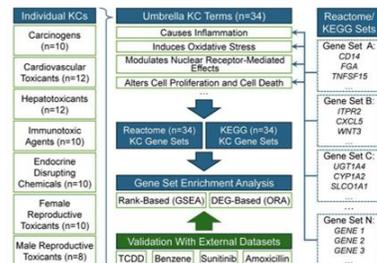
**Spotlight** article

Toxicological Sciences, 2025, 205(2), 310-325  
https://doi.org/10.1093/toxsci/kfuf036  
Advance Access Publication Date: March 20, 2025  
Research article



A workflow for human health hazard evaluation using transcriptomic data and Key Characteristics-based gene sets

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# 联合利华在中国的NGRA活动

科研合作

### Unilever's Journey in China from 2011

2011 TT21 Symposium

2014, Oct/Nov 2 TATT set-up

2015 PBPk training by CMU

NAMs/NGRA on Environmental Science (Sept 2024 @Tian)

NAMs/NGRA on Human Health (July, 2024 Shenyang)

教育培训

### 联合利华在中国的2025年教育和培训

第六届计算毒理学方法培训班及应用论坛  
新途径方法中的计算毒理学及其在下一代风险评估中的应用  
2025年06月26-29日 中国 杭州

Paul Carmichael  
联合利华英国安全、环境与法规科学中心  
新途径方法(NAMS)及下一代风险评估(NGRA)的十年进展

专设奖项

### 联合利华&中国毒理学会替代发展奖 (2016-2023) 延续至2025-2030

Previous Award Winners

9 Innovation award winners

2016 2017 2018 2019 2021 2023

案例交流

### 联合利华在中国的案例学术交流

基于新途径技术方法的下一代风险评估研究案例学术交流  
Academic Exchange of Case Studies on Next-Generation Risk Assessment Research  
Presentations Based on New Approach Methodologies

基于新途径技术方法的下一代风险评估研究案例学术交流  
2025年06月26-29日 中国 杭州



# Thank You

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Gavin Maxwell, Paul Hepburn, Mollie Lu, Adam  
Wood and the scientists at Unilever CECS

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