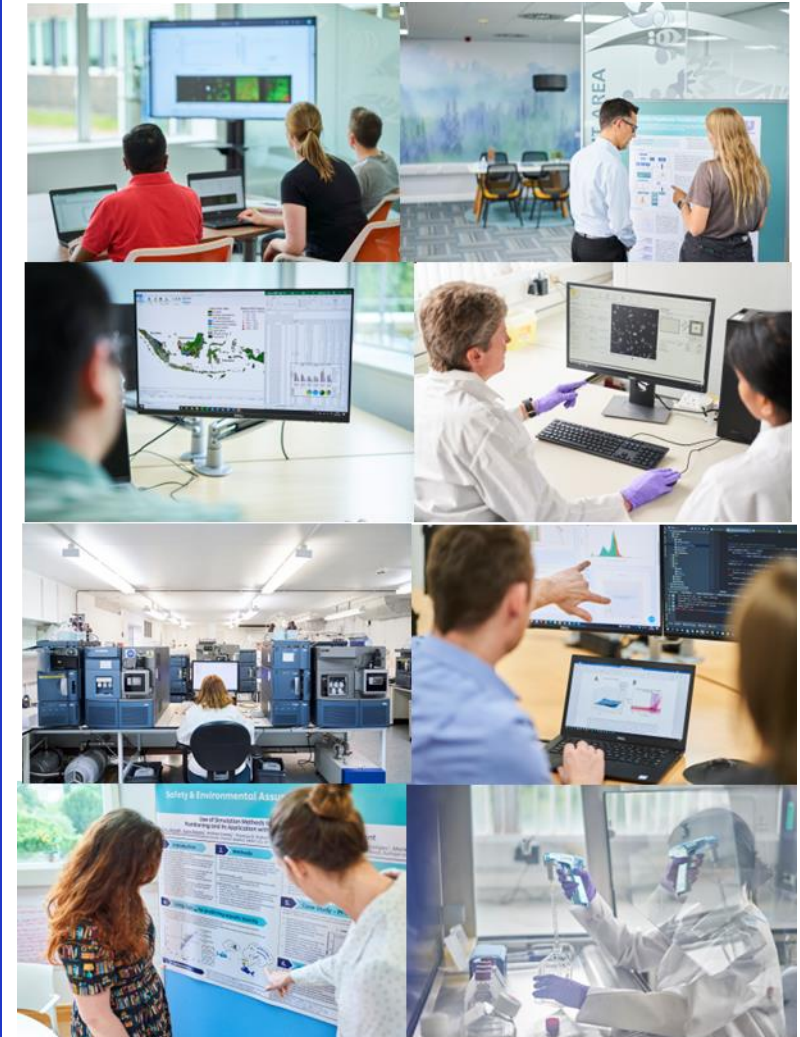


Closing the gap between advanced safety science and regulatory requirements

Dr Gavin Maxwell & Dr Julia Fentem MBE

CERJ Networking Day – 21st June 2024

Acknowledgement: >80 eco/toxicologists, biologists, chemists, computational modellers, data scientists & exposure / risk assessors in **Unilever's Safety & Environmental Assurance Centre (SEAC – seac.unilever.com)**




A good track record of collaboration over many years



UNIVERSITY OF
BIRMINGHAM

website link: [Safety & Environmental Sciences | Unilever](#)




Safety & Environmental Science


Unilever's Safety and Environmental Assurance Centre (SEAC)

Advances in science and technology mean that we can generate much more relevant safety data to protect people and the environment using modern non-animal approaches.


Our Science



Safety Without Animal Testing
Unilever is committed to ending animal testing globally. We use the latest non-animal safety science, not animals, to assure the safety of our products and the ingredients in them.



Environmental Sustainability Science
Unilever's ambition is to be the global leader in sustainable business. We have been using the Cycle Assessment (CA) approaches for many years to assess the environmental impacts of our products.




Case Studies
Real life and hypothetical case studies to demonstrate how our leading-edge safety and environmental sustainability science capabilities are applied.

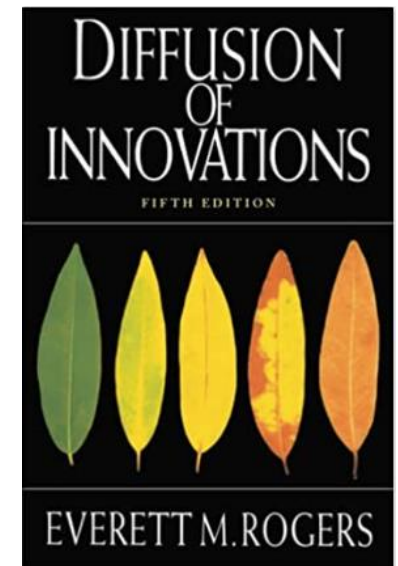
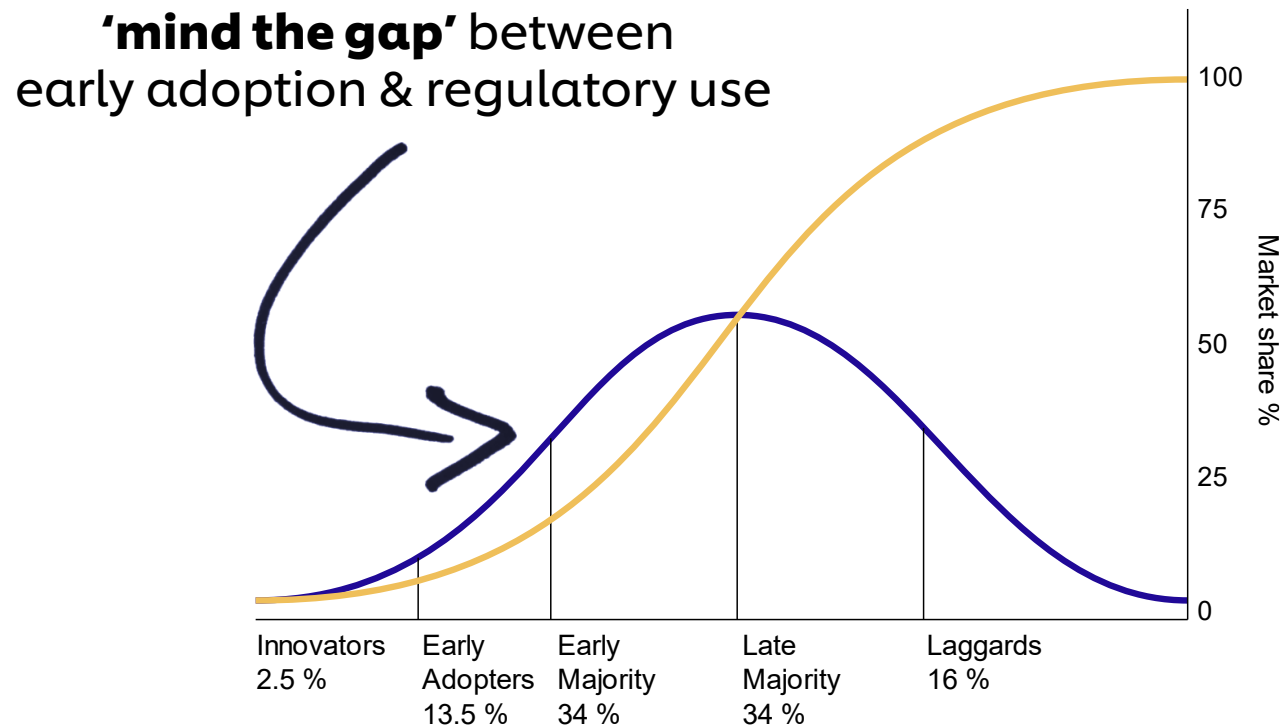
Partnerships & Collaborations

We are proud to be working closely with leading scientific authorities around the world, including academic and government scientists.

[Learn more about Partnerships & Collaborations](#)



1. Unilever Policy and Approach
2. Next Generation Risk Assessment (NGRA)
3. Applying NGRA to Cosmetic Safety Assessment
4. Accelerating the Transition



Unilever Policy & Approach

Safe & Sustainable Products without Animal Testing

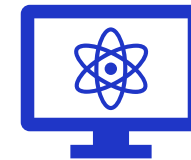
We say use science.
Not animals.



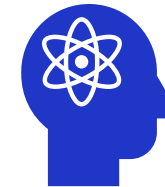
What we believe

- **Every Unilever product must be safe for people and our environment**
- **Animal testing is not needed to assess ingredient & product safety**
–wide range of non-animal alternatives available
- **We work to accelerate the global adoption of animal-free cosmetic safety assessment approaches**

How we do it



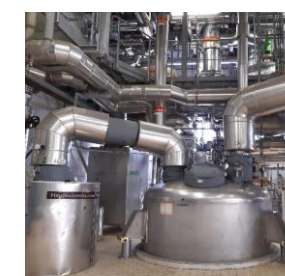
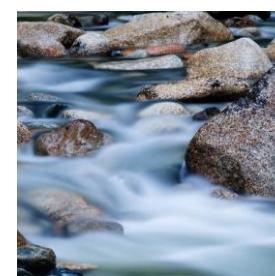
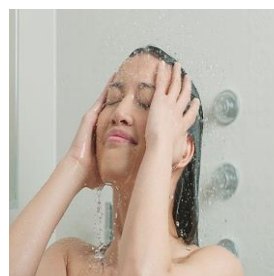
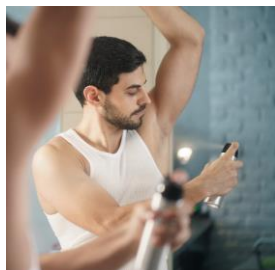
40+ years of developing non-animal safety science



70+ collaborations



600+ publications



20 years of "Assuring Safety without Animal Testing" research & advocacy

> Altern Lab Anim. 2004 Dec;32(6):617-23. doi: 10.1177/026119290403200612.

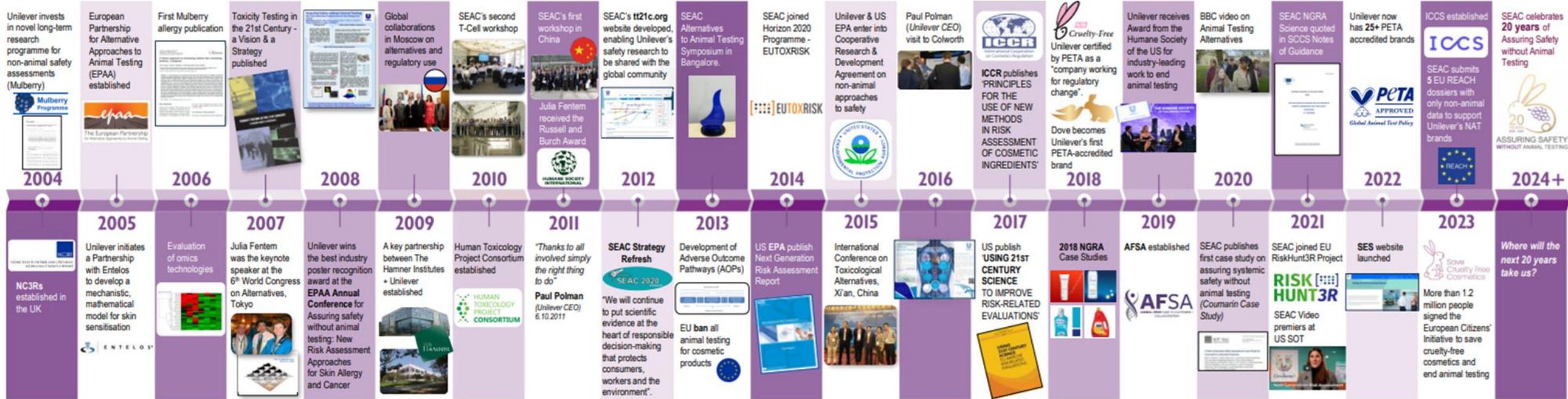
The feasibility of replacing animal testing for assessing consumer safety: a suggested future direction

Julia Fentem¹, Mark Chamberlain, Bart Sangster

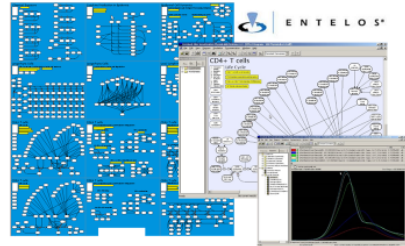
Next generation risk assessment for occupational chemical safety – A real world example with sodium-2-hydroxyethane sulfonate

Adam Wood^{a,*}, Catherine Breffa^b, Caroline Chaine^c, Richard Cubberley^a, Matthew Dent^a, Joachim Eichhorn^b, Susann Fayyaz^b, Fabian A. Grimm^b, Jade Houghton^a, Reiko Kiwamoto^d, Predrag Kucic^a, MounSook Lee^b, Sophie Malcomber^a, Suzanne Martin^a, Beate Nicol^a, Joe Reynolds^a, Gordon Riley^a, Sharon Scott^a, Colin Smith^e, Carl Westmoreland^a, Willemien Wieland^f, Mesha Williams^a, Kathryn Wolton^a, Tristan Zellmann^g, Steve Gutsell^a

Toxicology 506 (2024) 153835

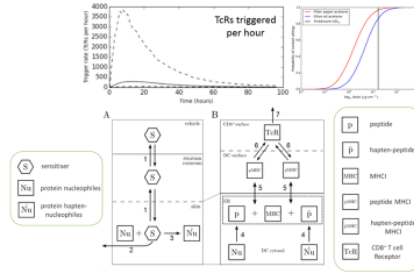


My background: NGRA for Skin Sensitisation



Entelos model

[Maxwell G. & MacKay C. 2008.](#)



SARA TKTD qAOP model

[Mackay et al. 2013](#)

SARA Bayesian Model

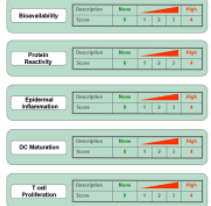
[Reynolds et al. 2019](#)

T cell Forum

[Kimber et al. 2012](#)

Integration of non-animal data

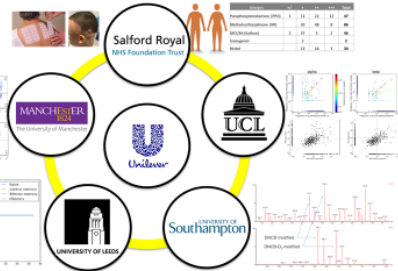
[Jowsey et al. 2006](#)



'Weight of Evidence' Predictions
Integration of different forms of *in vitro* and *in silico* data

Does the Ingredient have the potential to 'sensitize'?

Jowsey et al. 2006



My current roles:



Regulatory Science Strategy & Advocacy Lead, SEAC



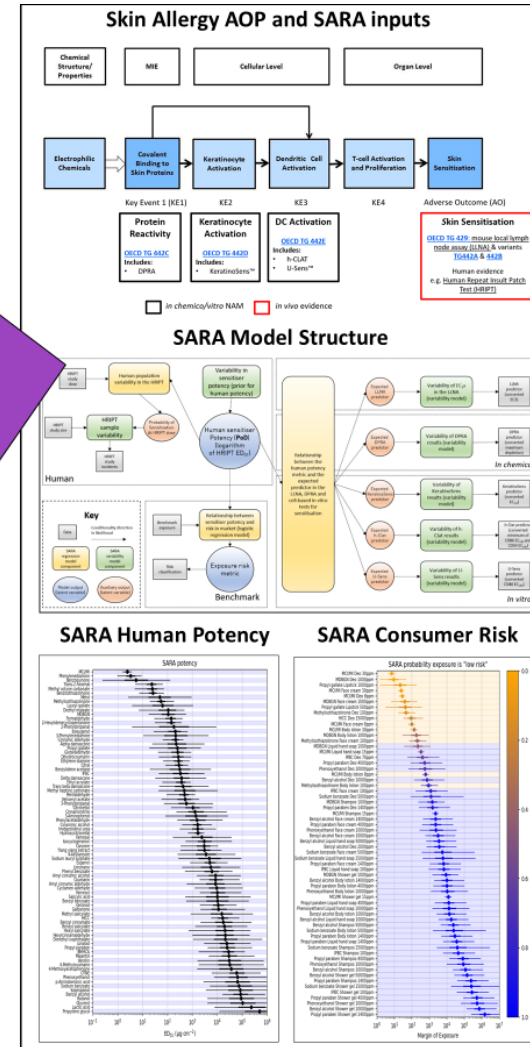
The European Partnership for Alternative Approaches to Animal Testing

Industry co-chair, EPAA

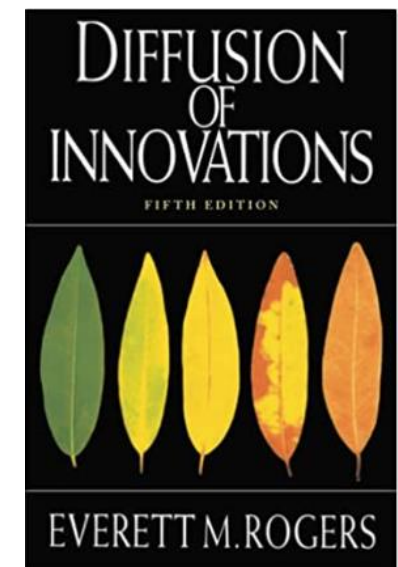
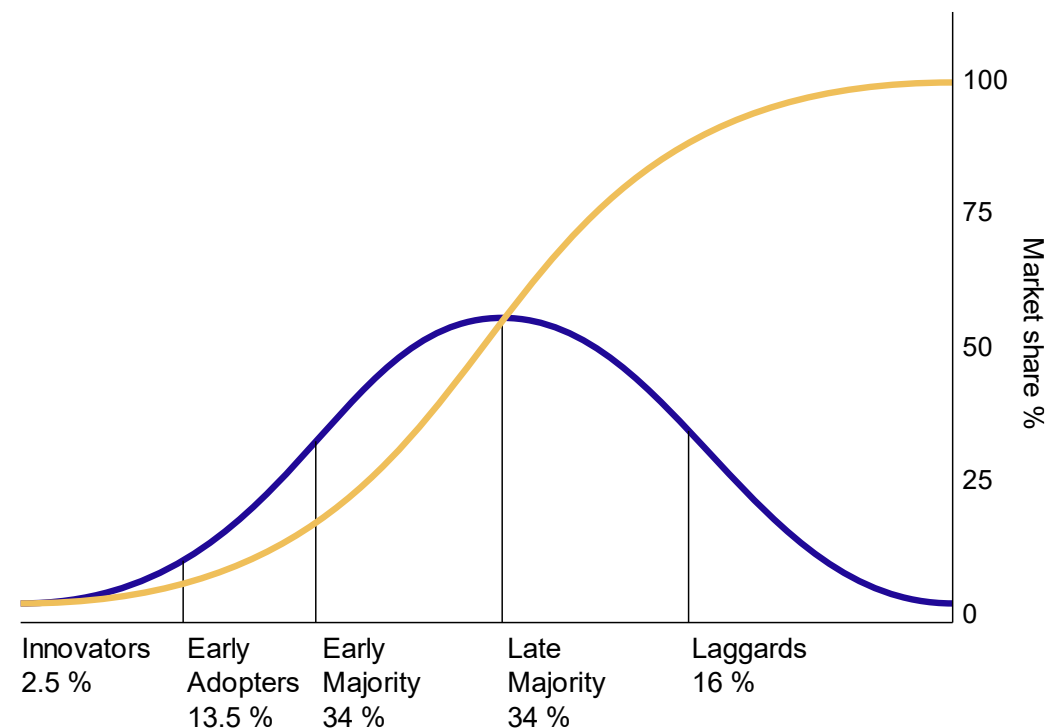


INTERNATIONAL COLLABORATION ON COSMETICS SAFETY

Core Acceptance Team vice chair, ICCS

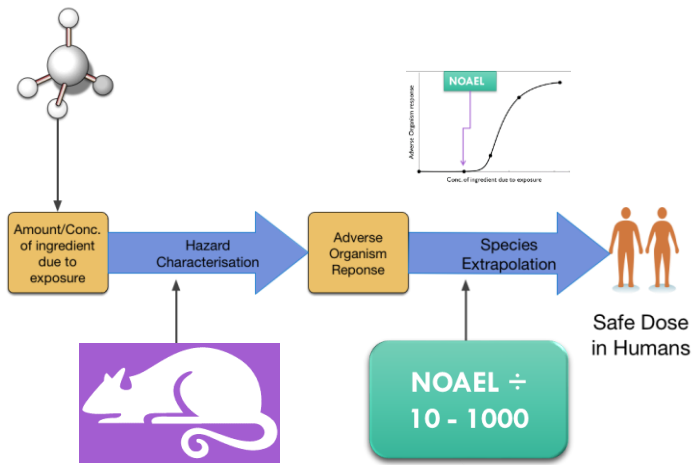


1. Unilever Policy and Approach
- 2. Next Generation Risk Assessment (NGRA)**
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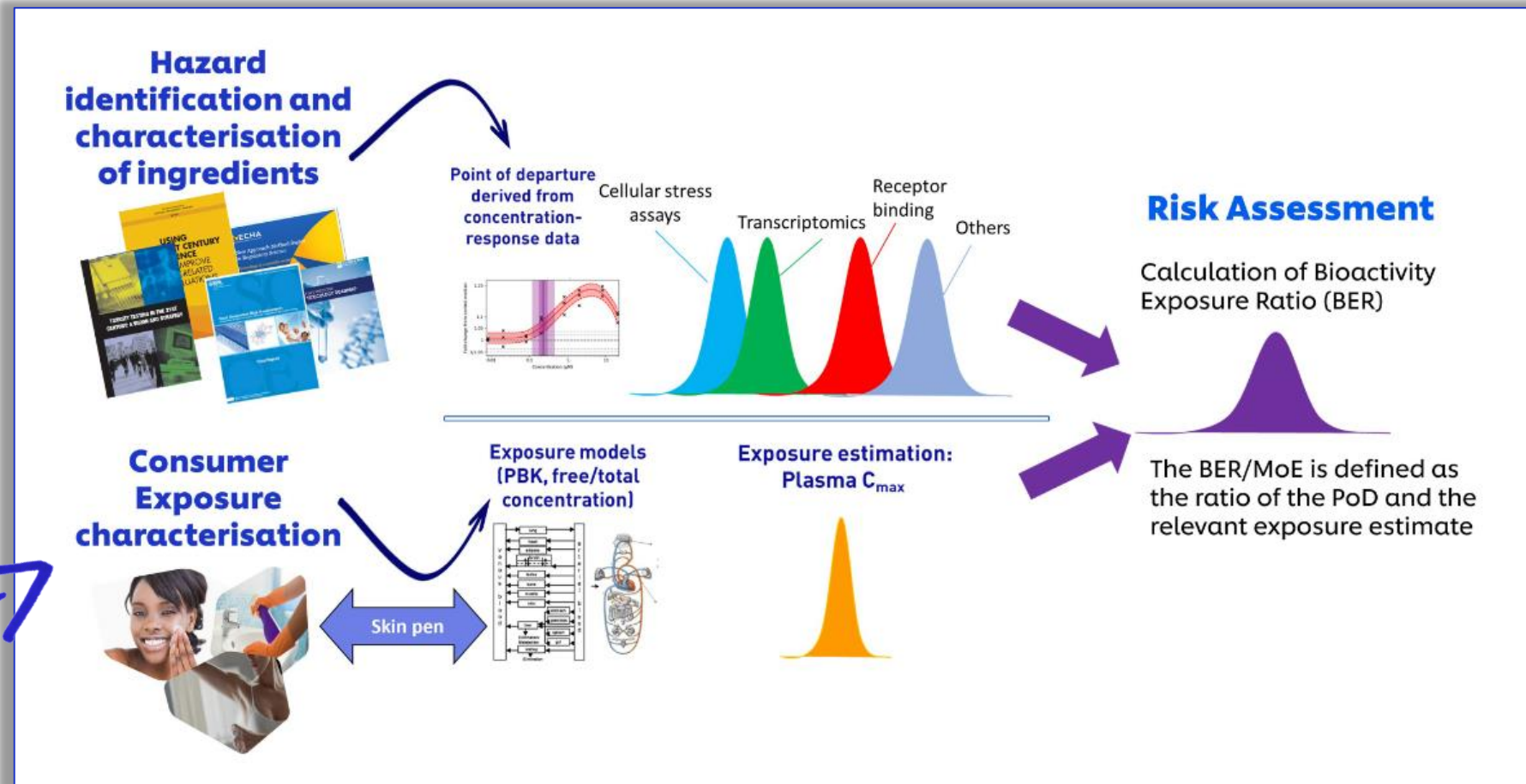


A global transition is underway as use of non-animal safety science increases & regulatory safety frameworks start to embed NAMs & NGRA approaches

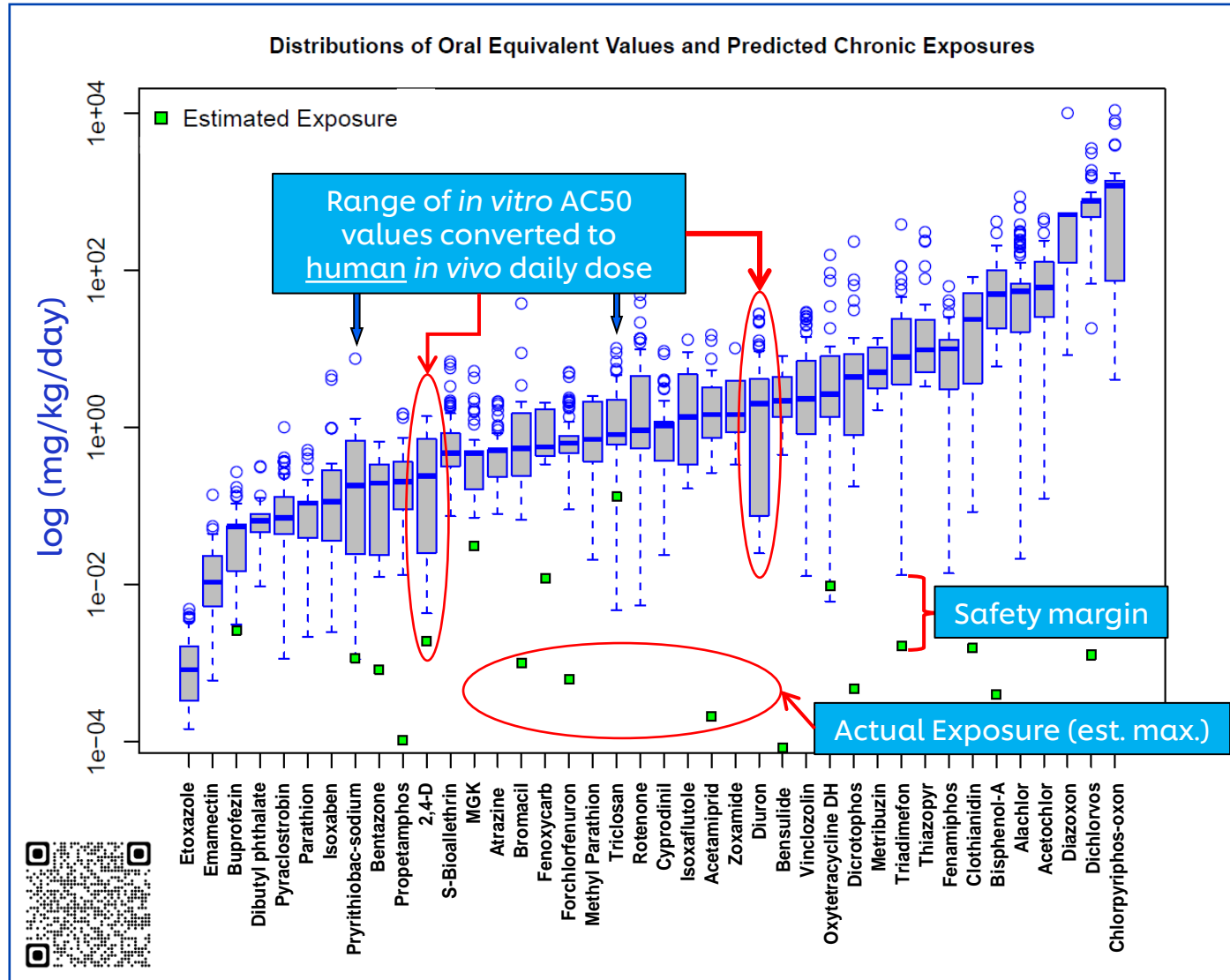
'Traditional' Risk Assessment



'Next Generation' Risk Assessment (NGRA)



NGRA: aim is protection, not prediction of animal data



The hypothesis underpinning NGRA is that **if no bioactivity is observed at consumer-relevant concentrations, there can be no adverse health effects.**

At no point does NGRA attempt to predict the results of high dose toxicology studies in animals.

NGRA uses new exposure science and understanding of human biology.



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

US EPA Next Generation Blueprint Tiered Testing Framework

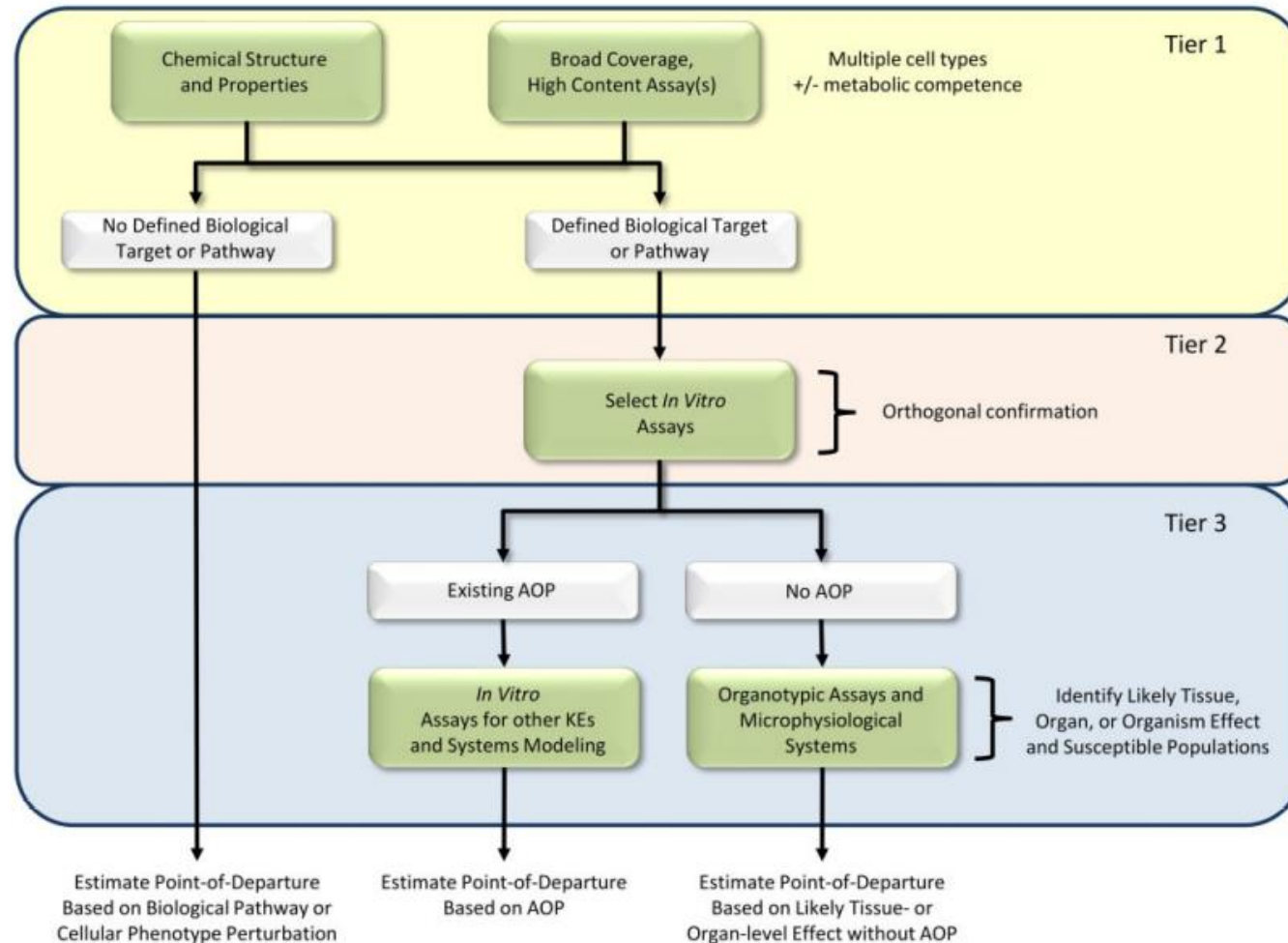


Figure 2. Tiered testing framework for hazard characterization. Tier 1 uses both chemical structure and broad coverage, high content assays across multiple cell types for comprehensively evaluating the potential effects of chemicals and grouping them based on similarity in potential hazards. For chemicals from Tier 1 without a defined biological target / pathway, a quantitative point-of-departure for hazard is estimated based on the absence of biological pathway or cellular phenotype perturbation. Chemicals from Tier 1 with a predicted biological target or pathway are evaluated Tier 2 using targeted follow-up assays. In Tier 3, the likely tissue, organ, or organism-level effects are considered based on either existing adverse outcome pathways (AOP) or more complex culture systems. Quantitative points-of-departure for hazard are estimated based on the AOP or responses in the complex culture system.



TOXICOLOGICAL SCIENCES, 169(2), 2019, 317–332

doi: 10.1093/toxsci/ktz058
Advance Access Publication Date: March 5, 2019
Forum

The Next Generation Blueprint of Computational Toxicology at the U.S. Environmental Protection Agency

Russell S. Thomas,^{*,1} Tina Bahadori,[†] Timothy J. Buckley,[‡] John Cowden,^{*} Chad Deisenroth,^{*} Kathie L. Dionisio,[‡] Jeffrey B. Frithsen,[§] Christopher M. Grulke,^{*} Maureen R. Gwinn,^{*} Joshua A. Harrill,^{*} Mark Higuchi,[¶] Keith A. Houck,^{*} Michael F. Hughes,[¶] E. Sidney Hunter, III,[¶] Kristin K. Isaacs,[‡] Richard S. Judson,^{*} Thomas B. Knudsen,^{*} Jason C. Lambert,^{||} Monica Linnenbrink,^{*} Todd M. Martin,^{||} Seth R. Newton,[‡] Stephanie Padilla,[¶] Grace Patlewicz,^{*} Katie Paul-Friedman,^{*} Katherine A. Phillips,[‡] Ann M. Richard,^{*} Reeder Sams,^{*} Timothy J. Shafer,[¶] R. Woodrow Setzer,^{*} Imran Shah,^{*} Jane E. Simmons,[¶] Steven O. Simmons,^{*} Amar Singh,^{*} Jon R. Sobus,[‡] Mark Strynar,[‡] Adam Swank,[‡] Rogelio Tornero-Valez,[‡] Elin M. Ulrich,[‡] Daniel L. Villeneuve,^{|||} John F. Wambaugh,^{*} Barbara A. Wetmore,[‡] and Antony J. Williams^{*}

^{*}National Center for Computational Toxicology, U.S. Environmental Protection Agency, Research Triangle Park, NC 27711, [†]National Center for Environmental Assessment, U.S. Environmental Protection Agency, Washington, D.C. 20004, [‡]National Exposure Research Laboratory, U.S. Environmental Protection Agency, Research Triangle Park, NC 27711, [§]Chemical Safety for Sustainability National Research Program, U.S. Environmental Protection Agency, Washington, D.C. 20004, [¶]National Health and Environmental Effects Research Laboratory, U.S. Environmental Protection Agency, Research Triangle Park, NC 27711, ^{||}National Center for Environmental Assessment, U.S. Environmental Protection Agency, Research Triangle Park, NC 27711, ^{|||}National Center for Environmental Assessment, U.S. Environmental Protection Agency, Research Triangle Park, NC 27711

Use of NAMs/NGRA for Chemical Screening & Safety Assessment:

Current status of regulatory acceptance



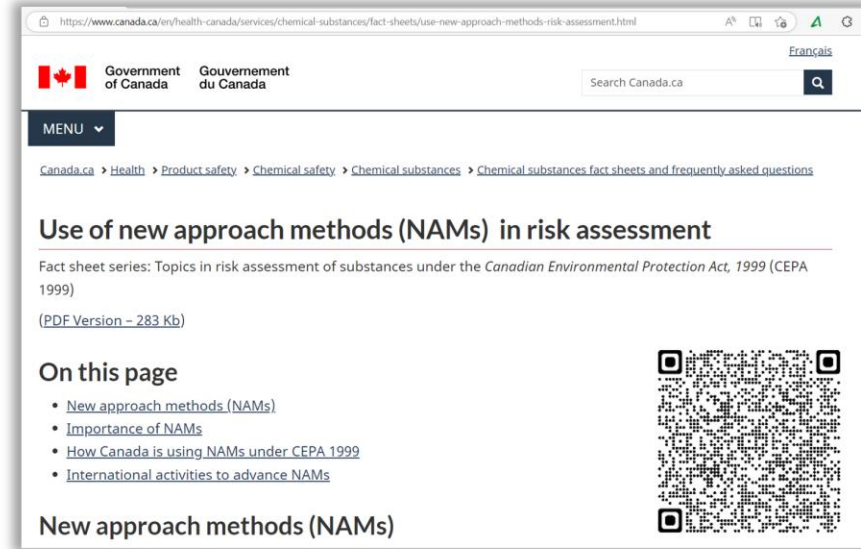
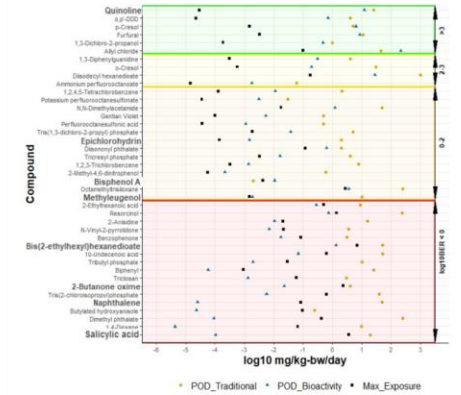
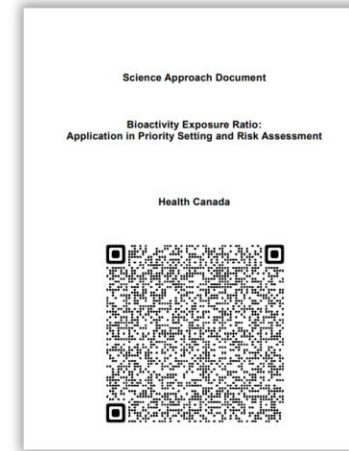
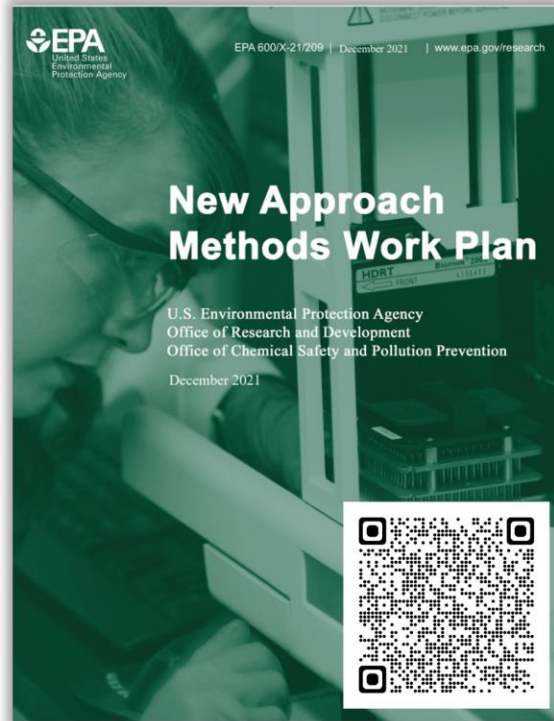
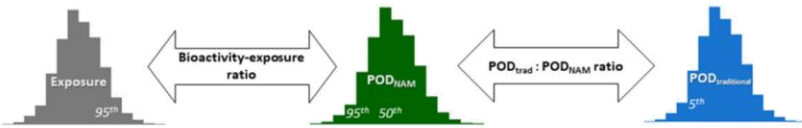
APCRA
ACCELERATING THE PACE OF
CHEMICAL RISK ASSESSMENT



ASTAR HIPPTox
EC10 (µM)

ToxCast AC50
(µM)

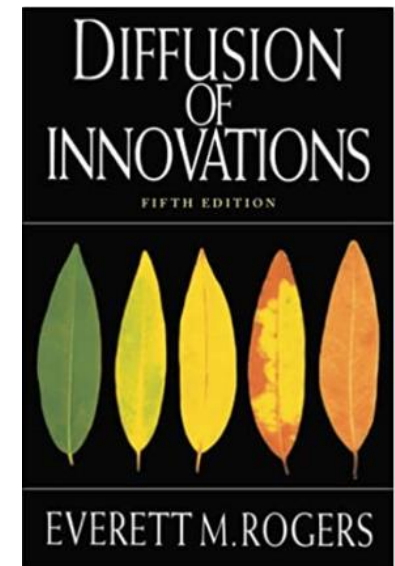
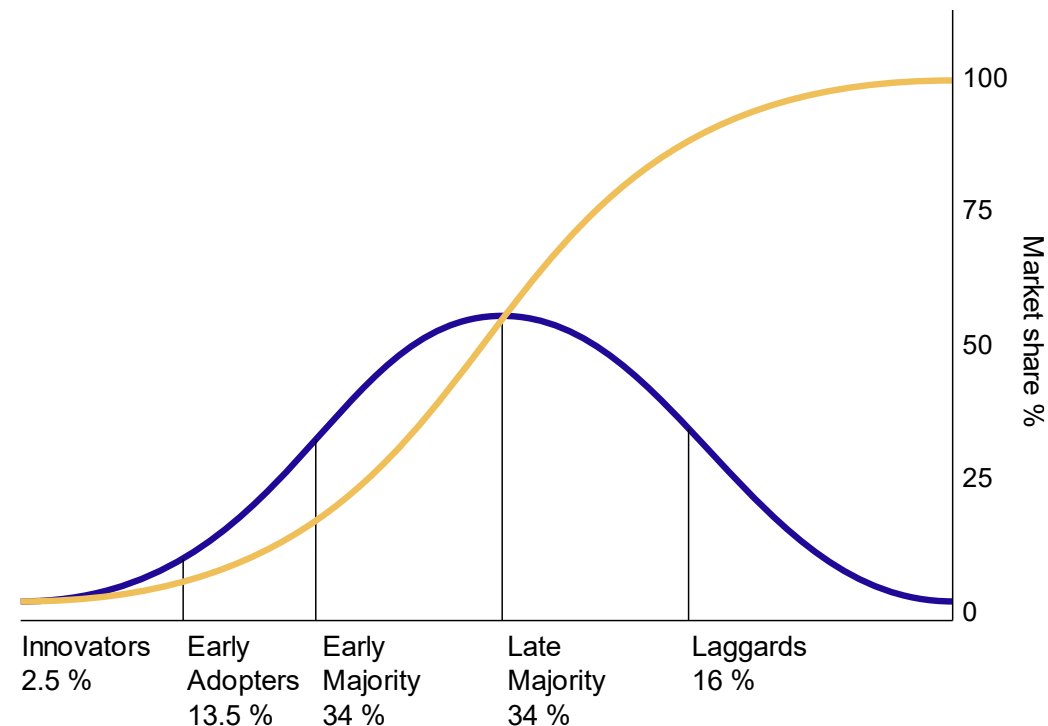
Apply high-throughput toxicokinetics (htk) to get mg/kg-bw/day



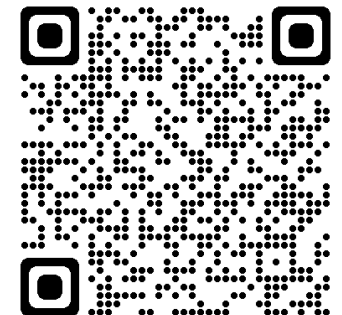
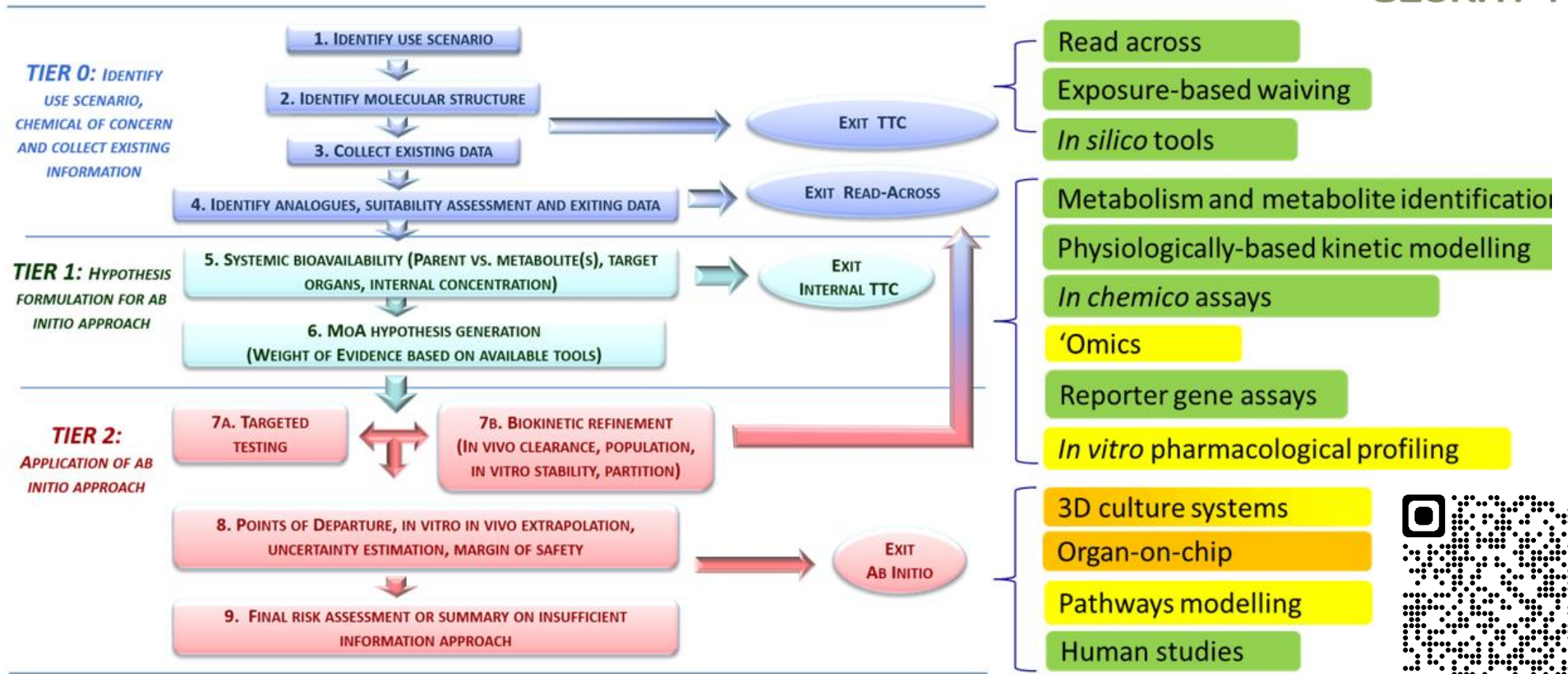
Paul Friedman et al. 2020

APCRA 'proof-of-concept' case study demonstrated the feasibility of applying a high throughput NAM-based approach for screening-level assessments - $POD_{NAM 95}$ value less than or equal to the $POD_{traditional}$ value for 89% chemicals. **Bioactivity-exposure ratio** useful metric for chemical prioritization

1. Unilever Policy and Approach
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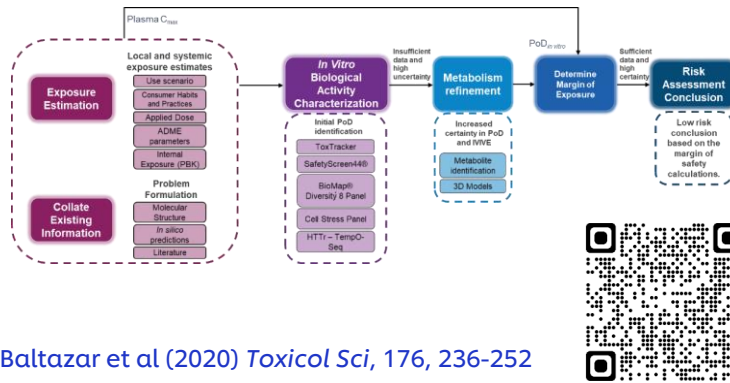
SEURAT-1 NGRA framework: tiered testing to support human health safety assessment



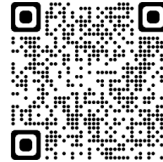
Unilever NGRA frameworks for Consumer Safety

Ongoing Evaluations

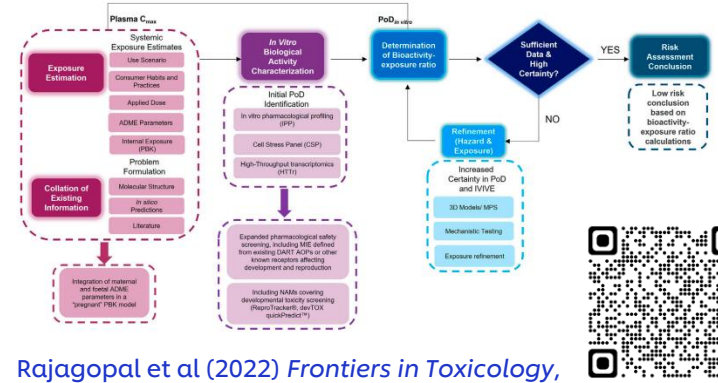
Systemic



Baltazar Habas et al (2020) *Toxicol Sci*, 176, 236-252



Developmental & Reproductive



Rajagopal et al (2022) *Frontiers in Toxicology*, doi: 10.3389/ftox.2022.838466



EPA and Unilever Announce Major Research Collaboration to Advance Non-animal Approaches for Chemical Risk Assessment

August 19, 2021

Contact Information
EPA Press Office (press@epa.gov)

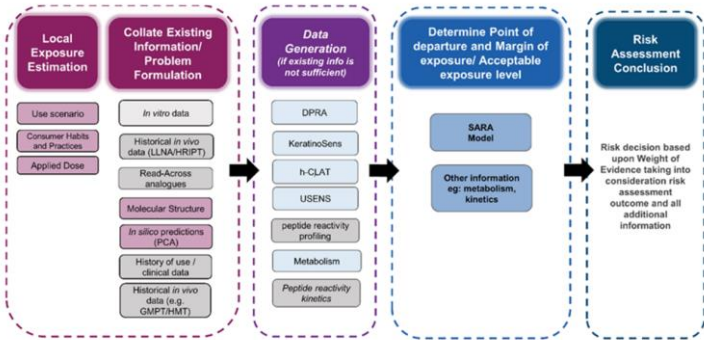
WASHINGTON - Today, the U.S. Environmental Protection Agency (EPA) and Unilever announced a collaborative agreement to explore better ways to assess chemical risks associated with consumer products. This agreement builds on prior cooperation between EPA and Unilever regarding New Approach Methods (NAMs), which are a promising alternative to conventional toxicity testing that are intended to reduce reliance on the use of animals.

EPA and Unilever have been jointly evaluating and using NAMs since 2015. 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.

"EPA is a pioneer in developing and applying NAMs to identify and quantify risks to human health, while reducing the use of animals in chemical toxicity testing," said **H. Christopher Frey**, Deputy Assistant Administrator for Science Policy in EPA's Office of Research and Development. "We are excited to continue the collaboration with Unilever, which enhances the robustness of our mutual research to demonstrate the use of NAMs."

The new collaborative effort aims to establish a framework for the Next Generation of Risk Assessments based on NAMs. Such assessments are intended to quantify health risks to humans with sufficient scientific rigor to replace conventional animal-based methods and to support EPA's mission to protect human health and the environment.

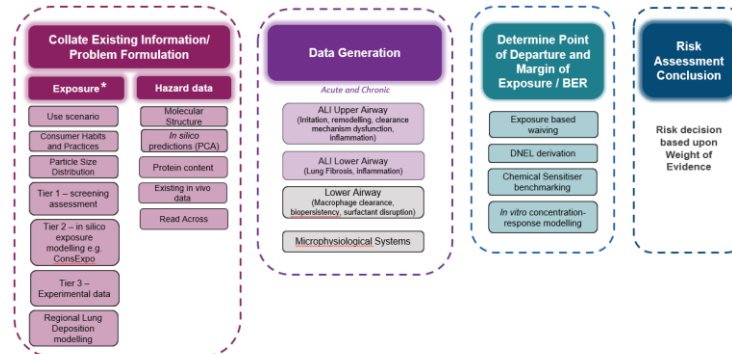
Skin Sensitisation



Reynolds et al (2021) *Reg. Toxicol Pharmacol* 127, 105075



Inhalation



NICEATM News - 2021 Issue 25: May 27

In this Newsletter:

NICEATM to Collaborate with Unilever on Development of Predictive Model for Skin Sensitization

NICEATM to Collaborate with Unilever on Development of Predictive Model for Skin Sensitization

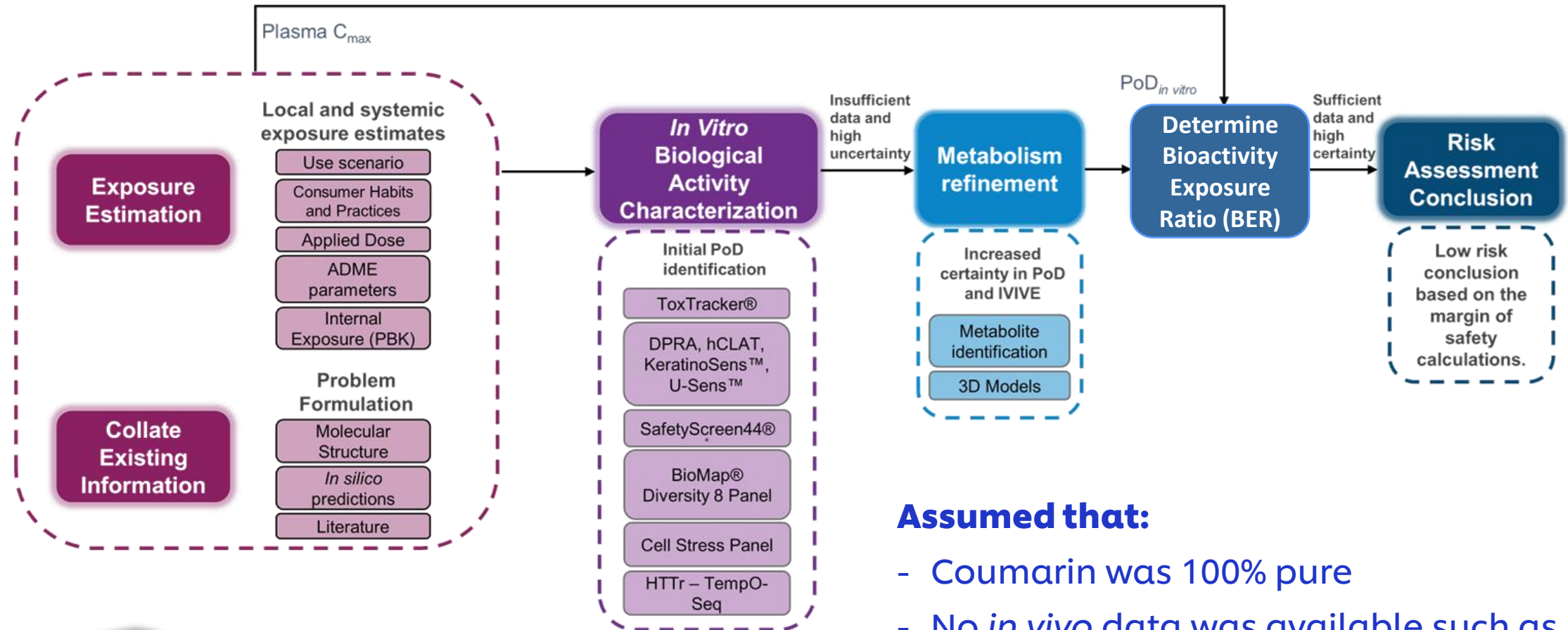
NICEATM has entered into an agreement with consumer products company Unilever to collaboratively test and further develop their Skin Allergy Risk Assessment (SARA) predictive model. SARA is a computational model that uses a variety of input data to estimate a probability that a chemical will cause an allergic skin reaction in humans. NICEATM will test the SARA model using a variety of chemical data sets, including chemicals of interest to U.S. and international regulatory agencies. NICEATM and Unilever will also work together to expand the SARA model to include data generated by NICEATM. The intent is to make the SARA model openly available for public use along with other NICEATM predictive models. Availability of the SARA model will help further reduce animal use for the endpoint of skin sensitization, and will improve upon existing efforts by providing points of departure for quantitative human risk assessment.

[Information about other NICEATM projects](https://ntp.niehs.nih.gov/op/ACDtest) to evaluate alternatives to animal use for skin sensitization is available at <https://ntp.niehs.nih.gov/op/ACDtest>.

Reference: [Reynolds et al](#), Probabilistic prediction of human skin sensitizer potency for use in next generation risk assessment. *Comput Toxicol* 9:36-49. <https://doi.org/10.1016/j.cotox.2018.10.004>

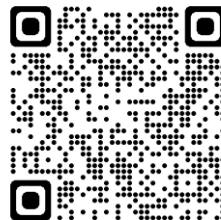
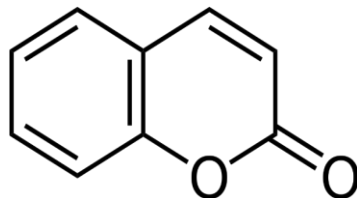


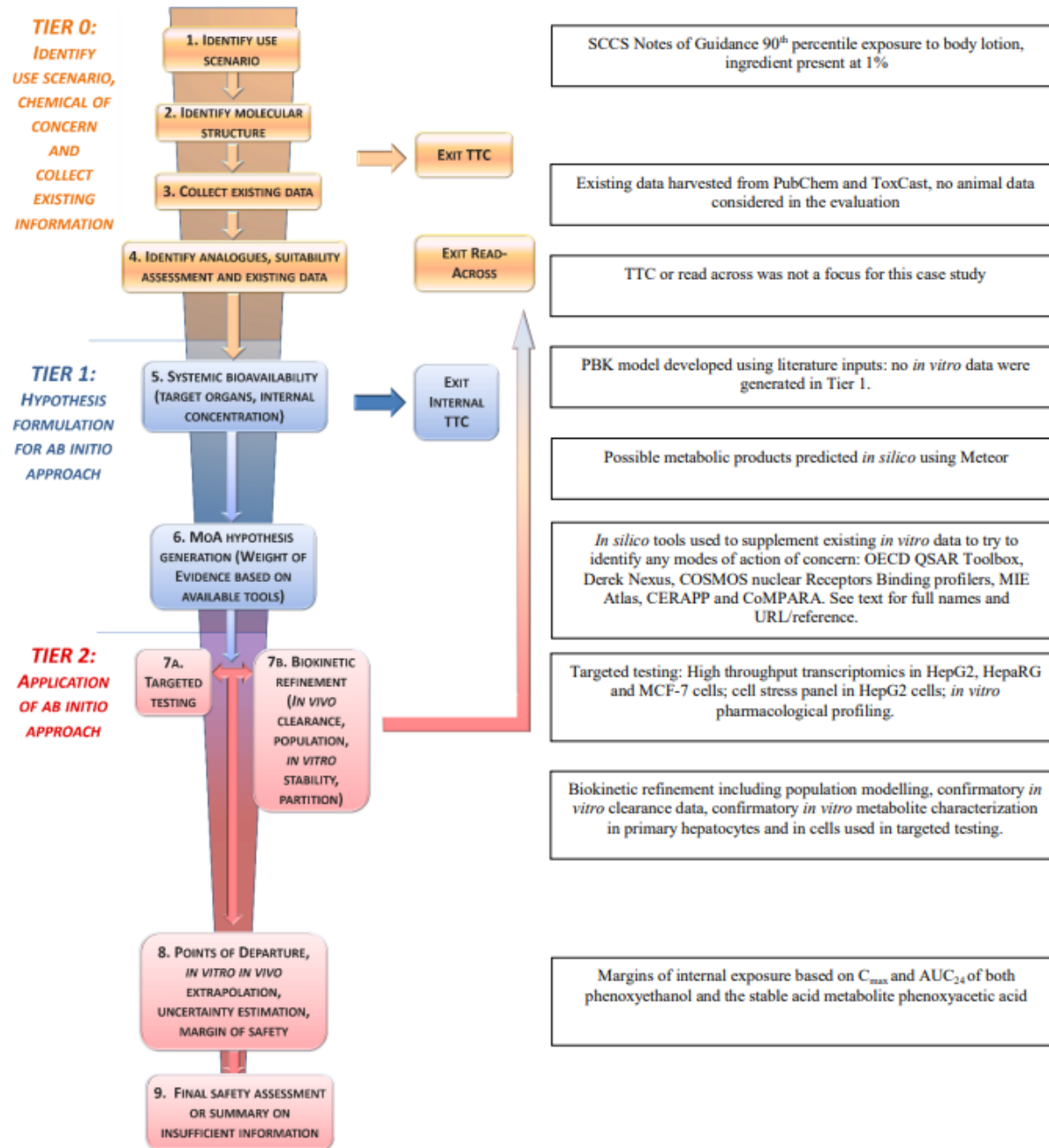
NGRA for Systemic Exposure & Effects: 0.1% coumarin in face cream



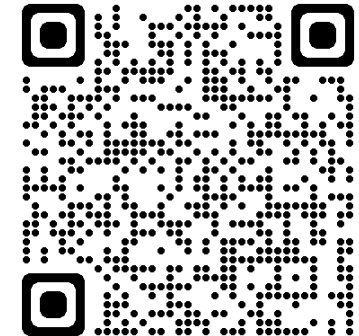
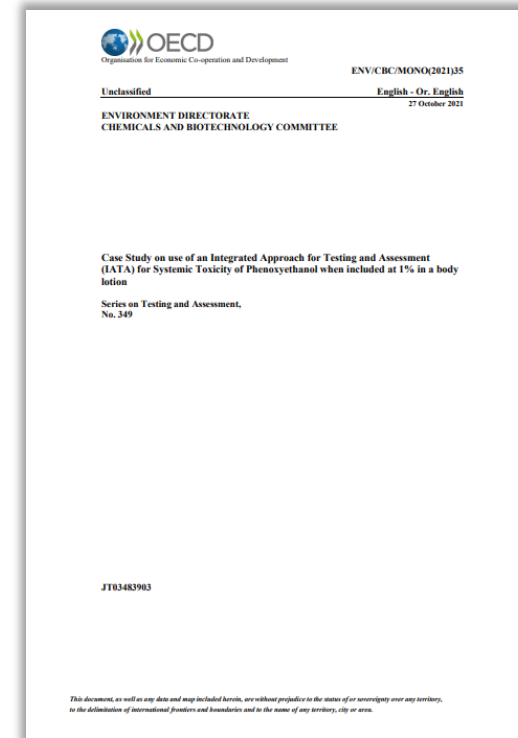
Assumed that:

- Coumarin was 100% pure
- No *in vivo* data was available such as animal data, history of safe use (HoSU) or clinical data or use of animal data in read across

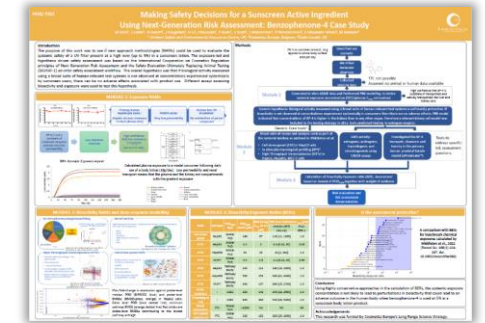
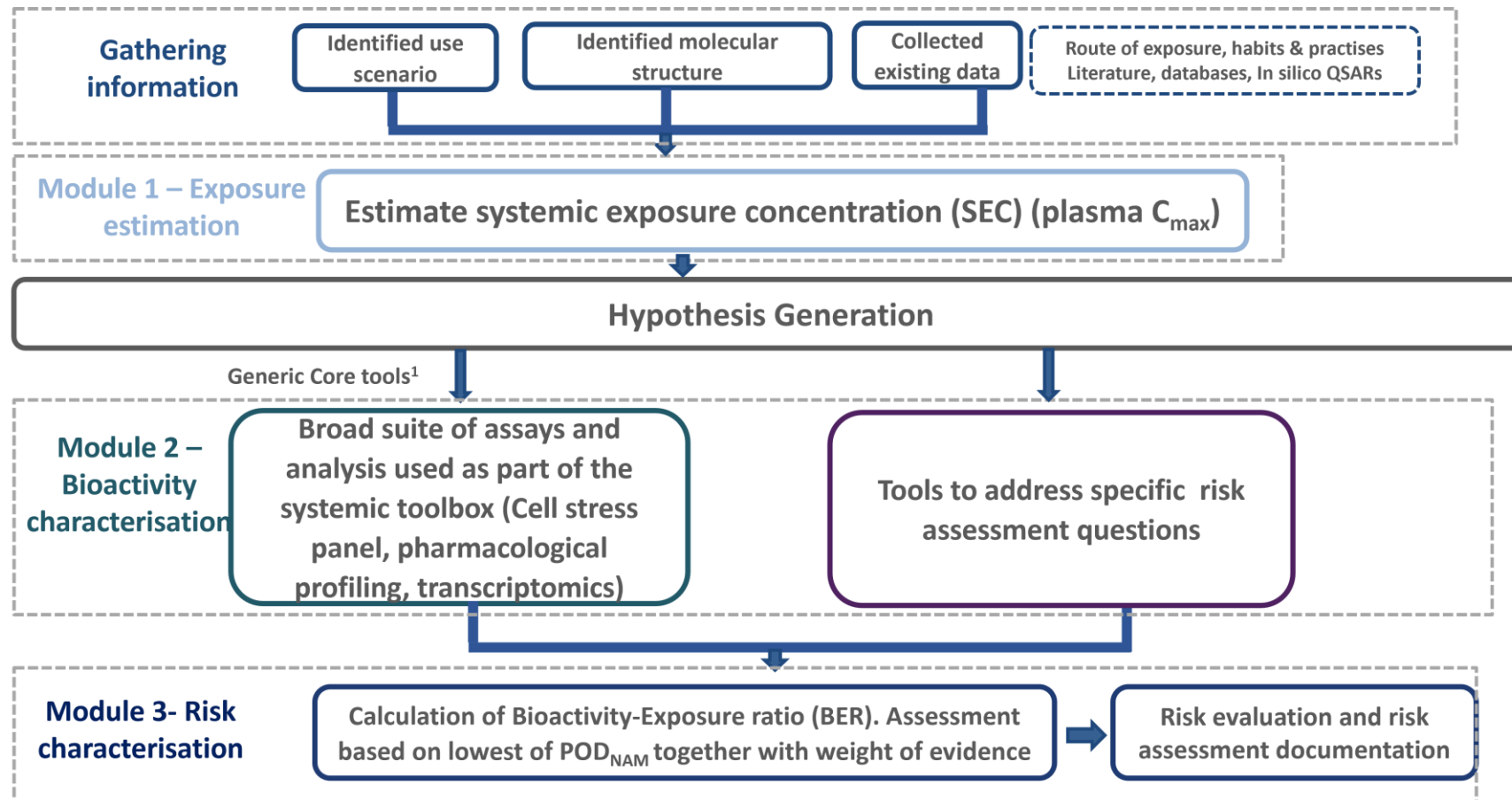




Case Study on use of an IATA for Systemic Toxicity of Phenoxyethanol when included at 1% in a body lotion Testing and Assessment Series, # 349



Making Safety Decisions for a Sunscreen Active Ingredient Using NGRA: Benzophenone-4 Case Study



Use of NAMs/NGRA for Cosmetic Safety Assessment: Current status of regulatory acceptance

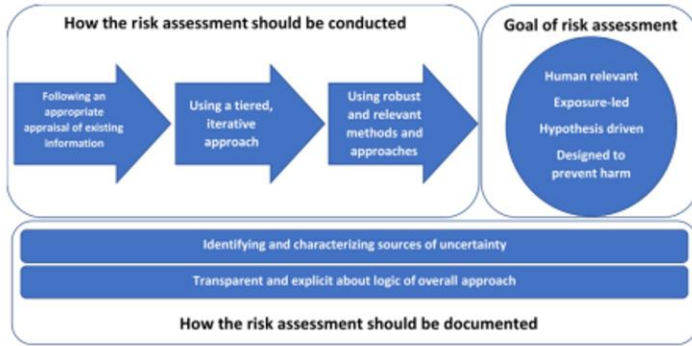
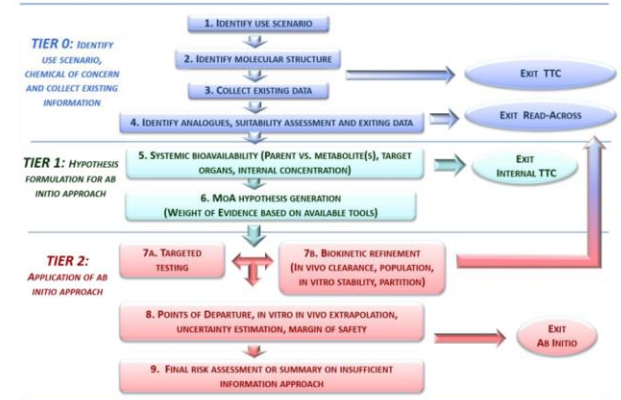


Fig. 1. Principles underpinning the use of new methodologies in the risk assessment of cosmetic ingredients.

- 4 Main overriding principles:**
- » The overall goal is a human safety risk assessment
 - » The assessment is exposure led
 - » The assessment is hypothesis driven
 - » The assessment is designed to prevent harm
- 3 Principles describe how a NGRA should be conducted:**
- » Following an appropriate appraisal of existing information
 - » Using a tiered and iterative approach
 - » Using robust and relevant methods and strategies
- 2 Principles for documenting NGRA:**
- » Sources of uncertainty should be characterized and documented
 - » The logic of the approach should be transparent and documented



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 of cosmetic ingredients

Matthew Dent^{a,*}, Renata Teixeira Amaral^b, Pedro Amores Da Silva^b, Jay Ansell^c, Fanny Boisleve^d, Masato Hatao^e, Akihiko Hirose^f, Yutaka Kasai^g, Petra Kern^h, Reinhard Kreilingⁱ, Stanley Milstein^j, Beta Montemayor^k, Julemaria Oliveira^l, Andrea Richarz^m, Rob Taalmanⁿ, Eric Vaillancourt^o, Rajeshwar Verma^p, Nashira Vieira O'Reilly Cabral Posada^q, Craig Weiss^r, Hajime Kojima^s

^aUnilever Safety and Environmental Assurance Centre, Colworth Science Park, Sharnbrook, Bedfordshire MK44 1LQ, UK
^bANVISA - Associação de Cosméticos, Tóxicos e Regulação Indústria (ASRT/RECI), Av. Paulista, 2333 Consórcio Citrus, São Paulo, SP 01311-000, Brazil
^cUS Personal Care Products Council (PCPC), 1620 L St. NW, Suite 1200, Washington, D.C. 20036, USA
^dJohnson & Johnson Saint Basil France, Division de Maternité, CS 10625, P-27126 VAL DE REUIL, Colas, France
^eJapan Cosmetic Industry Association (JCIA), Moten City Kamiyacho 6F, 3-1-5, Toranomon, Minato-ku, Tokyo 105-0001 Japan
^fNational Institute of Health Sciences, 1-18-1 Kamiyoga, Setagaya-ku, 158-8501 Tokyo, Japan
^gKao Corporation, External Relations & Government Affairs 2-1-3, Banri, Sameda-ku, Tokyo 131-8501 Japan
^hProcter and Gamble Service Company NV, Transdoken 100, B-1833 Overhokkebeek, Belgium
ⁱCharité - Universitätsmedizin Berlin, Charité - Universitätsmedizin Berlin, Charitéplatz 1, 10583 Berlin, Germany
^jUS Food and Drug Administration (US FDA), Office of Cosmetics and Colors (OCC/C), Center for Food Safety and Applied Nutrition (CFSA), 5001 Campus Drive, College Park, MD 20740, USA
^kCosmetics Alliance Canada, 420 Britannia Road East Suite 102, Mississauga, ON L4Z 3L5, Canada
^lBrazilian Health Regulatory Agency (ANVISA), Gerência de Produtos de Higiene, Perfumes, Cosméticos e Sanitários, SIA Trêche S, lote 200, Área Especial 57 - CEP 71205-050, Brazil
^mEuropean Commission, Joint Research Centre (JRC), Directorate for Health, Consumers and Reference Materials, Chemical Safety and Alternative Methods Unit, Via E. Fermi 2749, 21027 Segrate, VA, Italy
ⁿCosmetics Europe, Avenue Hermans Delbecq 40, 1160 Auderghem, Belgium
^oHealth Canada (HC), Consumer Product Safety Directorate, Healthy Environments and Consumer Safety Branch, 269 Laurier Ave. W., Ottawa, ON K1A 0K9, Canada
^pHealth Canada (HC), Consumer Product Safety Directorate, Healthy Environments and Consumer Safety Branch, 269 Laurier Ave. W., Ottawa, ON K1A 0K9, Canada
^qIndependent Cosmetics Manufacturing and Distributors (ICMAD), 21925 Field Parkway, Suite 2015, Deer Park, IL 60010, USA

ARTICLE INFO

Keywords:
 Next Generation Risk Assessment
 New approach methodologies
 Cosmetic risk assessment

ABSTRACT

Consumer safety is a prerequisite for any cosmetic product. Worldwide, there is an ever-increasing desire to bring safe products to market without animal testing, which requires a new approach to consumer safety. Next Generation Risk Assessment (NGRA), defined as an exposure-led, hypothesis driven risk assessment approach that integrates in silico, in chemico and in vitro approaches, provides such an opportunity. The customized nature of each NGRA means that the development of a prescriptive list of tests to assure safety is not possible, or appropriate. The International Cooperation on Cosmetic Regulation (ICCR) therefore tasked a group of scientists

Regulatory Toxicology and Pharmacology 125 (2021) 10

Contents lists available at ScienceDirect

Regulatory Toxicology and Pharm

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

Paving the way for application of next generation risk as decision-making for cosmetic ingredients

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ARTICLE INFO

ABSTRACT

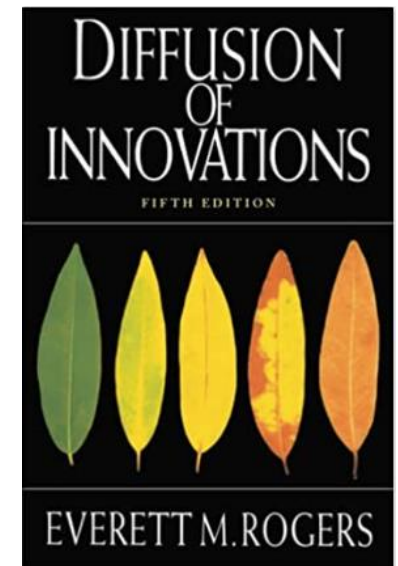
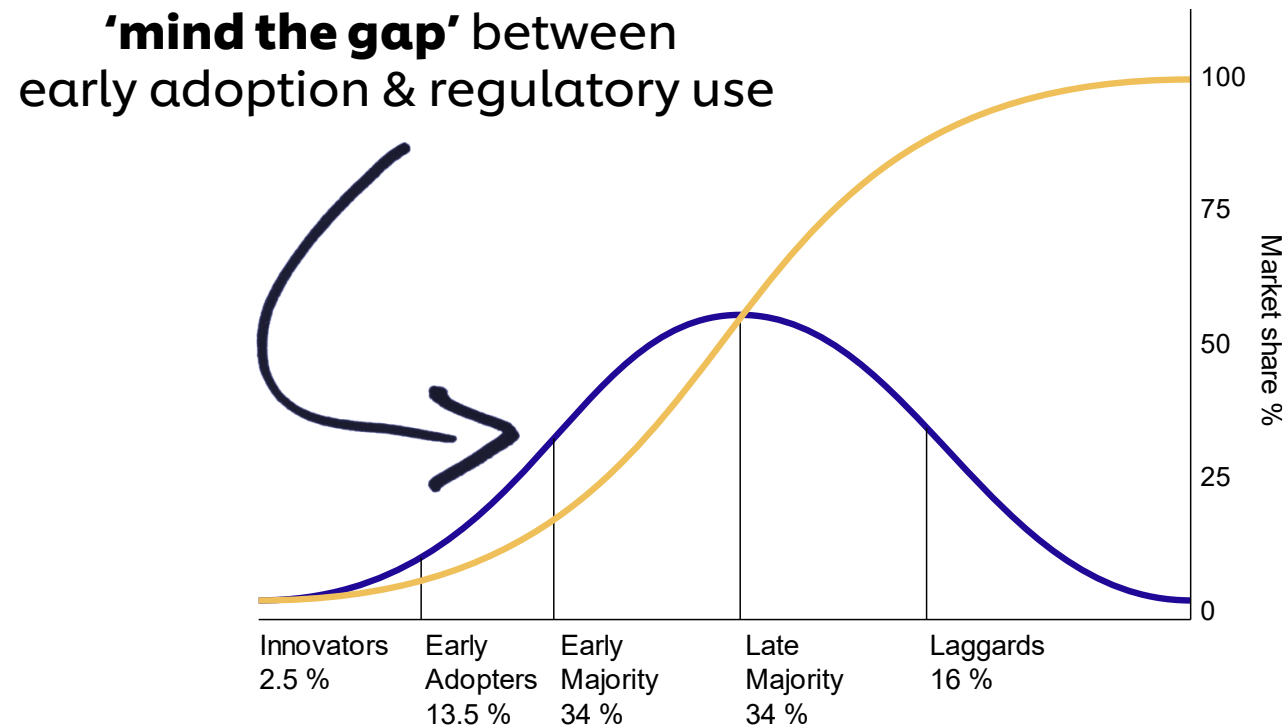
Scientific Committee on Consumer Safety

SCCS

THE SCCS NOTES OF GUIDANCE FOR THE TESTING OF COSMETIC INGREDIENTS AND THEIR SAFETY EVALUATION

12TH REVISION

1. Unilever Policy and Approach
2. Next Generation Risk Assessment (NGRA)
3. Applying NGRA to Cosmetic Safety Assessment
- 4. Accelerating the Transition**

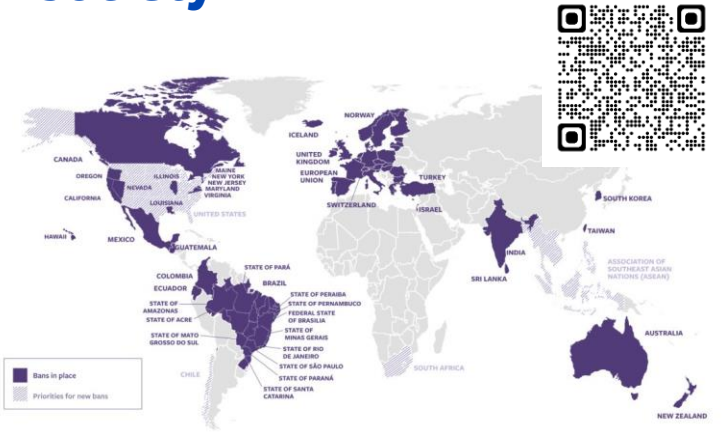


Why accelerate the transition to Animal-Free Safety Assessment?

- 1. Consumer concerns about the potential impacts of chemicals on their health & environment are high**
- 2. Move to more sustainable sources of chemicals (e.g. bio-based) is transforming chemical innovation & use**
- 3. Regulatory Animal Testing of Chemicals is increasingly seen as unjustifiable / unethical by the majority of society**

85% / 90% EU citizens are worried about the impact of chemicals present in everyday products on their health / the environment

Special Eurobarometer 501

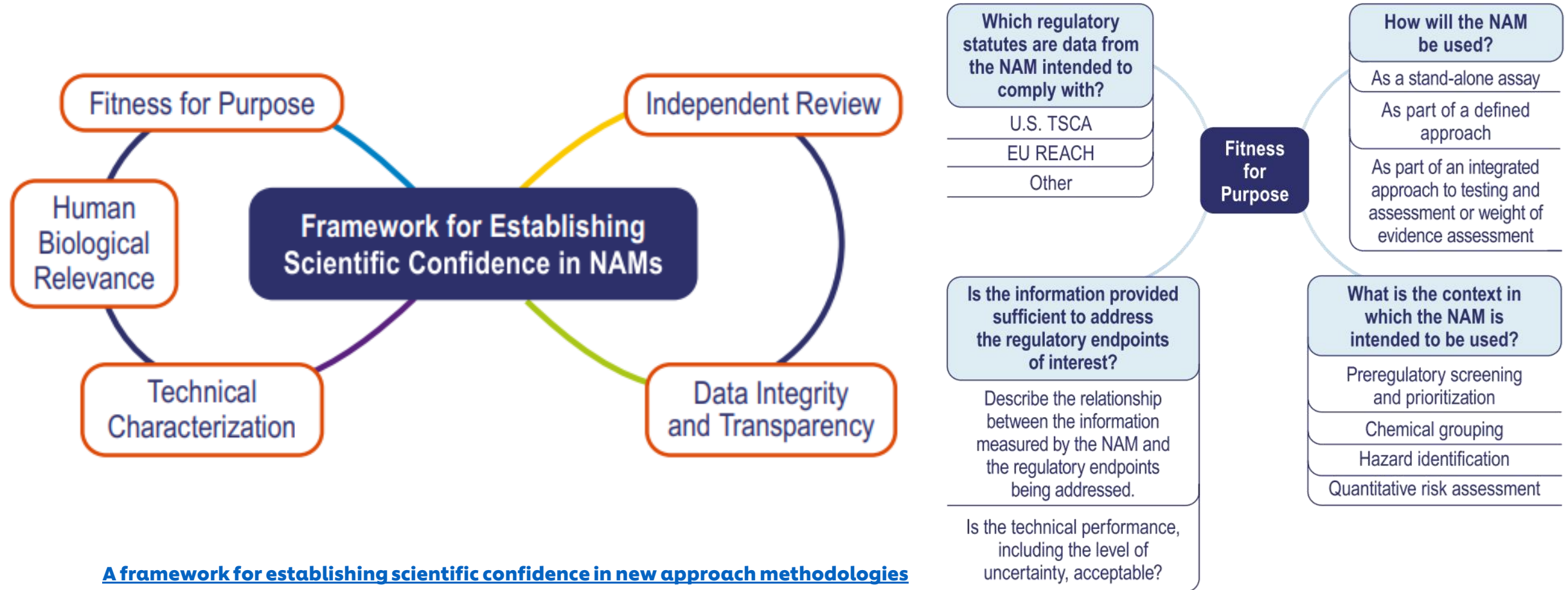



✓ Let's use Animal-free Safety Science to **rebuild consumer trust in cosmetic safety**

✓ Let's use Animal-free Safety Science to **ensure new chemicals are Safe & Sustainable**

✓ Let's use Animal-free Safety Science to **fully replace the need for regulatory animal testing**


1. Build confidence in NGRA frameworks by validating whether or not they are 'fit for regulatory use'



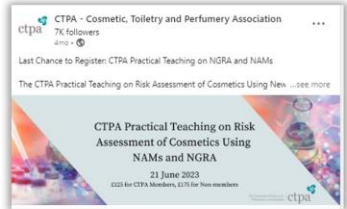
[A framework for establishing scientific confidence in new approach methodologies](#)

2. Co-create NGRA best practice through open industry: regulator scientific dialogue using NGRA case studies







BP4 NGRA dossier presented to SCCS – Feb 2023




CTPA training workshop – June 2023



ASCCT workshop – Oct 2023



DGK/IKW seminar – Nov 2023

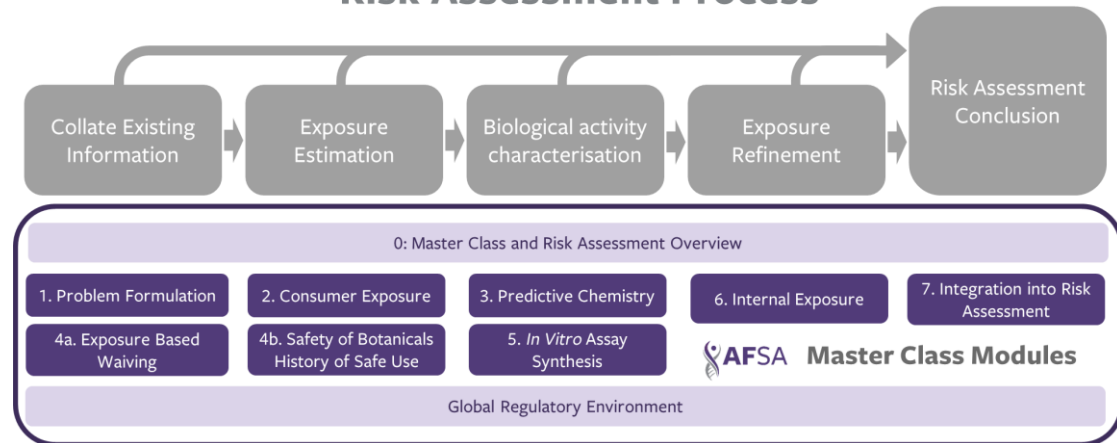


EPAA NAM User Forum – Dec 2023

3. Update toxicological training to include NGRA concepts and approaches



Risk Assessment Process



Module release date 2023	Online now	Aug '23	Fall '23
0: Intro: course overview	█		
1: Problem formulation	█		
2: Consumer exposure	█		
3: In silico tools	█		
4a: Exposure-based waiving	█	█	
4b: Safety of Botanicals: History of Safe Use	█	█	
8: Regulatory landscape	█	█	
5: In vitro data synthesis	█	█	█
6: Internal Exposure: Dosimetry	█	█	█
7: Risk assessment	█	█	█



4. Collaborate to pool resources, learn together & manage the change (EU Roadmap, UK NAMs strategy, EPA NAM workplan)



That's why we need you to join us and **sign the European Citizens' Initiative (ECI)** calling on the European Commission to:

- **Protect and strengthen the cosmetics animal testing ban**
- **Transform EU Chemicals Regulation**
- **Put forward a concrete plan to transition to non-animal science**

Save Cruelty Free Cosmetics

Commit to a Europe without animal testing



Workshop on the Roadmap towards phasing out animal testing for chemical safety assessments 11 - 12 December 2023, Brussels

Session 1 – Introduction and setting the scene
Session 2: How to replace animal testing for the concern of systemic human health effects?
Session 3: How to replace animal testing for the concern of long-term aquatic toxicity?
Session 4: Partnership for the Assessment of Risks from Chemicals (PARC) - Next-Generation Risk Assessment
Session 5: Enhancing the translation of non-animal methods into regulation
Session 6: Next steps and closing remarks

PARC workshop
"Guiding principles towards "Next-Generation Risk Assessment" (NGRA)-ready chemicals legislation in the EU"

European Commission - Press release

Commission acts to accelerate phasing out of animal testing in response to a European Citizens' Initiative
Brussels, 25 July 2023

Today, the Commission is responding to the European Citizens' Initiative (ECI) 'Save Cruelty-free Cosmetics - Commit to a Europe without Animal Testing'. The response provides a comprehensive overview of the EU's legislative and policy framework relevant to the use of animals for testing purposes. It also proposes additional actions to further reduce animal testing.

The Commission welcomes the initiative and acknowledges that animal welfare remains a strong concern for European citizens. It highlights the leading role of the EU in phasing out the use of animals in testing and improving animal welfare in general. This is especially reflected in the full ban of animal testing for cosmetics, which has been in place in the EU since 2013.

In addition, the Commission will launch a new roadmap with a set of legislative and non-legislative actions to further reduce animal testing, with the aim to ultimately move to an animal-free regulatory system under chemicals legislation (e.g. REACH, Biocidal Product Regulation, Plant Protection Products Regulation and human and veterinary medicines) and continue strongly supporting alternatives to animal testing.

In relation to the modernisation of science, the Commission will continue its strong support to research for the development of alternatives to animal testing and explore the possibility to coordinate the activities of Member States in this field.

The Commission outlines the following actions in response to specific objectives of the European citizens' initiative:

- **Protect and strengthen the cosmetics animal testing ban:** The Commission emphasises that the EU Cosmetics Regulation already prohibits the placing on the market of cosmetic products that have been tested on animals. However, this ban does not extend to safety tests required to assess risks from chemicals to workers and the environment under the EU Regulation on the Registration, Evaluation, Authorisation, and Restriction of Chemicals



PARC NGRARoute guiding principles and work streams. 18.12.2023

PARC NGRARoute guiding principles and work streams (2023-12-18)

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1 Introduction

1.1 Context

This document was developed in the context of NGRARoute, an activity under Work Package 2 ("A common science-policy agenda") of PARC, the European Partnership for the Assessment of Risks from Chemicals.

The overall vision of NGRARoute² is to develop a concrete and applicable roadmap proposal for implementing Next-Generation Risk Assessment (NGRA) as the default approach to chemical risk assessment in EU chemicals legislation by the end of April 2025.

The scope of NGRARoute includes all major chemicals legislation with a hazard, exposure or risk assessment component of their own. In addition, it pertains to both, human health and environmental risk assessment.

At this point in time, the conceptual development of NGRA for human health is slightly more advanced and therefore the present document is more comprehensive regarding issues relevant to human health risk assessment. However, it is expected that more conceptual content related to Next-Generation Environmental Risk Assessment (NGERA) will be added over time. In the end, the establishment of NG(E)RA in the legislation offers a particular chance to significantly improve integration of risk assessment for human health and the environment.

Since NGRARoute kicked off in the second half of 2022, the project team under PARC Task 2.2 ("Knowledge management and uptake into policy") performed initial research and developed the

¹ For more information on PARC, go to <https://www.eu-parc.eu/>. If you want to interact with PARC partners and other members of the chemical risk assessment community, you might also want to go to <https://www.epaa.eu/>.

² For more details, see https://www.eu-parc.eu/sites/default/files/2023-10/PARC_DT3.pdf.

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EPAA 'NAM Designation' Challenge for human systemic toxicity



EPAA 'Use of NAMs in Environmental Safety Assessment' Partners Forum

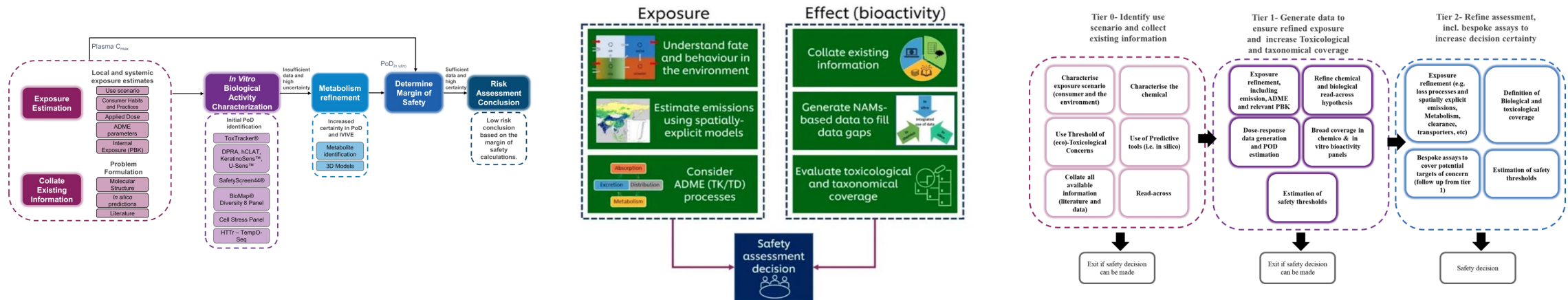


EPAA NAM User Forum



Conclusions

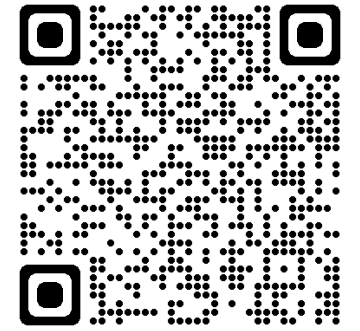
- A paradigm shift is well underway as use of NAMs and NGRA increases & moves beyond innovators/early adopters
- Translation of NGRA concepts into chemical regulatory frameworks, strategic plans & guidance is moving forward steadily
- We can accelerate the NGRA paradigm shift through increasing industry: regulator exchange, re-focusing validation, supporting training platforms & increased collaboration



Acknowledgements

Collaborators:

Logos include: **bts** (the british toxicology society), **ICCS** (INTERNATIONAL COLLABORATION ON COSMETICS SAFETY), **ASPIS**, **SHFDA**, **HUMANE SOCIETY INTERNATIONAL**, **cefic**, **ecetoc**, **EPSCRC** (Pioneering research and skills), **NTP** (National Toxicology Program), **cosmetics Europe**, **ICCR** (International Cooperation on Cosmetics Regulation), **EUROL** (European Union Reference Laboratory for Allergenicity of Animal Testing), **Scientific Committees**, **Unilever China CPSC Centre** (联合利华中 国消费者产品安全合作中心), **EPA**, **cyprotex** (an EVOTEC COMPANY), **Delphic HSE**, **国家药品监督管理局** (National Medical Products Administration), **ICAPO** (International Council on Animal Protection in OECD Programmes), **HORIZON 2020**, **EMBL-EBI**, **VHP4SAFETY** (virtual human platform for safety assessment), **NC 3R^s** (National Centre for the Replacement, Refinement & Reduction of Animals in Research), **eawag** (aquatic research), **epaa** (The European Partnership for Alternative Approaches to Animal Testing), **State Key Laboratory of Environmental Chemistry and Ecotoxicology**, **HUMAN TOXICOLOGY PROJECT CONSORTIUM**, **RISK HUNT3R**, **Universiteit Leiden**, **AFSA** (ANIMAL-FREE SAFETY ASSESSMENT COLLABORATION), **BROWN**, **GENESTACK**, **中国科学院生态环境研究中心** (Research Center for Eco-Environmental Sciences, Chinese Academy of Sciences), **UCL**, **INDOOR biotechnologies**, **BBSRC** (bioscience for the future), **Newcastle University**, **Université de Strasbourg**, **BPRC** (Beijing Proteome Research Center), **Home Office**, **DTU**, **UNIVERSITY OF CAMBRIDGE**, **Lhasa Limited**, **WAGENINGEN UNIVERSITY & RESEARCH**, **UNIVERSITY OF LEEDS**, **ATM**, **MERIEUX NutriSciences**, **军事医学科学院**, **toxys**, **Swansea University Prifysgol Abertawe**, **Bio:Clavis**, **UNIVERSITY OF BIRMINGHAM**, **UNIVERSITY OF SURREY**, **Bio:Spyder**, **SciBite**, **THE UNIVERSITY OF NOTTINGHAM**, **Celentyx**, **University of Southampton**, **CARDIFF UNIVERSITY**, **Bio:Spyder**, **Creme GLOBAL** (Expert Models For Decision Makers), **LIVERPOOL JOHN MOORES UNIVERSITY**, **SOLVO** (BIOTECHNOLOGY THE TRANSPORTER COMPANY), **康龙化成 PHARMARON**, **EP** (Epithelix), **IIVS** (Institute for In Vitro Sciences), **Stockholm University**, **XCellR8** (Redefining testing), **euofins**, **Brunel University London**, **Stockholm University**, **esqlABS** (WE EMPOWER HEALTH CARE), **OECD**, **UNIVERSITÄT LEIPZIG**, **NWO**.



<p>Systemic Safety To understand the safety of ingredients if they are absorbed into the body (systemic safety), we do not use an animal study to...</p>	<p>Skin Allergy Safety Some ingredients used in consumer products have the potential to cause allergic contact dermatitis (ACD), a type of skin allergy. To...</p>
<p>Immune Effects Safety We consider all potential adverse impacts on the human immune system resulting from exposure to an ingredient. These include...</p>	<p>Microbiological Safety Some of our consumer products have the potential to change the human microbiome or raise microbiological concerns...</p>
<p>Inhalation Safety A significant proportion of Unilever's products are aerosols and sprays which include underarm antiperspirants, hair sprays...</p>	<p>DART Safety Developmental and reproductive toxicity (DART) refers to potential adverse effects that exposure to an ingredient may have on...</p>
<p>Environmental Safety Unilever ingredients are often disposed of down the drain after use, so it is important for us to assess the environmental safety of...</p>	<p>Biodegradation Biodegradation is the process in which an ingredient is broken down through natural processes by microorganisms into simple substances...</p>

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