ANNUAL LECTURE – 16 NOV 2022

Safer chemicals and sustainable innovation will be achieved by regulatory use of modern safety science, not by more animal testing

JULIA FENTEM

HEAD OF UNILEVER's SAFETY & ENVIRONMENTAL ASSURANCE CENTRE (SEAC)

Thank You

Gavin Maxwell, Carl Westmoreland, Gemma Shaw, Maria Baltazar, Paul Carmichael, Matt Dent, Steve Gutsell, Sarah Hatherell, Predrag Kukic, Hequn Li, Alistair Middleton, Iris Müller, Ramya Rajagopal, Georgia Reynolds, Andrew White

& Unilever colleagues + collaborators

Our Ambition – Safe & Sustainable Chemicals without Animal Testing

Unilever

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Home ▸ All news stories ▸ Safe and sustainable ingredients and products – without animal testing

Safe and sustainable ingredients and products – without animal testing

Published: **06/07/2022** Average read time: **6 minutes**

The ingredients in our products must be safe for people and the planet – but we don't need to test on animals to achieve this. Here Dr Julia Fentem, Head of our Safety & Environmental Assurance Centre, explains why we're calling for chemical regulations to change.

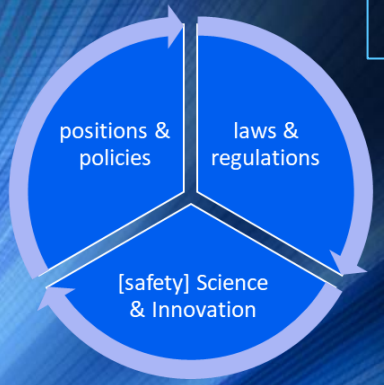
> Advances in science and technology mean that we can generate much more relevant safety data to protect people and the environment using modern non-animal approaches.

We say use science. Not animals.

Unilever

Advocating for an animal-free science-based approach to improve chemical safety

1. SAFETY SCIENCE
2. CHEMICALS REGULATIONS
3. CHEMICALS POLICY



Cosmetics design-europe.com

THE LONG READ: IN CONVERSATION WITH UNILEVER SAFETY & ENVIRONMENTAL ASSURANCE CENTRE (SEAC) EXECUTIVES

The future of animal-free chemical testing? There's a 'big frustration' in the scientific community, say Unilever execs

By Kacey Culliney

20-Oct-2021 - Last updated on 20-Oct-2021 at 09:54 GMT

ECHA EUROPEAN CHEMICALS AGENCY

REACH COMPLIANCE

Law–Not Science–Impedes Shift to Non-Animal Safety Testing

June 18, 2021, 9:01 AM

Listen

Testing products on animals is slowly ending, but there are still some obstacles to completely ending the practice, explains Gary E. Marchant, a professor at the Sandra Day O'Connor College of Law at Arizona State University. He discusses three impediments, including legal barriers from federal regulatory agencies.

Gary Marchant
Sandra Day O'Connor College of Law

High-Level Conference

EU Chemicals Policy 2030

Chemicals Strategy for Sustainability

The European Commission adopted its Chemicals Strategy for Sustainability on 14 October 2020. The strategy is part of the EU's zero pollution ambition – a key commitment of the European Green Deal – and aims to better protect citizens and the environment from harmful chemicals, and boost innovation by promoting the use of safer and more sustainable chemicals.

Common Framework: Framework Outline Agreement

Section A: What we are talking about

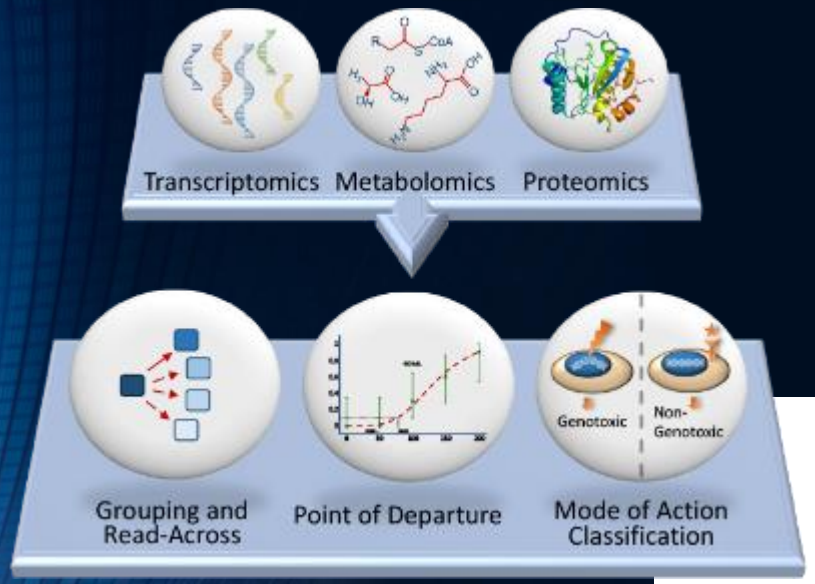
1. Policy area

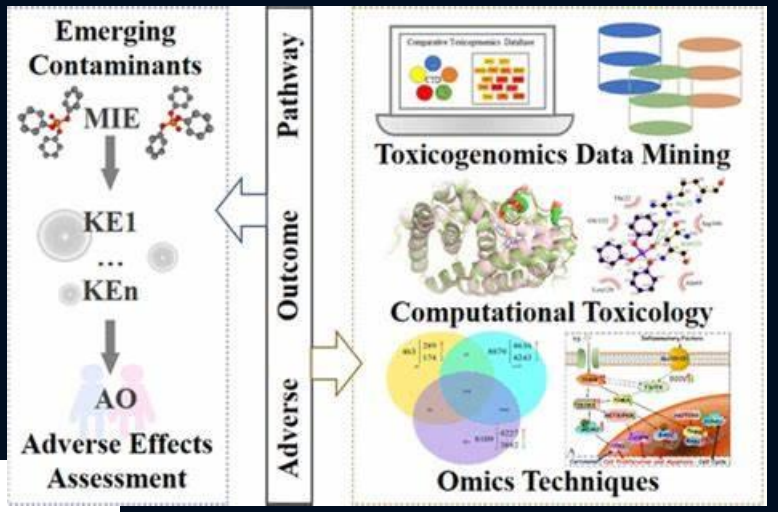
1.1. The policy area under consideration is chemicals regulation, including pesticides. For the purposes of this

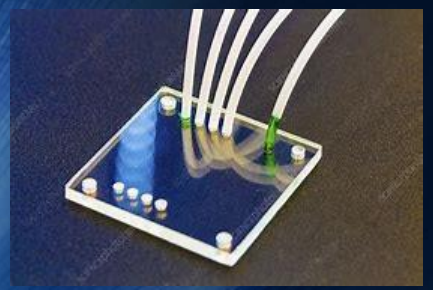
DEFRA confirms fresh delay to publication of Chemicals Strategy

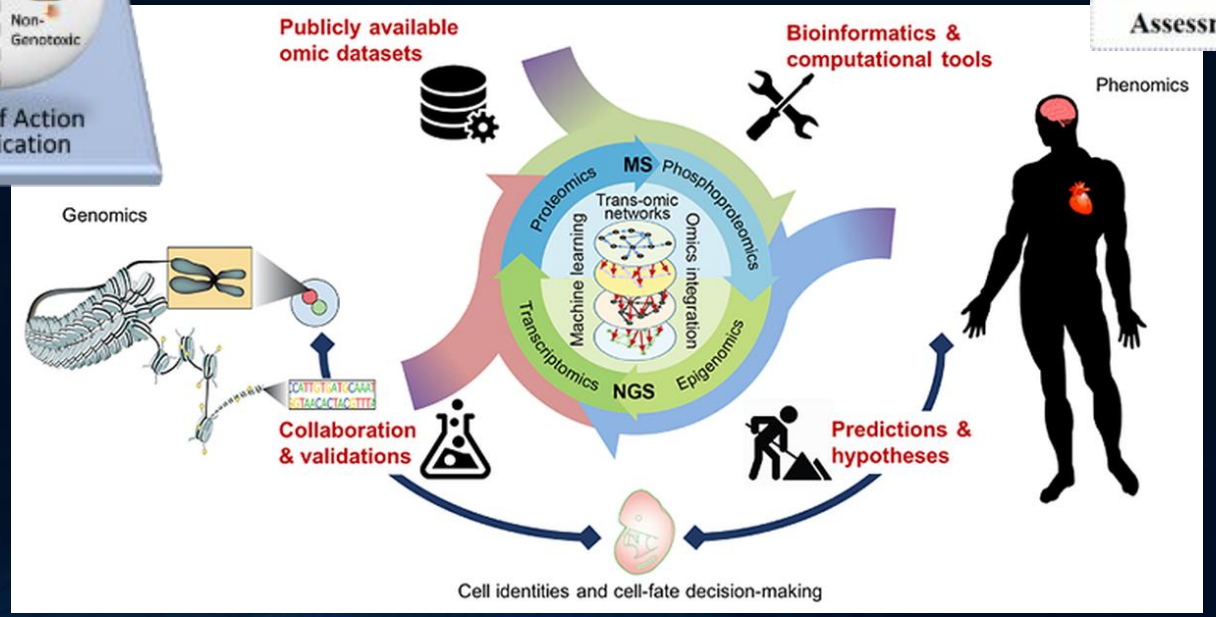
DEFRA has told ENDS that the publication of its serially-delayed Chemicals Strategy has been put back again, though roundtable talks will begin next month.

A 21st Century non-animal toolbox - exciting scientific developments accelerated availability of novel technologies & models





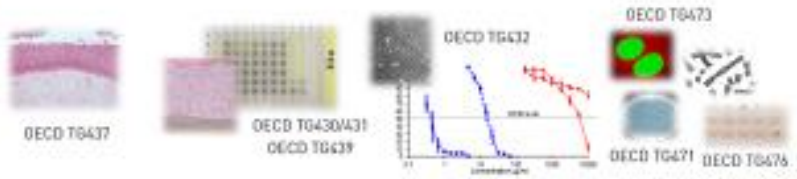




Assessing Consumer Safety of Cosmetics Ingredients
without new animal testing (EU Cosmetic Products Regulation)

Is the consumer exposure safe? A tiered approach is routine:

- Use all available safety data on the ingredient
  - clinical, epidemiological, animal (if dates permit), *in vitro*, etc.
- Exposure-based waiving (e.g. TTC – toxicological threshold of concern)
- *In silico* predictions
- History of safe use
- Read across from comparable ingredients
- Use of existing OECD *in vitro* approaches



- Next Generation Risk Assessment (NGRA)

1

SAFETY SCIENCE

Applying non-animal approaches in decision-making

ATLA 32, 617–623, 2004

Comment

The Feasibility of Replacing Animal Testing for Assessing Consumer Safety: A Suggested Future Direction

Julia Fentem, Mark Chamberlain and Bart Sangster

Safety & Environmental Assurance Centre, Unilever Colworth Laboratory, Sharnbrook, Bedfordshire, UK

Contents lists available at ScienceDirect

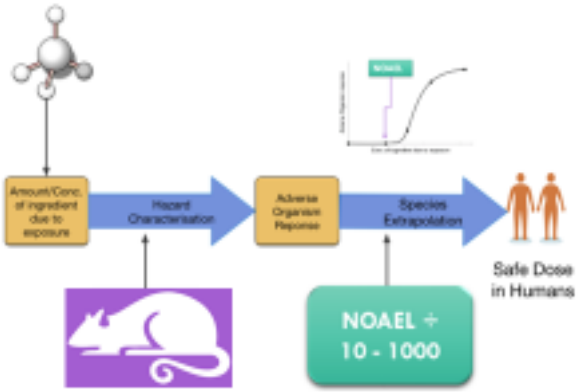
Computational Toxicology

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

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

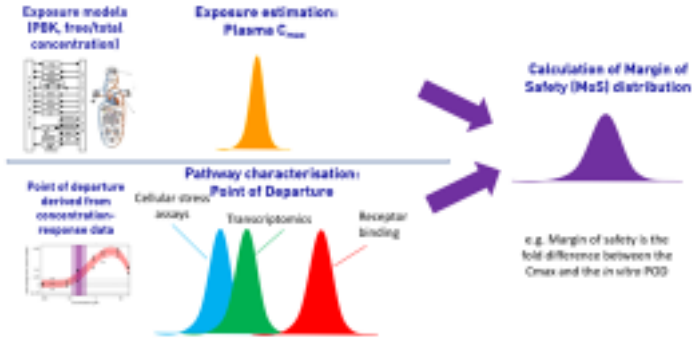
Matthew Dent[a,*], Renata Teixeira Amaral[b], Pedro Amores Da Silva[b], Jay Ansell[c], Fanny Boisleve[d], Masato Hatao[e], Akihiko Hirose[f], Yutaka Kasai[g], Petra Kern[h], Reinhard Kreiling[i], Stanley Milstein[j], Beta Montemayor[k], Julcemara Oliveira[l], Andrea Richarz[m], Rob Taalman[n], Eric Vaillancourt[o], Rajeshwar Verma[j], Nashira Vieira O'Reilly Cabral Posada[l], Craig Weiss[p], Hajime Kojima[f]

'Traditional' Risk Assessment



'Next Generation' Risk Assessment

based on advances in human biology and in vitro/computational modelling



SCCS/1628/21

Scientific Committee on Consumer Safety

SCCS

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

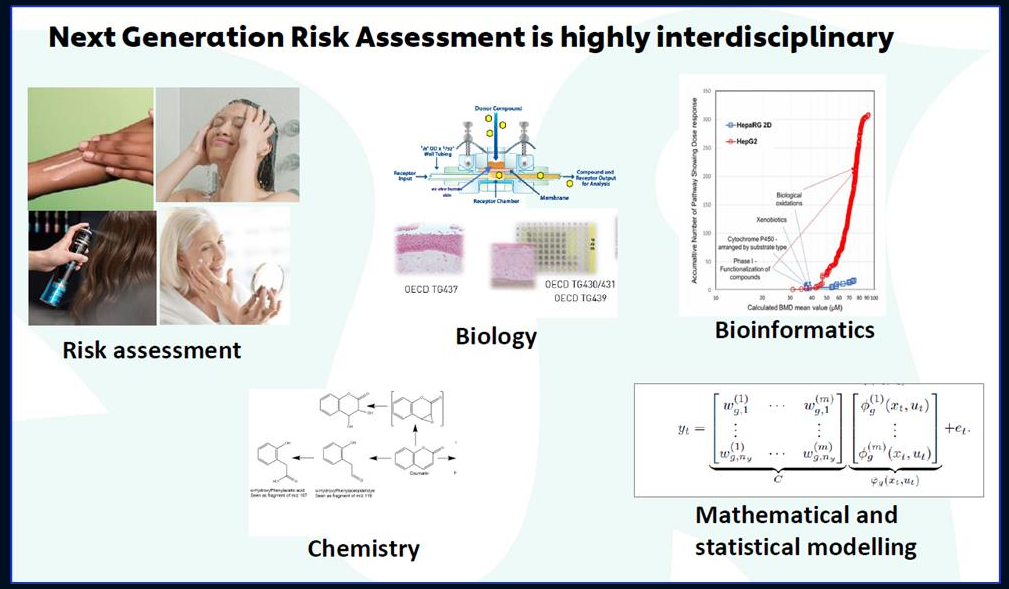
11TH REVISION

Scientific Committees

The SCCS adopted this guidance document at its plenary meeting on 30-31 March 2021

Next Generation Risk Assessment (NGRA)

NGRA is defined as an exposure-led, hypothesis-driven risk assessment approach that integrates New Approach Methodologies (NAMs) to assure safety without the use of animal testing



[Unilever, Safety & Environmental Assurance Centre (SEAC) – YouTube] US SoT March 2020 – NGRA concept & approach

[Unilever - Safety & Environmental Assurance Centre at Unilever Global IP Limited – YouTube] US SoT March 2022 – integrating NAMs in NGRA for consumer safety decisions

Using NGRA for assessing cosmetics safety

Dent *et al* (2018), Computational Toxicology, 7, 20-26

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

ICCR
International Cooperation on Cosmetics Regulation

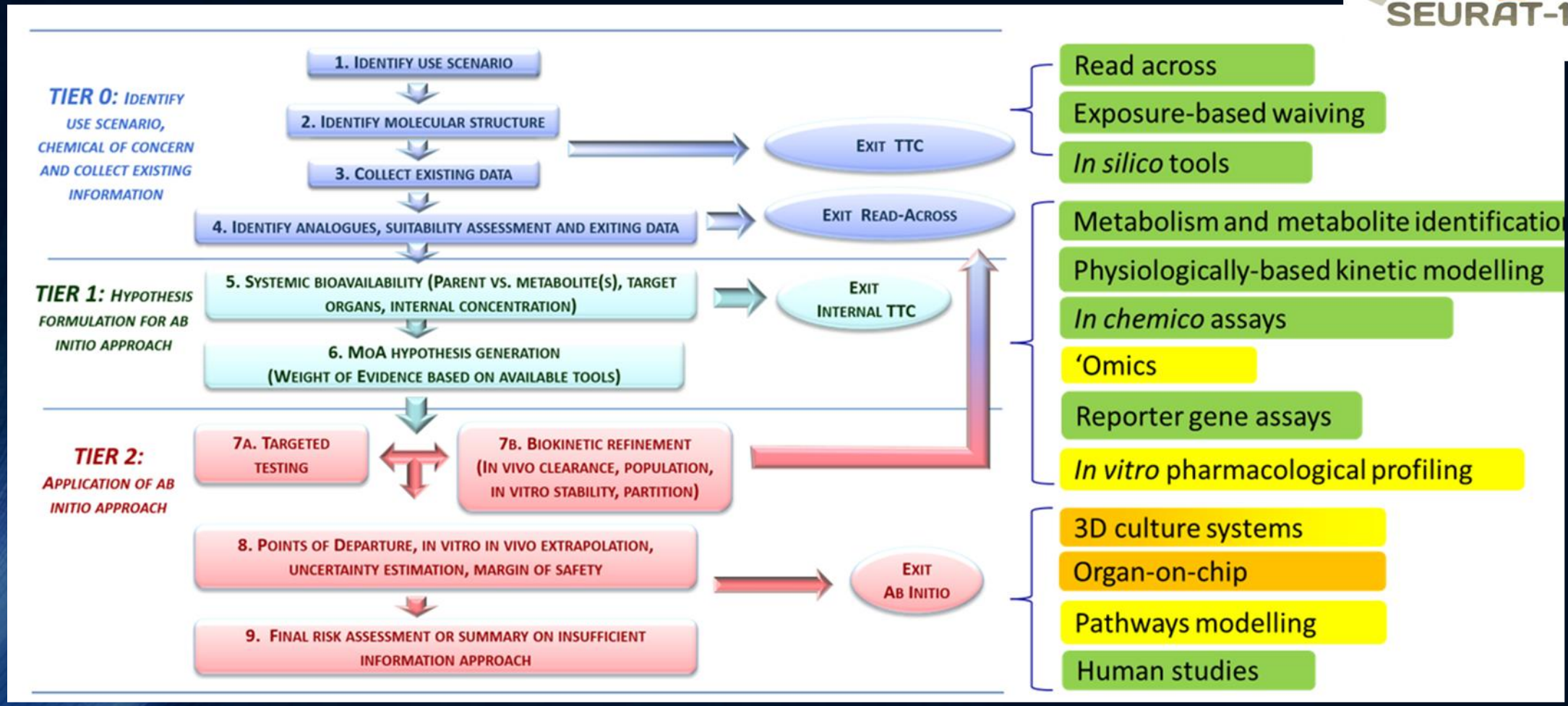
3 Principles describe how a NGRA should be conducted:

- 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 transparently documented

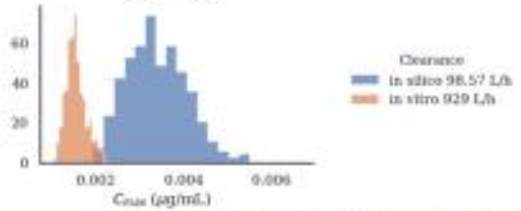
Tiered testing and human health assessment approach



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

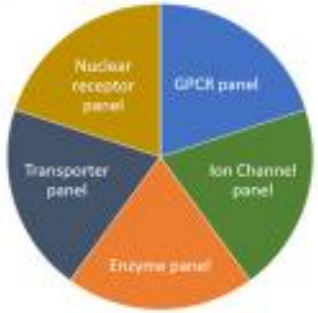
Our NGRA toolbox for systemic effects – key tools

PBK Modelling



Toxicology in Vitro (2020), 63, 104746

In vitro pharmacological profiling

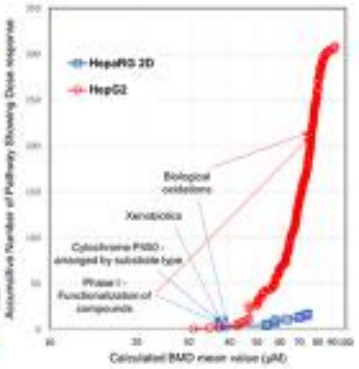


eurofins | Cerep

Transcriptomics

- Use of full human gene panel ~ 21k
- 24 hrs exposure
- 7 concentrations
- 3 cell lines HepG2/ HepaRG/ MCF7
- 3D HepaRG spheroid

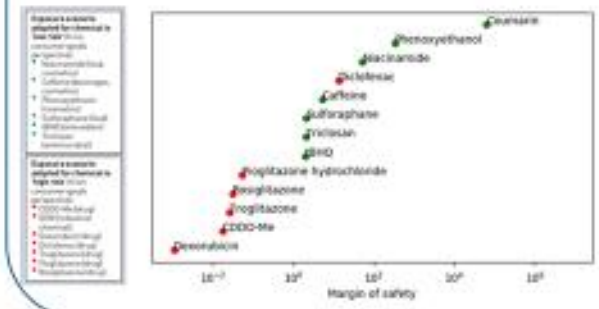
BMDexpress 2

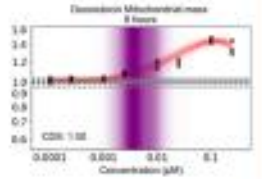


Cellular Stress Pathways

13 chemicals, 36 Biomarkers; 3 Timepoints; 8 Concentrations; ~10 Stress Pathways

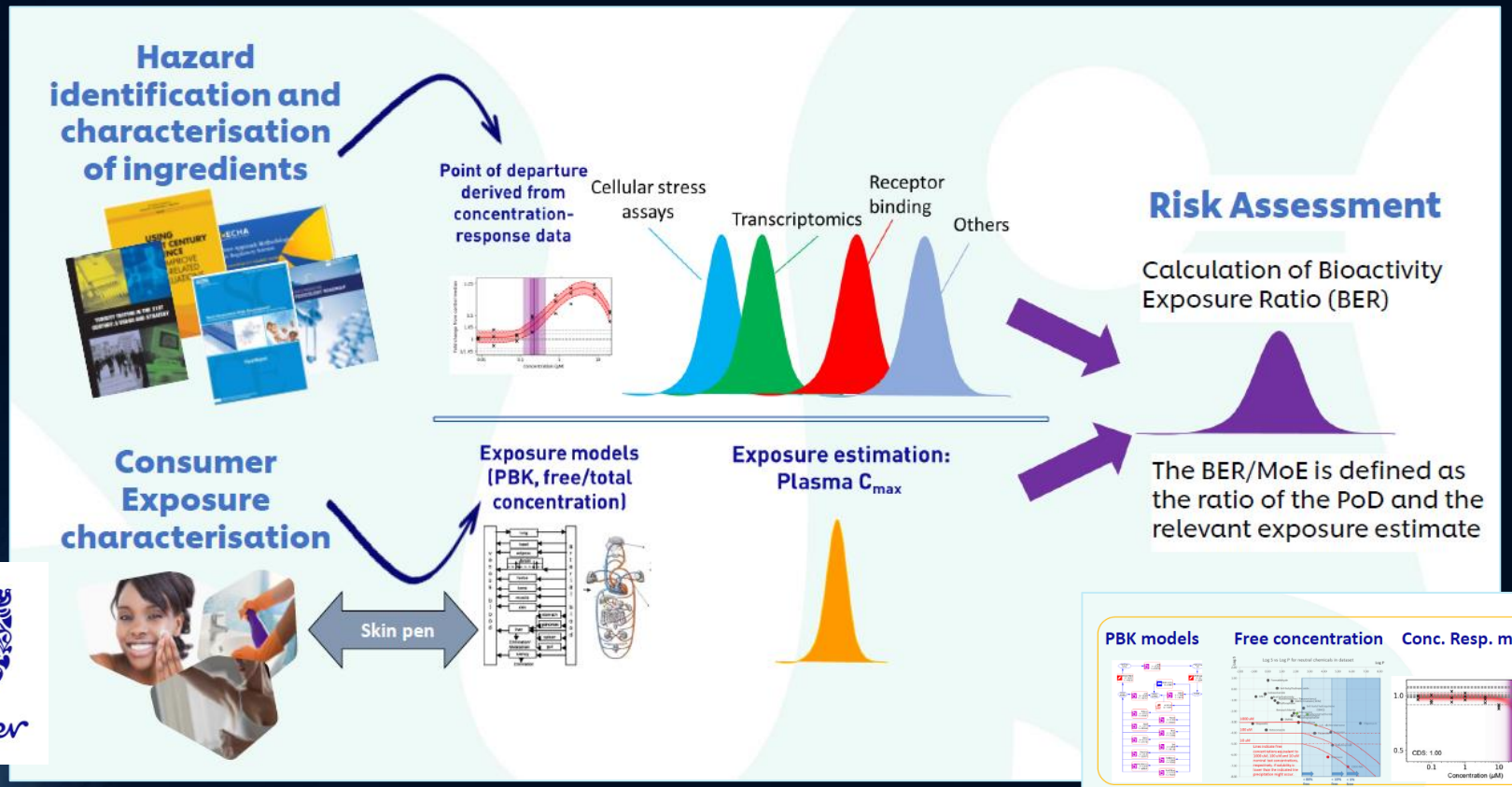
cyprotex

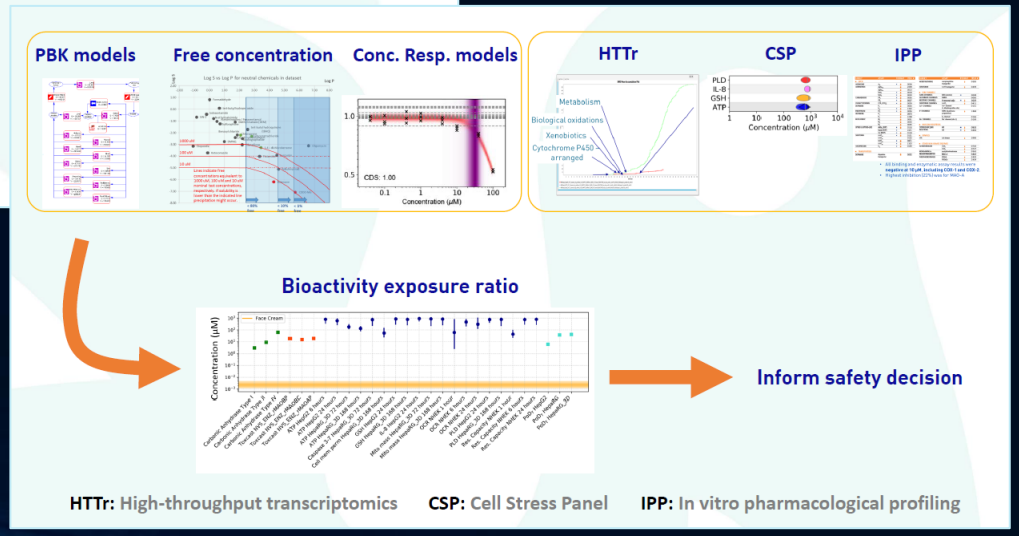




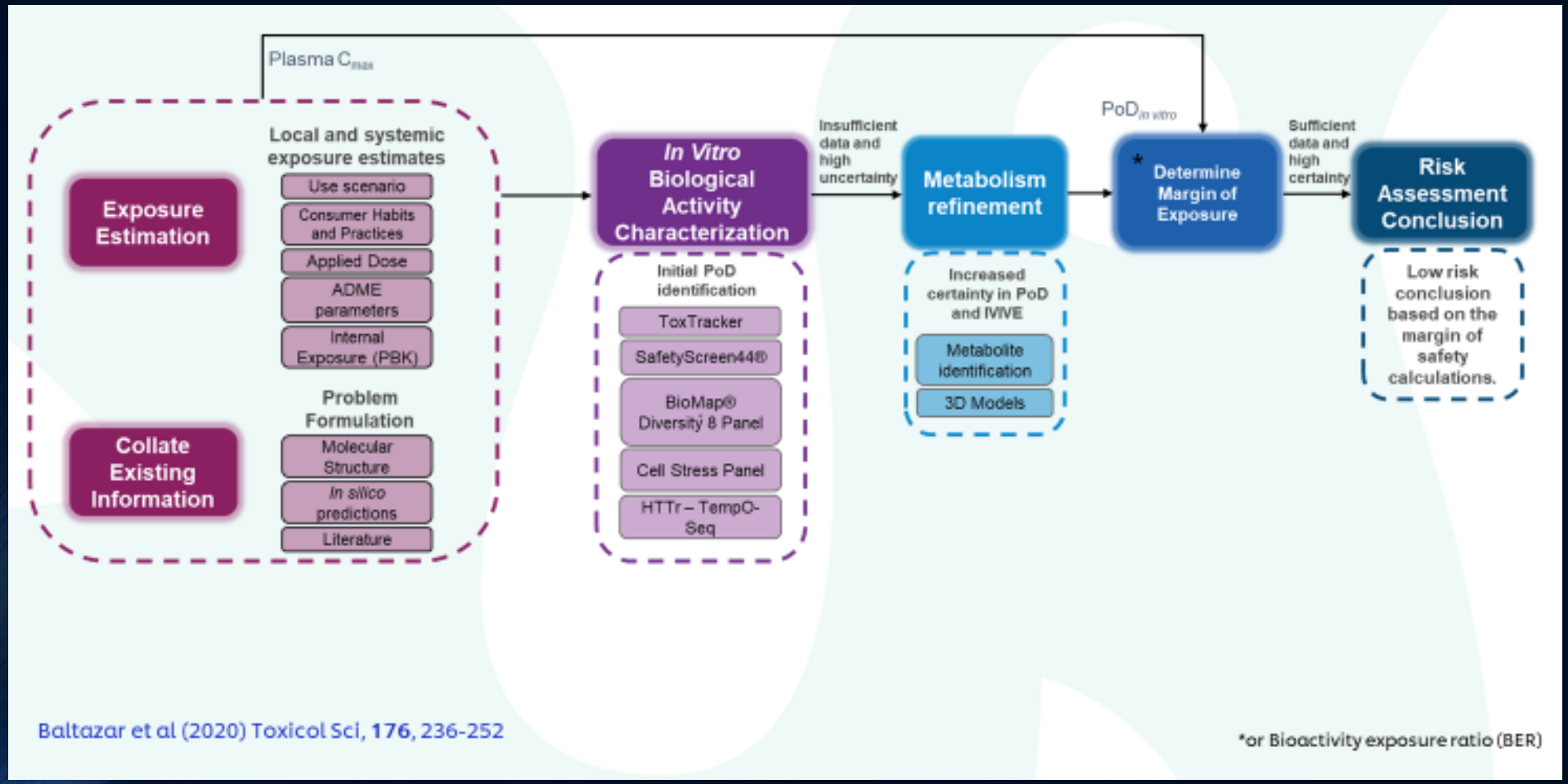
Toxicol Sci (2020), 176, 11-33

Integrating these approaches to make safety decisions

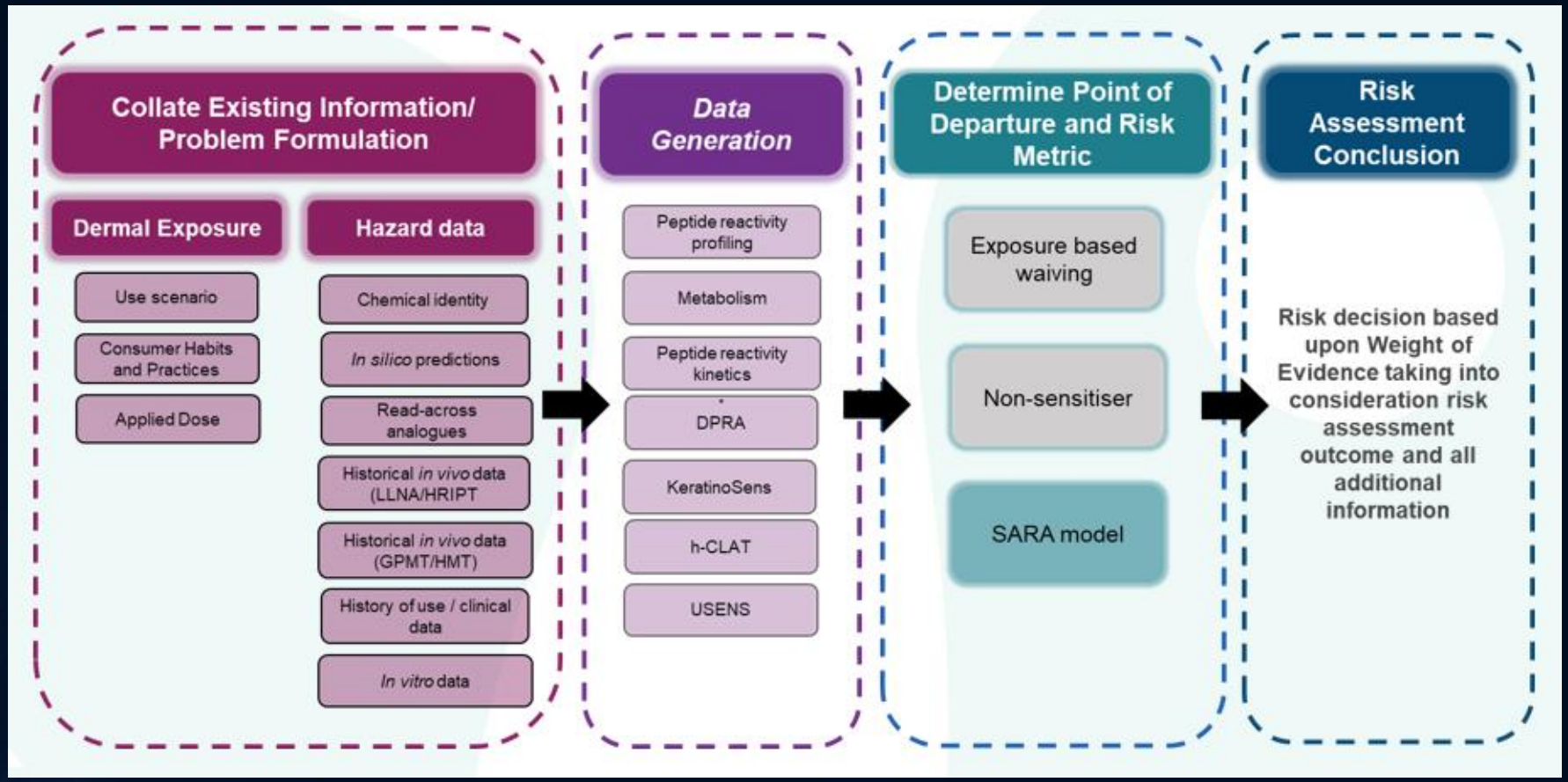




NGRA – case study workflow for systemic effects



NGRA – framework for skin allergy

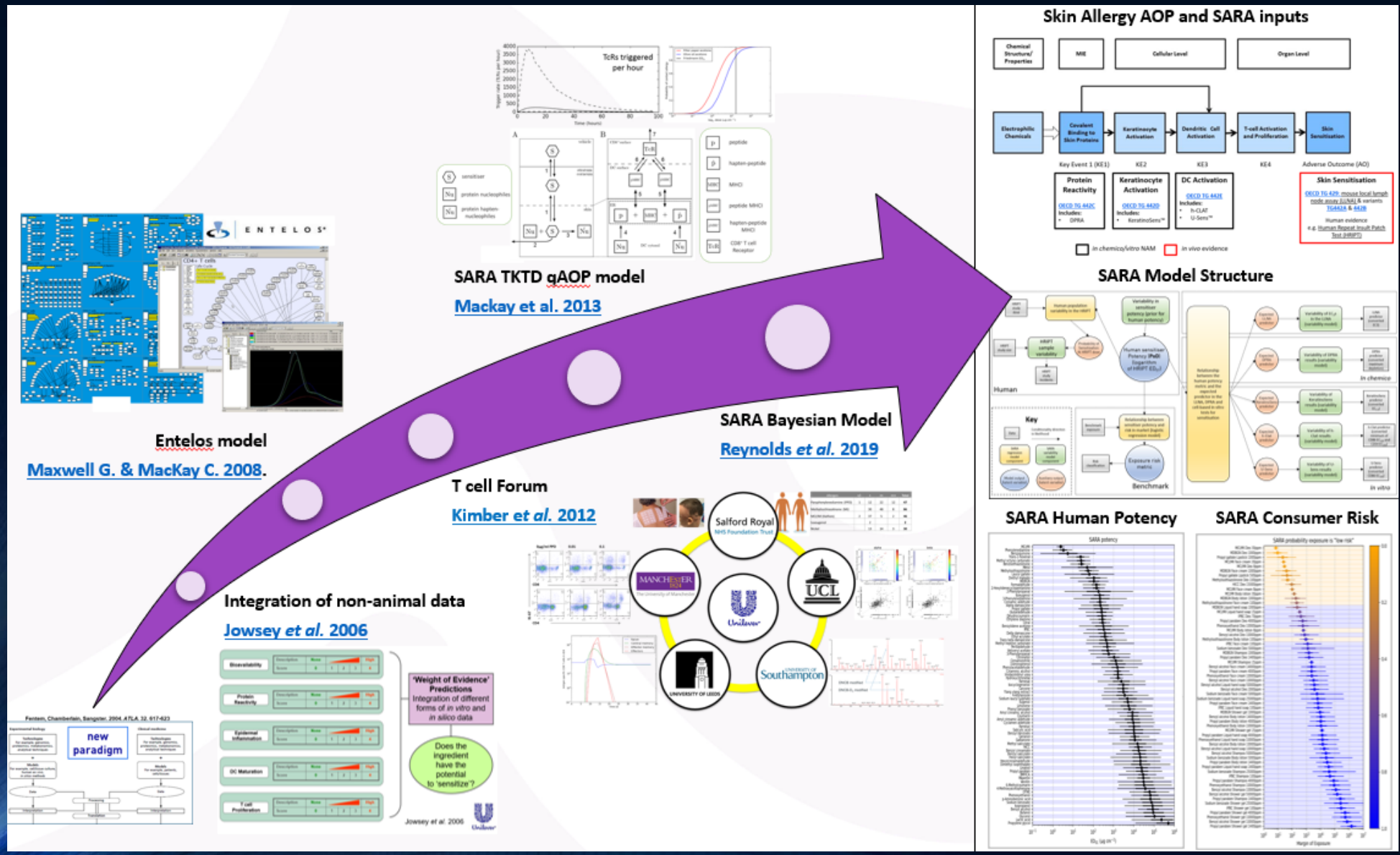


Unilever

Reynolds *et al* (2021) *Reg Tox Pharmacol*, **127**, December 2021, 105075

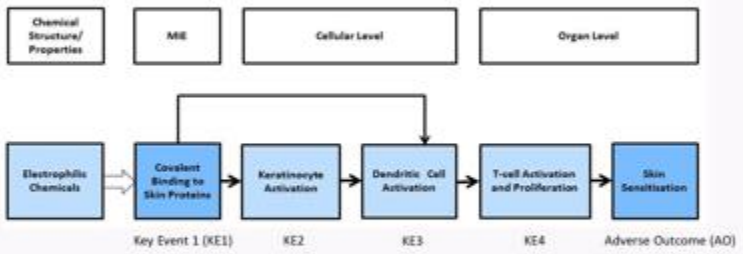
Gilmour *et al* (2022) Reg Tox Pharmacol **131**, June 2022, 105159

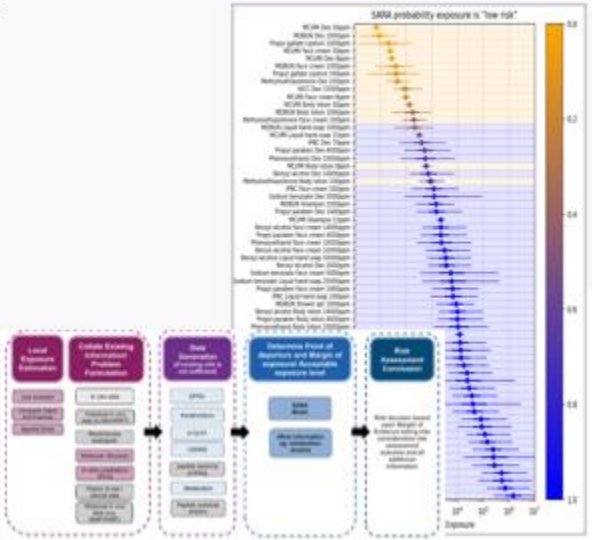
Transforming our approach for skin allergy risk assessment (SARA)



Non-animal strategy for skin allergy risk assessment (SARA)

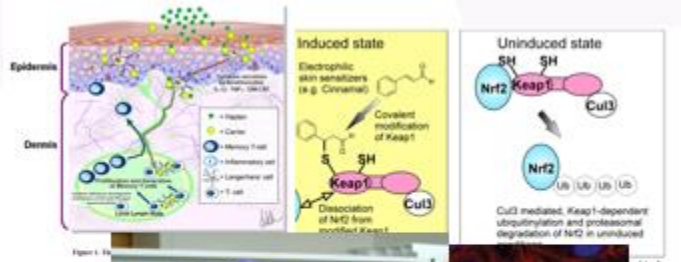
Determining the **biological pathway** behind the adverse skin allergy reaction ...

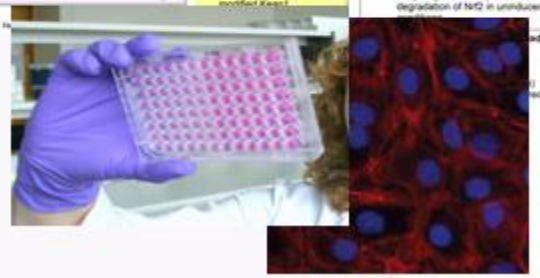




Unilever's **SARA Model** – developed as a computational approach to integrate information from the historical data and various cell-based experiments ...

SARA Model published and collaboration with US Gov. group (NICEATM) to adapt the model for **regulatory use**.





Developing **cell-based** experiments to measure activation of different parts of the biological pathway ...

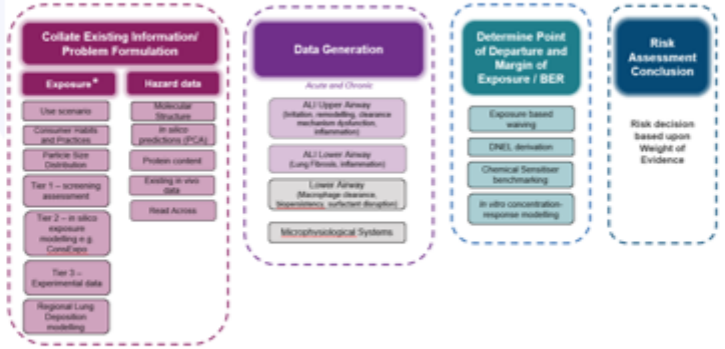
Developing a **risk assessment framework** ...

Unilever NGRA frameworks for using NAMs for consumer safety decisions

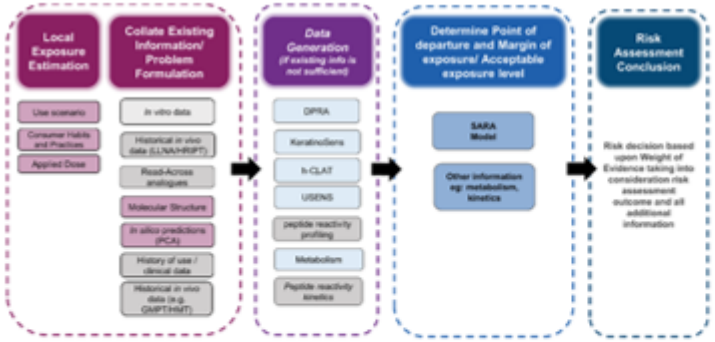
Developmental & Reproductive

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

Inhalation

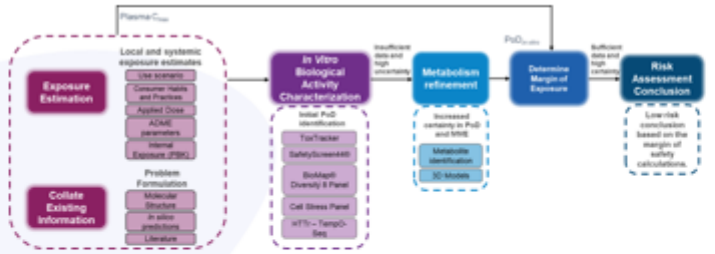


Skin Sensitisation



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

Systemic

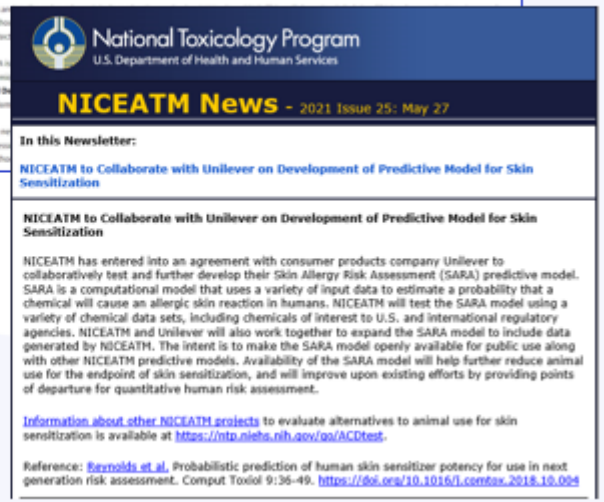


Baltazar et al (2020) *Toxicol Sci*, 176, 236-252

Ongoing Evaluations - Unilever working with government agencies

EPA

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



National Toxicology Program
U.S. Department of Health and Human Services

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 to evaluate alternatives to animal use for skin sensitization is available at https://ntp.niehs.nih.gov/go/ACDtest.

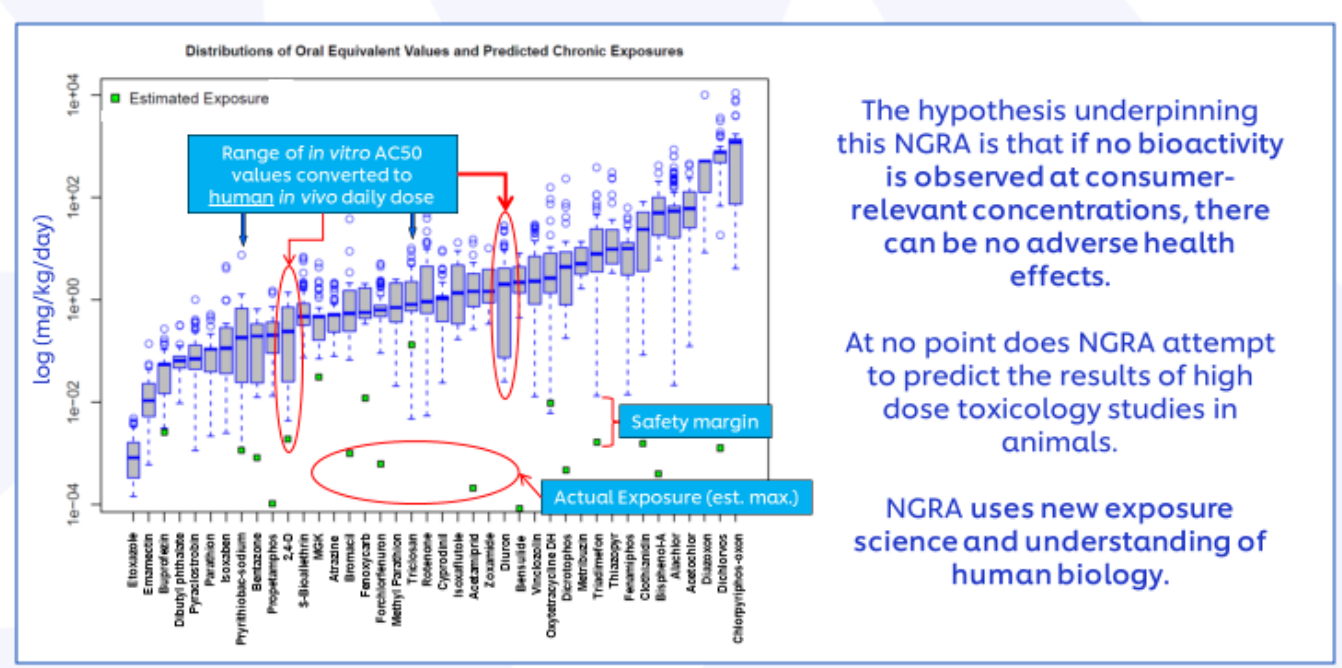
Reference: Reynolds et al. Probabilistic prediction of human skin sensitizer potency for use in next generation risk assessment. Comput Toxiol 9:36-49. https://doi.org/10.1016/j.comtox.2018.10.004

Aim of NGRA is **protection** of health, *not* prediction of animal data

Not a prescriptive set of tools, but **driven by the safety assessment**

Exposure tools to inform level of Systemic Exposure

Bioactivity tools to provide Points of Departure: ***Bioactivity - Exposure Ratio***



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

Hatherell *et al* (2020) Toxicological Sciences, **176,** 11-33

Moxon *et al* (2020) Toxicology in Vitro, **63** 104746

Li *et al* (2022) Toxicol. Appl. Pharmacol., **442** 115992

Unilever

Interpreting NAMs data for assessing chemical safety:
Bioactivity – Exposure Ratio (BER) approach

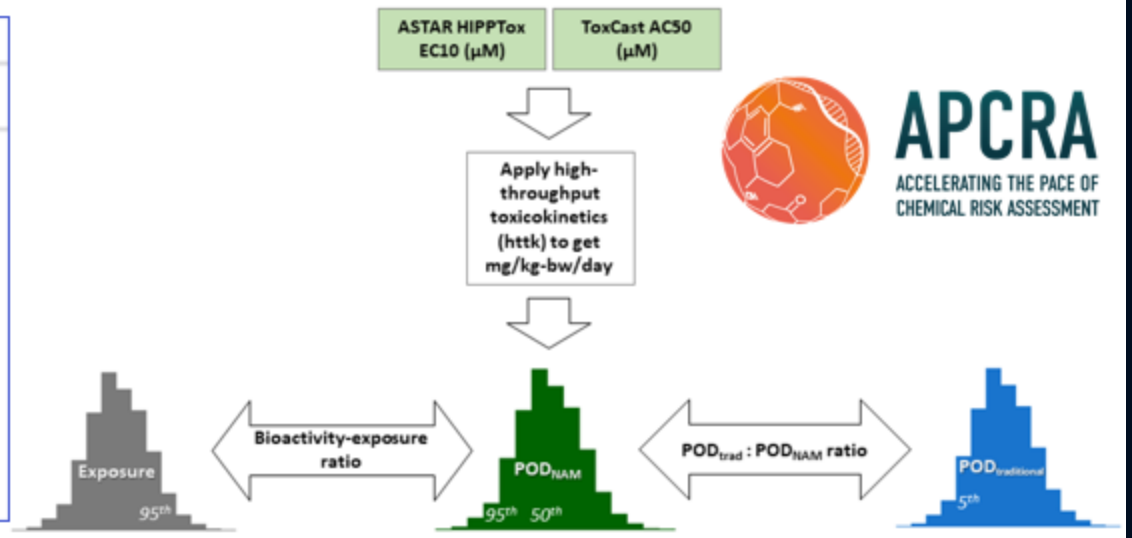
OXFORD SOT Society of Toxicology academic.oup.com/toxsci Tox Spotlight article

TOXICOLOGICAL SCIENCES, 173(1), 2020, 202–225

doi: 10.1093/toxsci/kfz201
Advance Access Publication Date: September 18, 2019
Research Article

Utility of *In Vitro* Bioactivity as a Lower Bound Estimate of *In Vivo* Adverse Effect Levels and in Risk-Based Prioritization

Katie Paul Friedman ,*,[1] Matthew Gagne,[†] Lit-Hsin Loo,[‡] Panagiotis Karamertzanis,[§] Tatiana Netzeva,[§] Tomasz Sobanski,[§] Jill A. Franzosa,[¶] Ann M. Richard,[*] Ryan R. Lougee,[*,||] Andrea Gissi,[§] Jia-Ying Joey Lee,[‡] Michelle Angrish,[|||] Jean Lou Dorne,[|||] Stiven Foster,[#] Kathleen Raffaele,[#] Tina Bahadori,[‖] Maureen R. Gwinn,[*] Jason Lambert,[*] Maurice Whelan,[**] Mike Rasenberg,[§] Tara Barton-Maclaren,[†] and Russell S. Thomas *



- Evaluation of *in vitro* NAMs, exposure modelling and dose-response models
- For 89% chemicals NAM PoD was **more conservative** than traditional PoD
- **Bioactivity - Exposure ratios (BERs) approach useful to accelerate screening and chemicals assessment using NAMs for hazard and exposure**

Evaluating our NAMs Toolbox for Systemic Safety Assessments

Toxicological Sciences SOT | Society of Toxicology

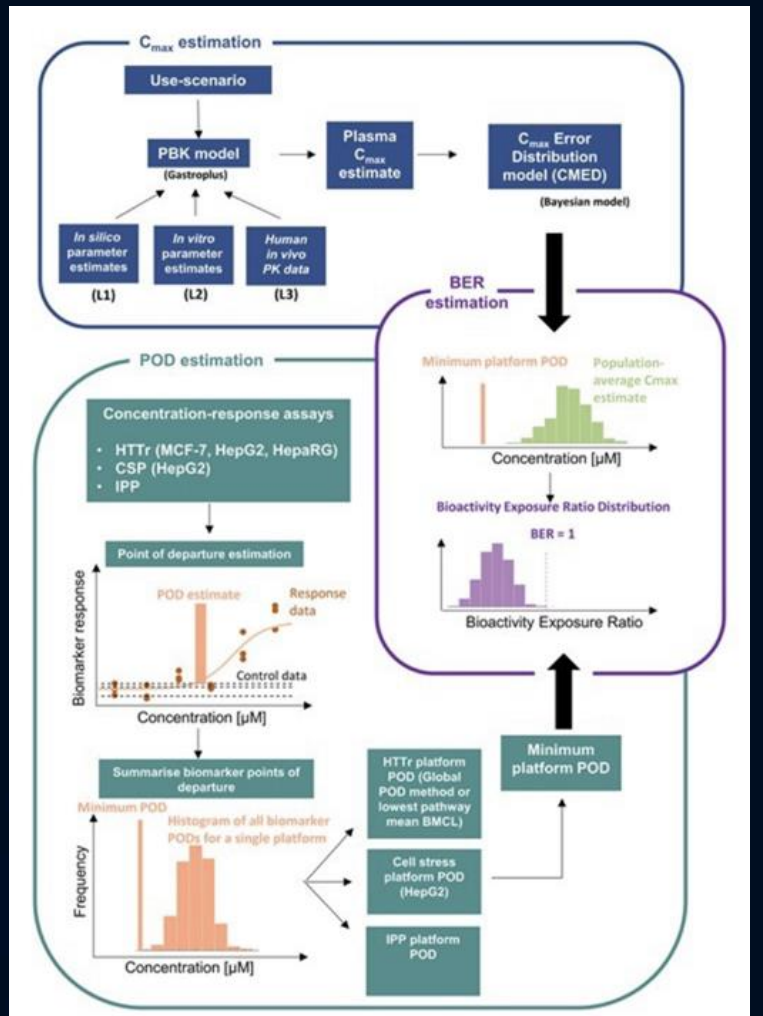
Article Navigation

JOURNAL ARTICLE FEATURED

Are Non-animal Systemic Safety Assessments Protective? A Toolbox and Workflow

Alistair M Middleton ✉, Joe Reynolds, Sophie Cable, Maria Teresa Baltazar, Hequn Li, Samantha Bevan, Paul L Carmichael, Matthew Philip Dent, Sarah Hatherell, Jade Houghton, Predrag Kukic, Mark Liddell, Sophie Malcomber, Beate Nicol, Benjamin Park, Hiral Patel, Sharon Scott, Chris Sparham, Paul Walker, Andrew White

Toxicological Sciences, Volume 189, Issue 1, September 2022, Pages 124–147,
https://doi.org/10.1093/toxsci/kfac068
Published: 13 July 2022



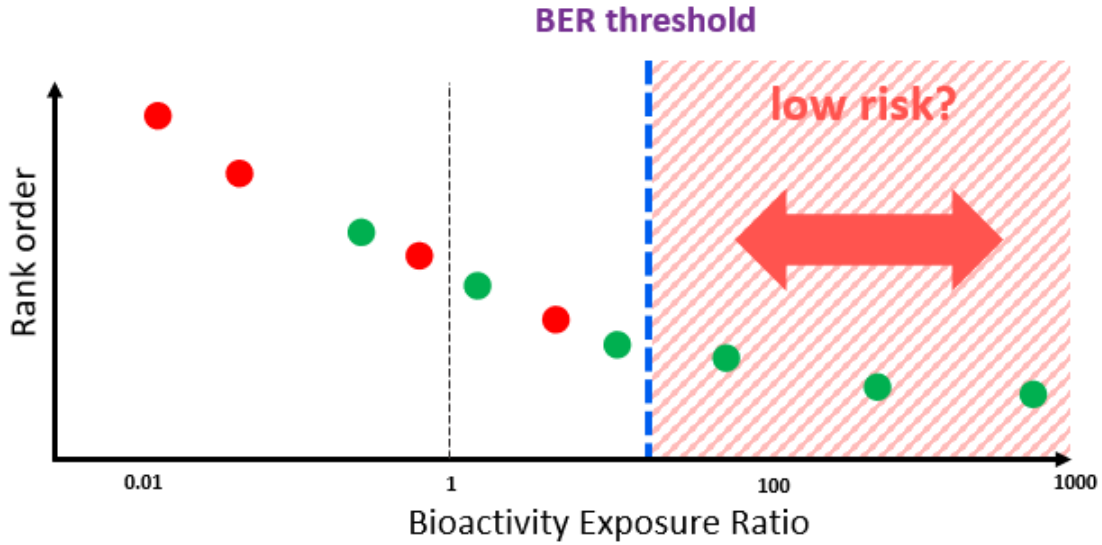
Are Non-animal Systemic Safety Assessments Protective? A Toolbox and Workflow - Abstract. A...

academic.oup.com • 2 min read

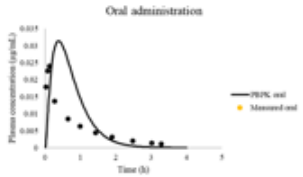
Benchmarking against historical safety decisions to evaluate how protective the toolbox & workflow are

Chemical exposures scenarios

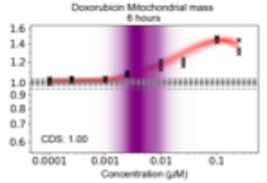
- 'Low' risk (from consumer goods perspective) – e.g. foods, cosmetics
- 'High' risk (from consumer goods perspective) – e.g. drugs



Define typical use-case scenarios & benchmark chemical-exposures; mix of high and low risk



PBK models of systemic exposure



in vitro assays, estimate PoDs

Calculate the Bioactivity-Exposure Ratio (BER)

Can we establish a BER threshold above which we consider a chemical exposure scenario to be low risk?

Unilever

Scientific partnership & publication underpin our approach

Details of SEAC's presentations & publications on www.tt21c.org

Unilever : U.S. EPA and Unilever Announce Major New Research Collaboration to Advance Non-Animal Approaches for Chemical Risk Assessment

09/08/2015 | 09:01am EDT

Research collaboration will develop ground-breaking scientific approaches to better assess the safety of chemicals found in some consumer products without using animal data

EPA United States Environmental Protection Agency

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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."

Adoption of NGRA / NAMs for assessing safety of cosmetic ingredients - promoting use of similar approaches for chemicals registration

ICCR International Cooperation on Cosmetics Regulation

International Cooperation on Cosmetics Regulation (2018)

Scientific Committee on Consumer Safety (2021)

Use of new approach methodologies (NAMs) to meet regulatory requirements for the assessment of industrial chemicals and pesticides for effects on human health

Advances in our non-animal safety science capability enabled a change in Unilever's animal testing policy in July 2018

Unilever's approach: science-based safety, claims & advocacy - working with others to end animal testing of consumer products

1 Use Science, Not Animals

We use science, not animals – our industry leading capability in animal-free safety science means we do not need to use animal testing to ensure safety.

2 Independent Brand Certification

Building consumer confidence through NGO accreditation and consumer-facing no animal testing claims.
Starting with Dove in 2018, we have 31 NGO-certified cruelty free brands.

3 Partnerships

Our partnerships – with global animal protection NGOs, leading research teams, other companies and government scientists – support wider acceptance and use of alternatives to animal testing.

4 Advocate for Regulatory Change

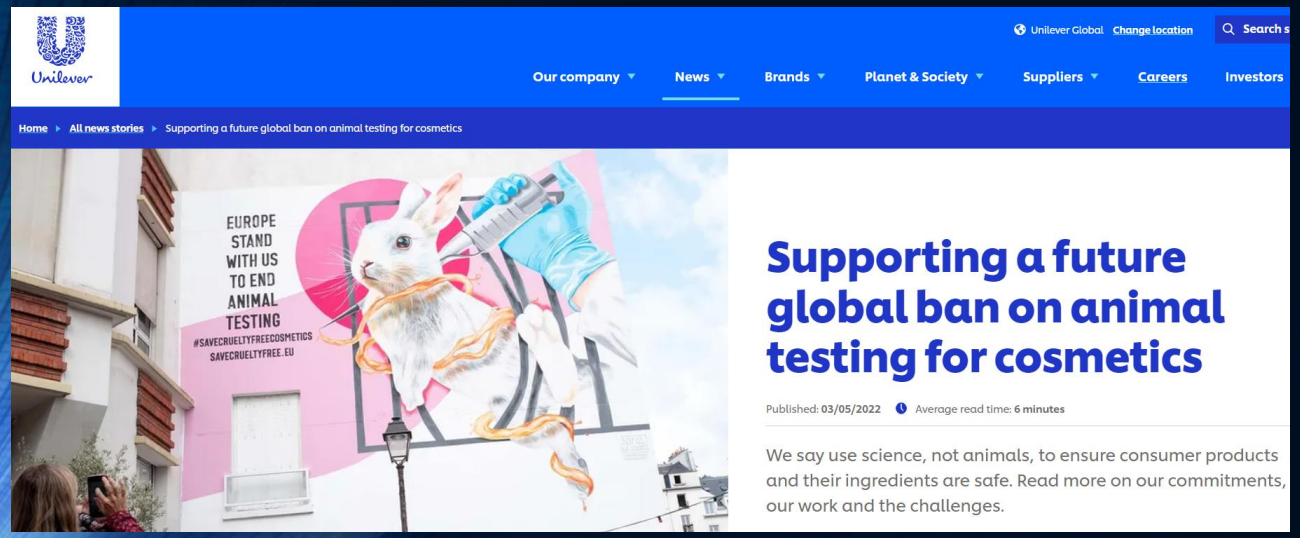
We work to end the animal testing of consumer products worldwide.

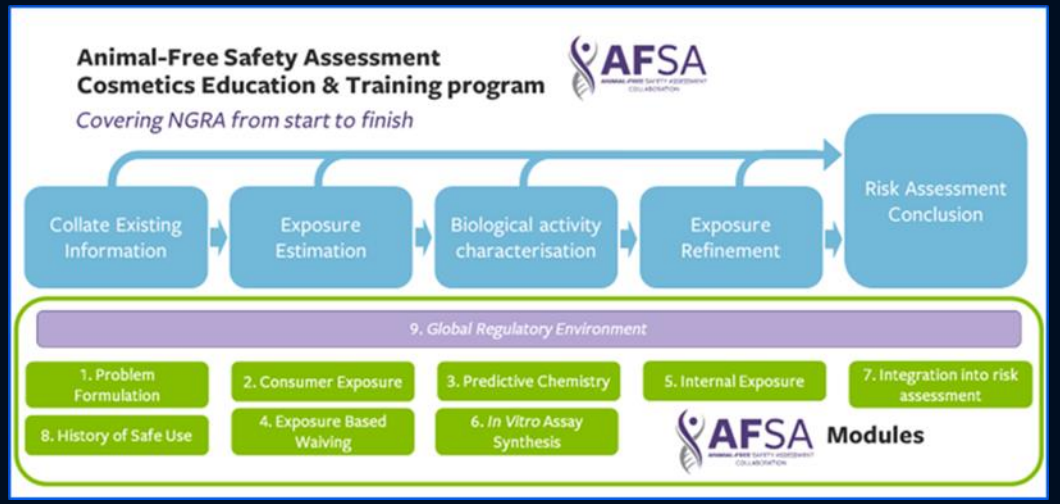
We are recognised by PETA as a company working for regulatory change.

Working towards a global ban on animal testing for cosmetics

Unilever supports calls for a worldwide animal testing ban on cosmetics

Published: **09/10/2018** Average read time: **3 minutes**





In **October 2018** Unilever was the first major international company to announce its support for a global ban on the animal testing of cosmetics. But the new proposals from ECHA appear to contradict it. In August 2020, ECHA said that certain substances must be tested on animals even if they are solely for use in cosmetics.

No animal testing, Unilever brands and the EU's chemicals regulati...
www.unilever.com/news/news-search/2020/no-animal-testing-unilever-brands-a...

EU & UK animal testing bans for cosmetics are being destroyed

New EU rule says cosmetics MUST be tested on animals despite the chemicals being used in hundreds of 'cruelty free' products supported by ambassadors such as Leona Lewis

- Eurocrats said chemicals in 'cruelty-free' cosmetics must be tested on animals
- Protesters say it destroys the EU-wide ban on animal experiments for cosmetics
- The two chemicals are used by High Street brands Dove, Body Shop and L'Oreal

By JON UNGOED-THOMAS FOR THE MAIL ON SUNDAY
PUBLISHED: 00:50, 30 August 2020 | **UPDATED:** 01:40, 30 August 2020

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The ban became EU-wide in 2013 but the European Chemicals Agency, a branch of the EU, now claims that separate regulations on the use of chemicals means substances still must be tested, even if exclusively for cosmetic use, to assess any risks to workers on the production line.

The two chemicals involved in this case are the ultra-violet filters homosalate and 2-ethylhexyl salicylate, also known as octisalate. Both have already been approved by EU safety watchdogs for use in cosmetics and are widely used in hundreds of popular cosmetic products.

Consumer giant Unilever last night condemned the European Chemicals Agency's decision and warned it may now be forced to reformulate some of its cosmetic products.

Its safety chief Julia Fentem said: 'We don't agree that animal testing is necessary to protect workers and the environment, and strongly encourage the use of non-animal data.

UK could allow animal tests for cosmetic ingredients for first time since 1998

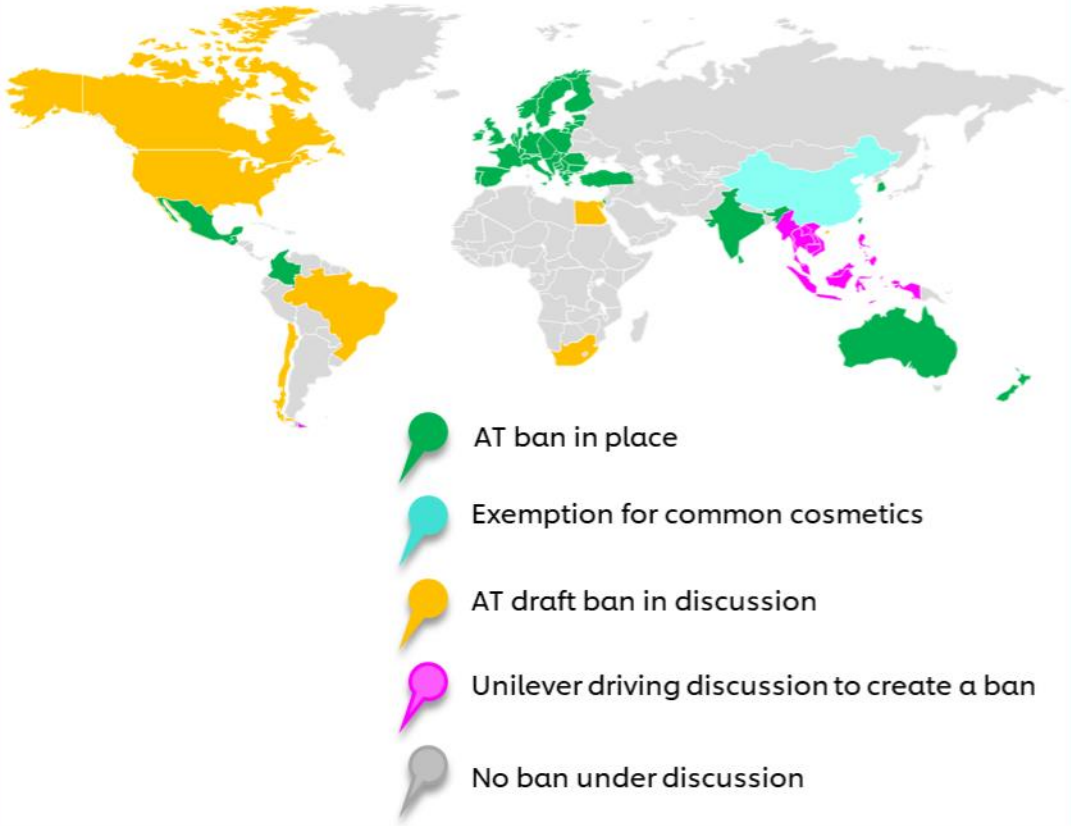
Exclusive: campaigners say aligning with EU ruling on chemical testing will 'blow a hole' in UK leadership on cruelty-free cosmetics

The UK banned animal testing of cosmetic ingredients in 1998. Photograph: Steven Senne/AP

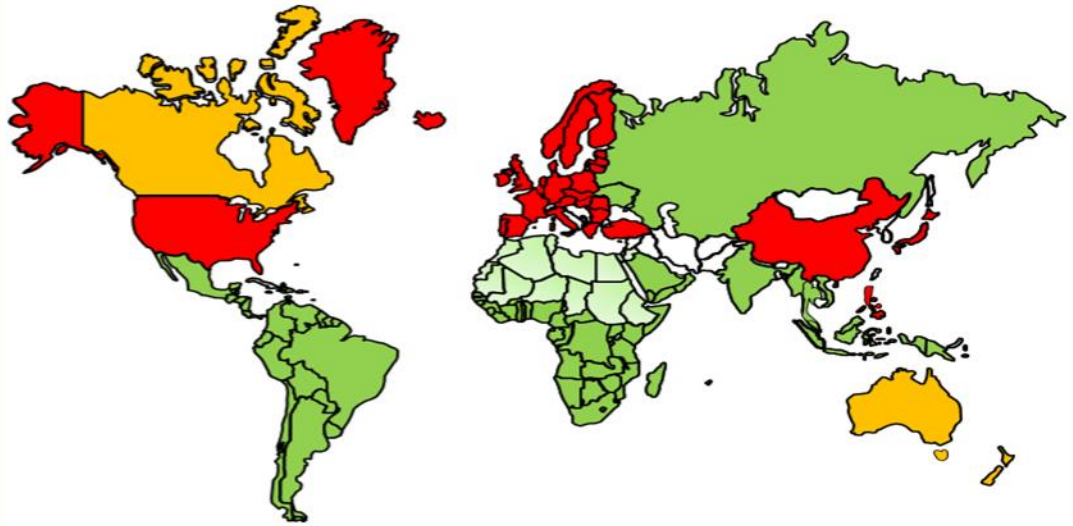
Ministers have opened the door to expanding the use of animal testing for ingredients used in cosmetic products for the first time in 23 years, an animal welfare charity has said.

Some regulations ban animal tests, others require them

COSMETICS
Animal testing bans since 1998



CHEMICALS



US, EU, China, Japan, Philippines & UK typically require AT

Canada & Australia registrations may require AT

No current requirements for AT

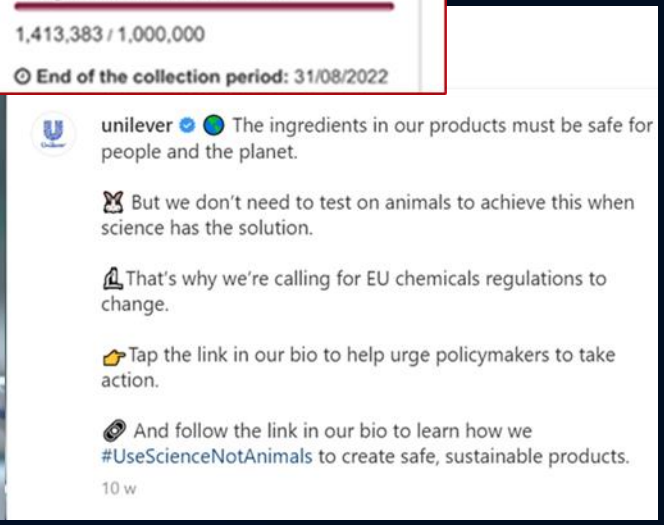
Advocating for regulatory use of innovative animal-free safety science

Unilever: EU needs 'paradigm shift' in chemical safety assessment methods

By Kacey Culliney
23-Sep-2021 - Last updated on 23-Sep-2021 at 14:59 GMT

RELATED TAGS: Animal testing, Animal testing alternatives, non-animal testing methods, REACH, Chemicals, Regulation, next-generation safety assessments, Unilever, safety assessment

A complete shift in the safety assessment of chemicals will be necessary if the EU is to uphold its 'animal testing as a last resort' policy under the European Chemicals Agency's REACH regulation – a critical aspect to maintaining the wider cosmetics animal testing ban, say Unilever execs.



Taking on the "close the gap" challenge: regulatory use

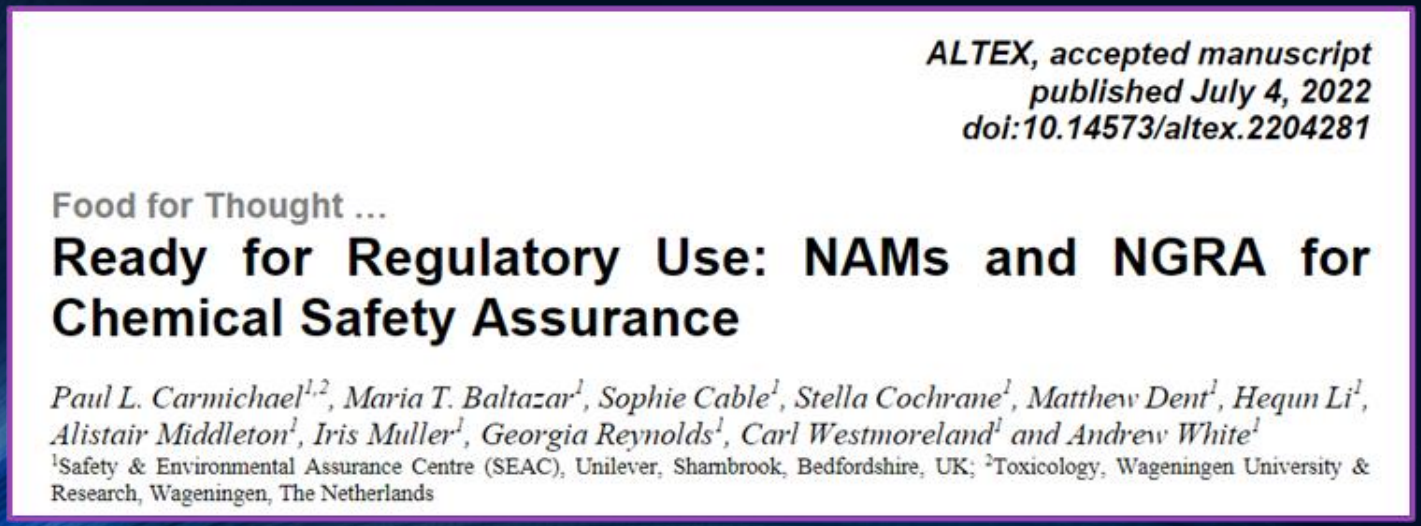
Comment

Upholding the EU's Commitment to 'Animal Testing as a Last Resort' Under REACH Requires a Paradigm Shift in How We Assess Chemical Safety to Close the Gap Between Regulatory Testing and Modern Safety Science

Alternatives to Laboratory Animals
2021, Vol. 49(4) 122–132

DOI: 10.1177/02611929211040824
journals.sagepub.com/home/atd
SAGE

Julia Fentem, Ian Malcomber, Gavin Maxwell and Carl Westmoreland



ALTEX, accepted manuscript published July 4, 2022
doi:10.14573/altex.2204281

Food for Thought …

Ready for Regulatory Use: NAMs and NGRA for Chemical Safety Assurance

Paul L. Carmichael[1,2], Maria T. Baltazar[1], Sophie Cable[1], Stella Cochrane[1], Matthew Dent[1], Hequn Li[1], Alistair Middleton[1], Iris Muller[1], Georgia Reynolds[1], Carl Westmoreland[1] and Andrew White[1]
[1]Safety & Environmental Assurance Centre (SEAC), Unilever, Shambrook, Bedfordshire, UK; [2]Toxicology, Wageningen University & Research, Wageningen, The Netherlands

Time to re-think our approach …

1. Conducting an animal test because it's a (perceived) regulatory requirement isn't adequate scientific justification

2. Current laws and regulations, not science, are impeding the paradigm shift to using modern animal-free safety science

3. Change regulatory approach to chemical safety to strengthen the protection of people (workers & consumers) and our environment, without that being anchored in predicting the apical toxicity effects seen in high-dose animal studies

Aligning materials suppliers with Unilever policy & partnering on advocating for changes in chemicals regulations

SUPPLIER WEBINARS - 2022

6 September
Partnering for a future with no animal testing

26 September
Animal testing as a last resort under REACH

18 October
NAT in REACH and consortia approaches

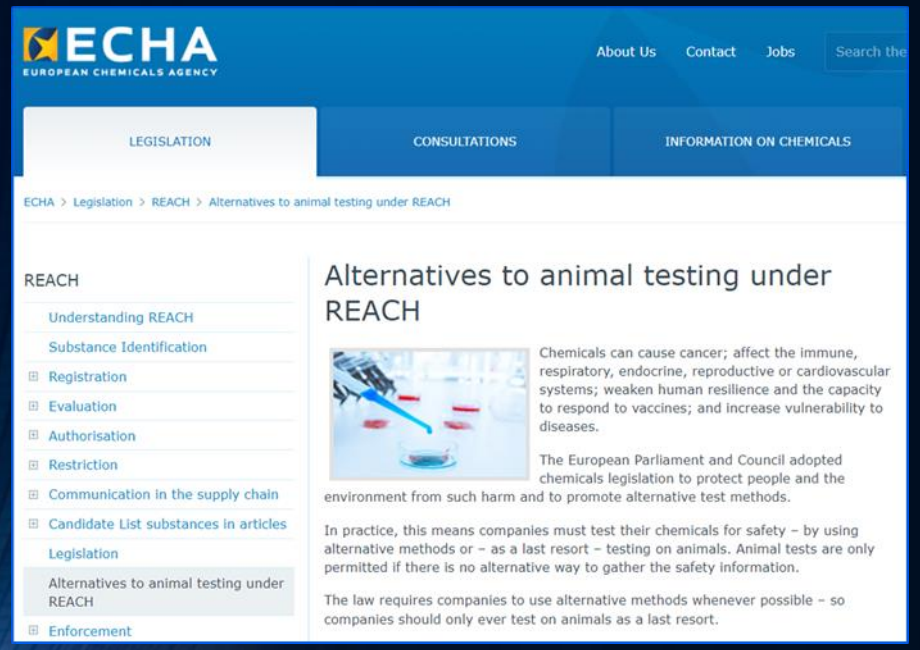
3 November
Next Generation approaches and REACH

6 December
Innovating for Biodegradability

2

CHEMICALS REGULATIONS

Principles of EU regulatory approach – protection from harm & use of non-animal tests



EU REACH legislation has been in place for 15 years. It was introduced to protect people & the environment from harm and to promote alternative test methods.

Science & technology have advanced hugely since June 2007. Chemicals regulations need to catch up ⟶ framework for using most relevant scientific data for safety decisions.

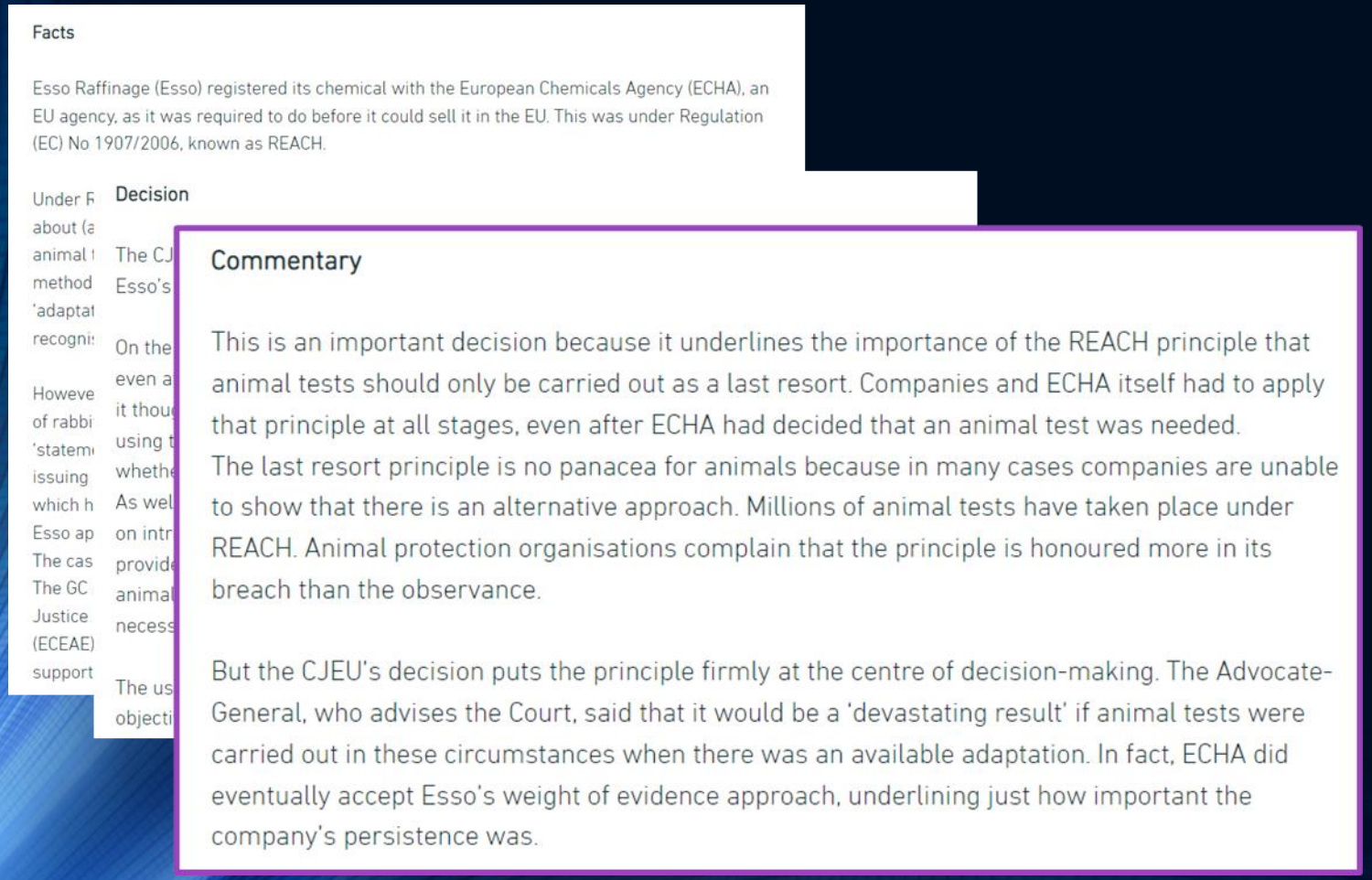
Regulations are based on animal testing for characterising chemical hazards

REACH, Article 25: '*In order to avoid animal testing, testing on vertebrate animals for the purposes of this regulation shall be undertaken only as a last resort*'

Upholding "animal testing as a last resort" is challenging

European Court of Justice C-471/18 P - 21 January 2021

Federal Republic of Germany v Esso Raffinage and Others (advocates-for-animals.com)



Facts

Esso Raffinage (Esso) registered its chemical with the European Chemicals Agency (ECHA), an EU agency, as it was required to do before it could sell it in the EU. This was under Regulation (EC) No 1907/2006, known as REACH.

Decision

Commentary

This is an important decision because it underlines the importance of the REACH principle that animal tests should only be carried out as a last resort. Companies and ECHA itself had to apply that principle at all stages, even after ECHA had decided that an animal test was needed.
The last resort principle is no panacea for animals because in many cases companies are unable to show that there is an alternative approach. Millions of animal tests have taken place under REACH. Animal protection organisations complain that the principle is honoured more in its breach than the observance.

But the CJEU's decision puts the principle firmly at the centre of decision-making. The Advocate-General, who advises the Court, said that it would be a 'devastating result' if animal tests were carried out in these circumstances when there was an available adaptation. In fact, ECHA did eventually accept Esso's weight of evidence approach, underlining just how important the company's persistence was.

European Court of Justice - 11 September 2015

Decision in case 1606/2013/AN on how the European Chemicals Agency applies rules concerning animal testing

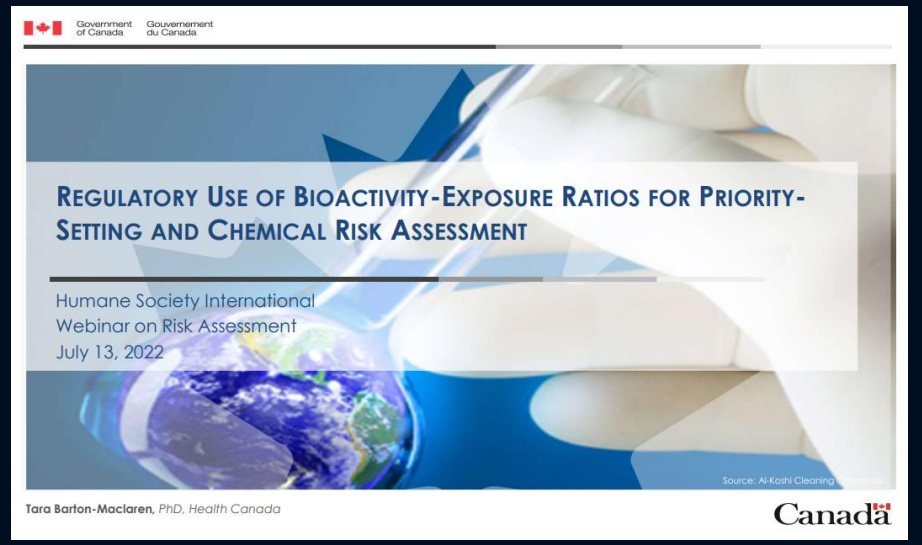
Decision
Case 1606/2013/AN - **Opened on** 20/11/2013 - **Decision on** 11/09/2015 - **Institution concerned** European Chemicals Agency (Friendly solution) |

The Ombudsman's inquiry concluded that ECHA's interpretation of its role was too strict and did not take into account the fact that the avoidance of animal testing was, together with the protection of human health and the environment, one of the guiding principles of the Regulation. The Ombudsman thus proposed to ECHA (i) that it require all registrants to show that they have tried to avoid animal testing and (ii) that it provide registrants with all the information at its disposal which could allow them to avoid animal testing.

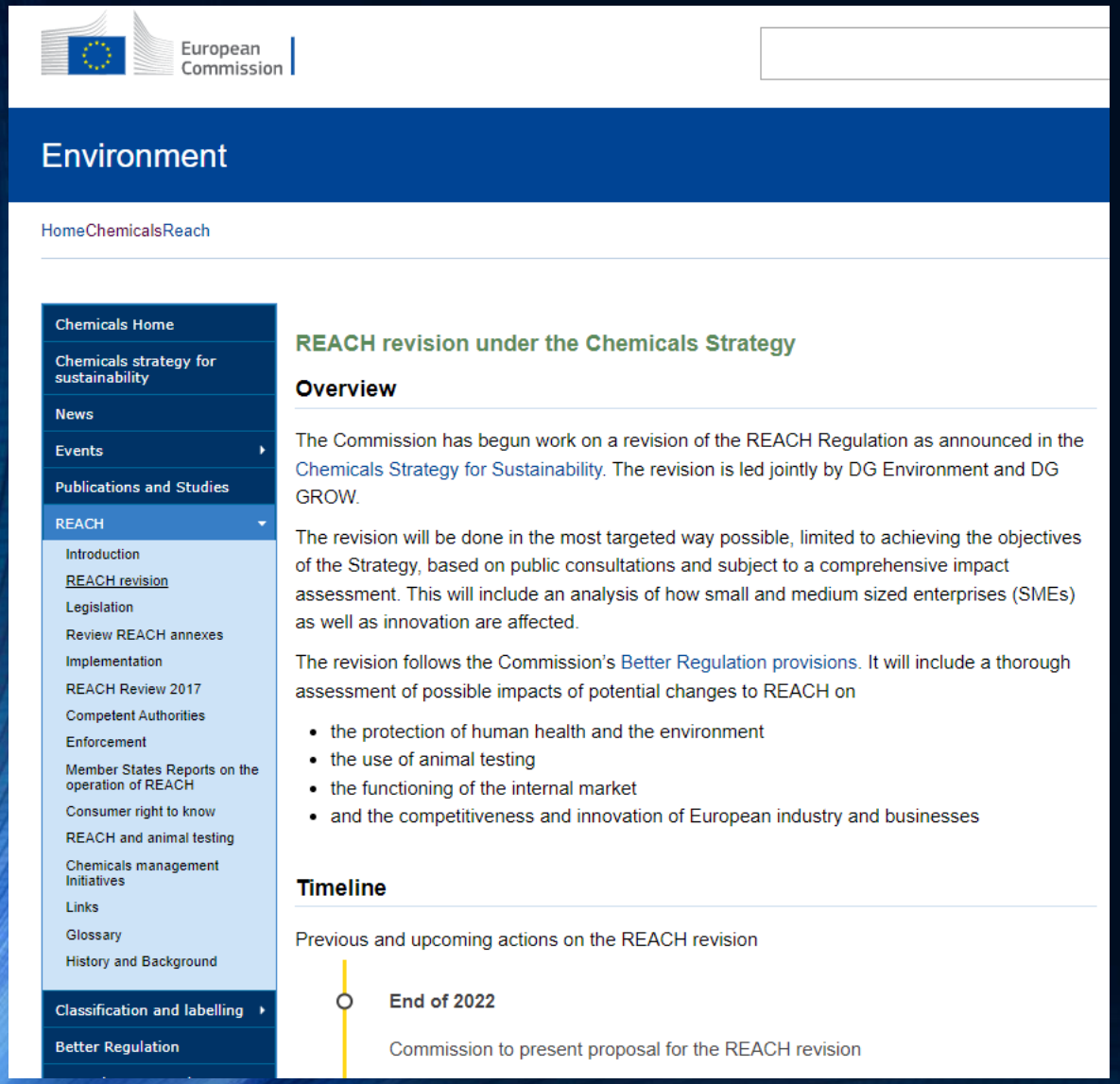
Decisions on Chemical Safety – Next Generation Risk Assessment (NGRA) integrating data from New Approach Methodologies (NAMs)

Data are needed for decisions on:

1. safety of **consumers** exposed to chemicals in **products**
2. safety of **workers** exposed to chemicals during product **manufacture**
3. safety of **people & non-human species** if exposed to chemicals in the **environment**



REACH is being revised under the EU Chemicals Strategy



European Commission

Environment

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- Better Regulation

REACH revision under the Chemicals Strategy

Overview

The Commission has begun work on a revision of the REACH Regulation as announced in the Chemicals Strategy for Sustainability. The revision is led jointly by DG Environment and DG GROW.

The revision will be done in the most targeted way possible, limited to achieving the objectives of the Strategy, based on public consultations and subject to a comprehensive impact assessment. This will include an analysis of how small and medium sized enterprises (SMEs) as well as innovation are affected.

The revision follows the Commission's Better Regulation provisions. It will include a thorough assessment of possible impacts of potential changes to REACH on

- the protection of human health and the environment
- the use of animal testing
- the functioning of the internal market
- and the competitiveness and innovation of European industry and businesses

Timeline

Previous and upcoming actions on the REACH revision

End of 2022

Commission to present proposal for the REACH revision

Unilever's perspective on the REACH revision

In line with the vision presented in the Chemical Strategy for Sustainability (CSS), we believe we need a paradigm shift to strengthen chemical safety using best available science and technology that rebuilds trust in chemical safety. To this end, the revision of REACH (Regulation (EC) No 1907/2006) will be a key opportunity, and we would like the following elements to be fully considered as part of the impact assessment.

Accelerating use of New Approach Methods (NAMs) and ensuring animal tests are a last resort

Scientific and technological advances mean we can generate much more relevant data on the safety of chemicals using New Approach Methodologies (NAMs) than animal tests. **We see the REACH review as a unique opportunity to break free of the belief that animal models are the best experimental tools available to protect European citizens and the environment and start the paradigm shift towards widespread use of NAMs for chemical regulatory testing**.

UK REACH is work in progress – good discussions on NAMs

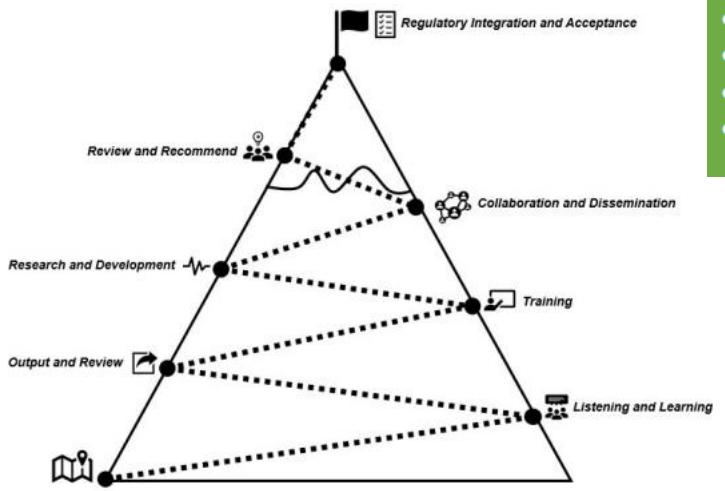
The REACH etc. (Amendment) Regulations 2021

Regulation (EC) No 1907/2006 of the European Parliament and of the Council of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals ("the EU REACH Regulation") forms part of retained EU law by virtue of the European Union (Withdrawal) Act 2018. The retained version of the EU REACH Regulation is referred to as the UK REACH Regulation.

From: Department for Environment, Food & Rural Affairs
Published 29 June 2021
Last updated 27 July 2021 — See all updates

Paving the way for a UK Roadmap:

Development, Validation and Regulatory Acceptance of New Approach Methodologies (NAMs) in Chemical Risk Assessment



2021

Food Standards Agency

Overall objectives of the roadmap are to:

- identify latest available NAMs for optimal risk assessment
- learn from other regulatory agencies and beyond
- validate through case studies
- build confidence in NAMs in the regulatory setting
- develop skills and training
- implement and integrate NAMs in the regulatory setting

Non-animal safety science can support sustainable chemical innovation → **evolve chemical safety assessment frameworks to embrace use of NAMs / embed NGRA concepts**

ECHA is responding to calls for more regulatory use of non-animal safety science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Czech EU presidency seeks way out of deadlock on European digital identity powered by EURACTIV Czechia

Home / Opinions / Health / Accelerating uptake of non-animal safety science into European chemical legislation

Accelerating uptake of non-animal safety science into European chemical legislation

DISCLAIMER: All o

By Sirpa Pietikäinen | EPAA Oct 3, 2022


C&EN CHEMICAL & ENGINEERING NEWS

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TOXICOLOGY

Can Europe replace animal testing of chemicals?

As revisions to the EU's regulatory system look certain to increase toxicity tests on animals, the region ponders whether it will ever be able to conduct chemical safety assessments with alternative methods

by *Vanessa Zainzinger, special to C&EN*

August 15, 2022 | A version of this story appeared in Volume 100, Issue 28


A 10-POINT PLAN FOR TARGETED AND EFFECTIVE REVISION OF REACH

cefic

REACH is the cornerstone of the EU chemicals legislation. Revising REACH means changing the very foundation of the world-leading chemicals management system that we have in Europe. This 10-point action plan outlines how this can be done in a targeted and efficient way so that it effectively tackles areas where improvement is needed in line with the objectives set in the Chemicals Strategy for Sustainability.

Action 1

Introduce a new safety assessment scheme where reliable and human-relevant non-animal safety assessment methods have a prominent place (New Assessment Methods).

Why? Accuracy and reliability of non-animal methods have improved considerably over the past decade.

Result:
- Legislation reflects the latest advancements in the field of toxicology.
- Unnecessary animal testing is avoided.


Regulatory Toxicology and Pharmacology 136 (2022) 105278

Contents lists available at ScienceDirect

Regulatory Toxicology and Pharmacology

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

ELSEVIER

REACHing for solutions: Essential revisions to the EU chemicals regulation to modernise safety assessment

Marina Pereira, Donna S. Macmillan *, Catherine Willett, Troy Seidle

Humane Society International/Europe, Research & Toxicology, Av. des Arts 50, 1000, Brussels, Belgium

UK is a scientific powerhouse in innovative animal-free safety approaches

- embed animal-free safety science & innovation in *UK Chemicals Strategy* (DEFRA)
  - ensure active participation of UK thought leaders across academia, companies & NGOs
  - invest in knowledge transfer, capability & capacity building
  - clear focal point in government (current complex split of responsibilities)

➢ shape a progressive new framework for UK chemicals regulations that ensures "AT as a last resort" is upheld by all stakeholders whilst improving safety

Building confidence with the regulatory community is key

Archives of Toxicology (2022) 96:2865–2879
https://doi.org/10.1007/s00204-022-03365-4

REVIEW ARTICLE

A framework for establishing scientific confidence in new approach methodologies

Anna J. van der Zalm[1] · João Barroso[2] · Patience Browne[3] · Warren Casey[4] · John Gordon[5] · Tala R. Henry[6] · Nicole C. Kleinstreuer[7] · Anna B. Lowit[6] · Monique Perron[8] · Amy J. Clippinger[1]

Received: 17 May 2022 / Accepted: 11 August 2022 / Published online: 20 August 2022

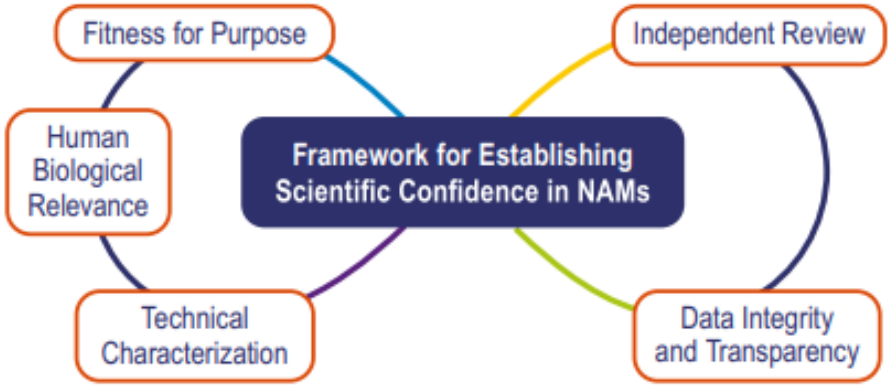

Fig. 1 Schematic illustrating the interconnectedness of the five essential elements for establishing scientific confidence in NAMs for assessing human health effects

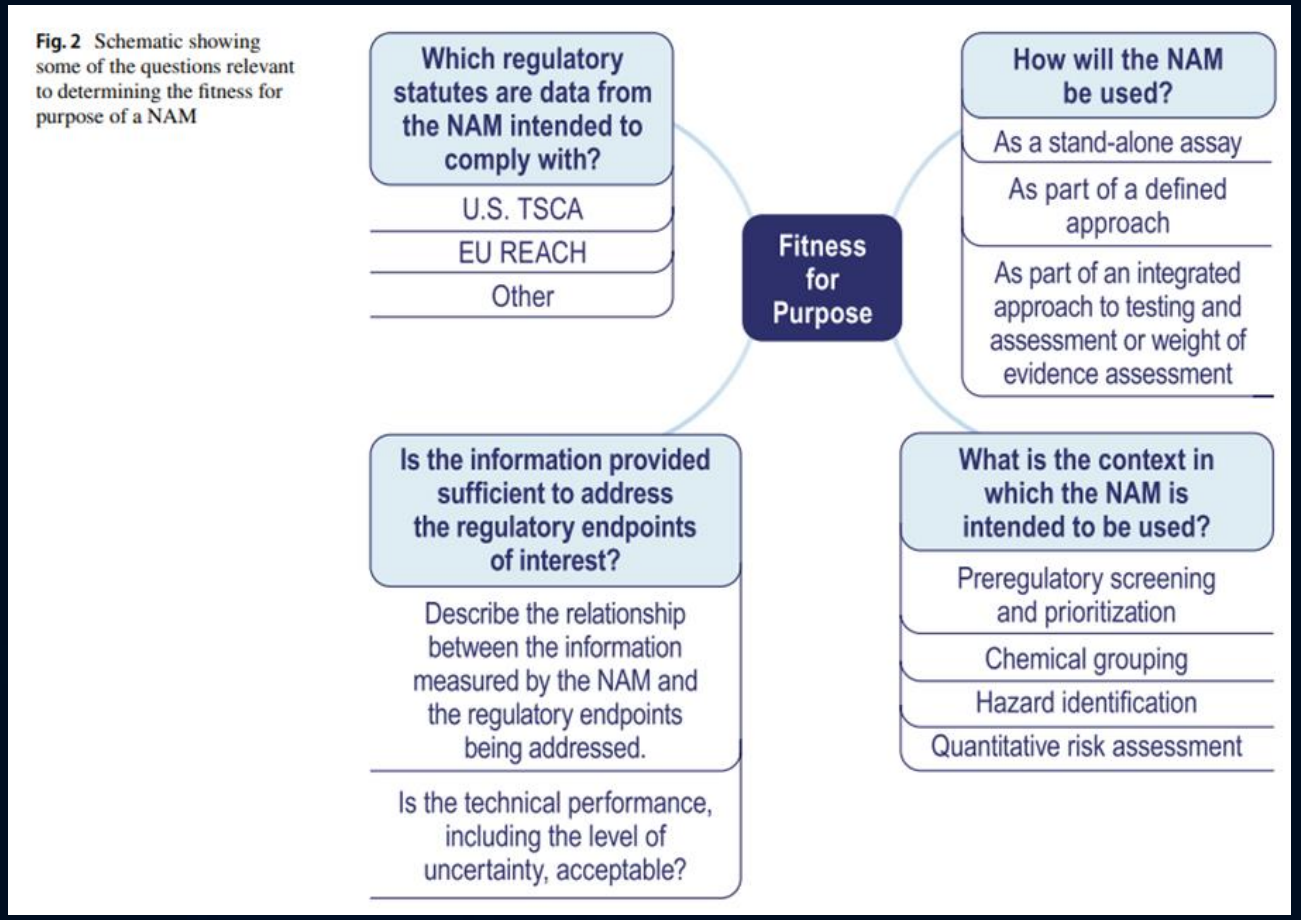

Fig. 2 Schematic showing some of the questions relevant to determining the fitness for purpose of a NAM

Challenging the positioning of animal data as gold standard

NATIONAL ACADEMIES Sciences Engineering Medicine

SEARCH

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Variability and Relevance of Current Laboratory Mammalian Toxicity Tests and Expectations for New Approach Methods (NAMs) for use in Human Health Risk Assessment

ASCCT

American Society for Cellular and Computational Toxicology

Archived Webinar

Using NAMs in Risk Assessment

Presenters:
Katie Paul Friedman, PhD, Center for Computational Toxicology and Exposure, Office of Research and Development, US EPA
George E. N. Kass, PhD, European Food Safety Authority (EFSA)

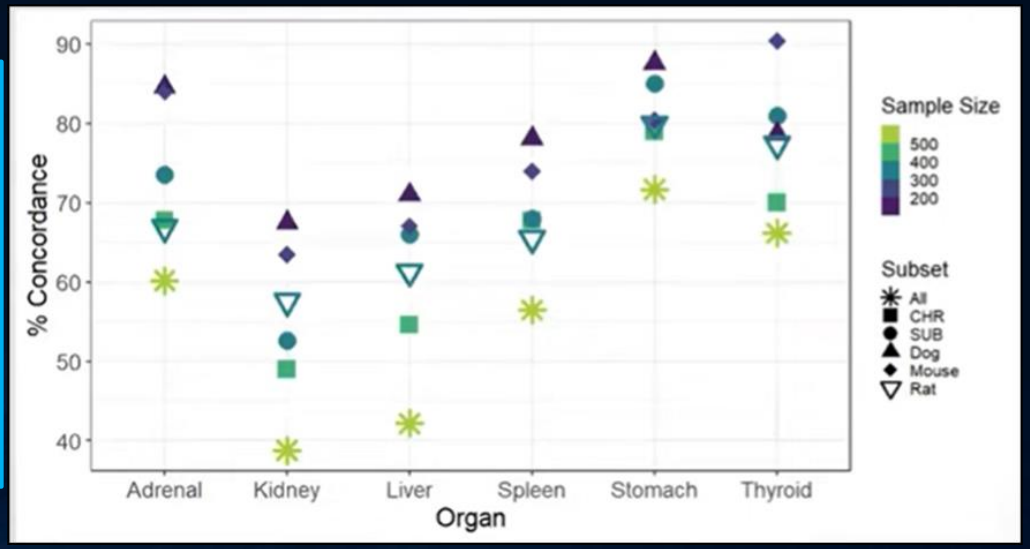
STATE OF THE SCIENCE ON DEVELOPMENT AND USE OF NAMS FOR CHEMICAL SAFETY TESTING

Location: U.S. Environmental Protection Agency
William Jefferson Clinton East Building
William D. Ruckelshaus Conference Center

EPA

Date: October 12-13, 2022

If attempting to use a NAM-based predictive model for prediction of a reference systemic effect level value of 10 mg/kg/day, it is likely that given the variability in reference data of this kind, that a model prediction of somewhere between 1 and 100 mg/kg/day would be the greatest amount of accuracy achievable.



Paul Friedman et al. (unpublished). Reproducibility of organ-level effects in repeat dose animal studies.

Primary Research Question	Statistical approaches
How concordant are organ-level effects for multiple repeat dose study observations?	Calculate concordance of findings between replicate studies when grouped by chemical and organ; chemical, organ, and species; and chemical, organ, and study type

- Qualitative reproducibility of organ-level effect observations in repeat dose studies of adult animals was 33-88%, depending on grouping

3

CHEMICALS POLICY

Implementing EU Chemicals Strategy for Sustainability *[& a new UK Chemicals Strategy ?]*

- High-level Roundtable on the chemicals strategy
- Promoting safe and sustainable by design chemicals
- Chemicals and the circular economy: towards non-toxic material cycles
- Strengthening the EU's open strategic autonomy
- Tackling the most harmful substances
- Essential uses
- Endocrine disruptors
- PFAS
- Chemical mixtures
- One substance, one assessment
- Zero-tolerance approach to non-compliance
- Research, innovation and funding
- Indicators

Legal revisions

- Revision of the Regulation on the Registration, Evaluation, Authorisation and Restr… Chemicals (REACH)
- Revision of EU legislation on hazard classification, labelling and packaging of chemicals (CLP)

European Commission

JRC TECHNICAL REPORT

Safe and Sustainable by Design chemicals and materials

Framework for t… criteria and eval… procedure for ch… materials

Caldeira, C. Farcal, R., Gar… Mancini, L., Tosches, D., A… Rauscher, H., Riego Sintes

2022

Chemicals Strategy for Sustainability

The European Commission adopted its Chemicals Strategy for Sustainability on 14 October 2020. The strategy is part of the EU's zero pollution ambition – a key commitment of the European Green Deal – and aims to better protect citizens and the environment from harmful chemicals, and boost innovation by promoting the use of safer and more sustainable chemicals.

SESSION 1: CURRENT UK POLICY

Introduction and welcome

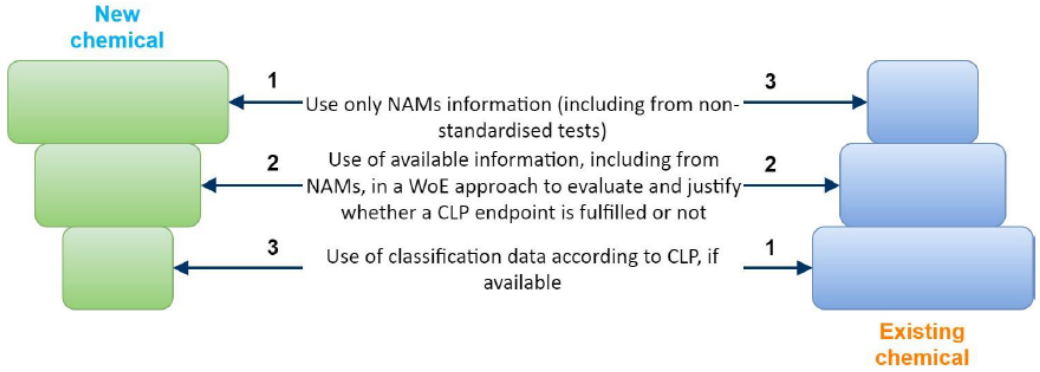
UK chemicals strategy
Representative from Defra

Update on UK REACH
Representative from HSE

Industry views on policy
Updates from CIA and CBA:

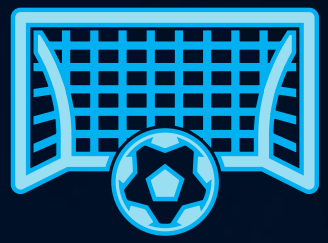
- Latest developments impacting the chemicals supply chain
- How chemicals policy could facilitate innovation and growth in the UK

Figure 24. Tiered approach regarding the information requirements and use of NAMs data for new or existing chemicals



In general, NAMs provide an opportunity for rapid and reliable toxicological profiling of chemicals and materials, including in the design phase. Further consideration should be given to the use of NAM-derived data within the SSbD framework, including the many cases where NAMs provide mechanistic information which is not directly comparable to endpoints from traditional *in vivo* studies.

Chemicals policies needed to stimulate progress in implementing modern safety science for chemicals regulatory purposes



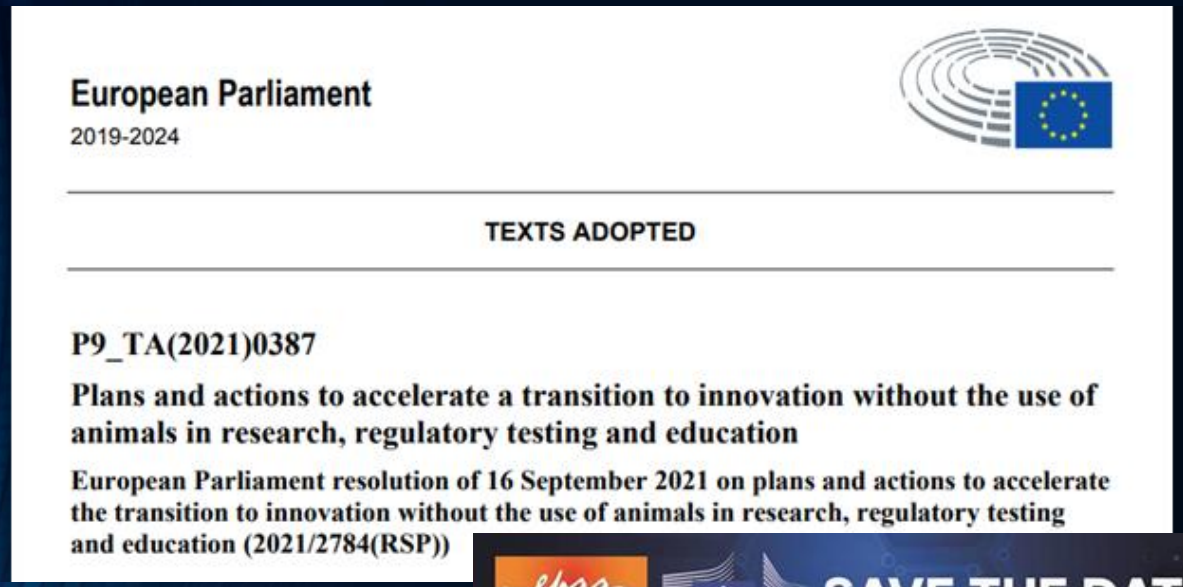
Scientifically justify 'animal testing as a last resort'
+
Paradigm shift in how we assess chemical safety

Best science & most relevant data for human health & environmental assessments
=
Safer Chemicals

- [x] Get creative using relevant NAMs to generate data
- [ ] Modernise legal & regulatory requirements
- [ ] Develop NAM-based regulatory frameworks

Can we embed use of NGRA / NAMs within Safe & Sustainable by Design Chemicals?

Accelerating the transition to animal-free sustainable innovation



European Parliament
2019-2024

TEXTS ADOPTED

P9_TA(2021)0387

Plans and actions to accelerate a transition to innovation without the use of animals in research, regulatory testing and education

European Parliament resolution of 16 September 2021 on plans and actions to accelerate the transition to innovation without the use of animals in research, regulatory testing and education (2021/2784(RSP))

Strengthening "AT as a last resort" …
Define & execute a Roadmap to phase out AT for EU chemicals regulatory compliance purposes

1. immediately pause all animal tests on existing **cosmetics ingredients** → use NGRA/NAMs
2. establish open dialogue on, and transparent scientific evaluation of, **NAM strategies** for specific chemicals / chemical groups
3. accelerate **knowledge transfer & training** in advanced safety science and NAM-based chemical assessments
4. stimulate EU **capacity building** to increase service provision of NAMs toolbox
5. develop a **modern, science-based, chemicals regulatory framework**, which facilitates use of NGRA/NAMs in weight-of-evidence approaches

ECI calls on the European Commission to manage chemicals without new animal testing requirements

European Union
EUROPEAN CITIZENS' INITIATIVE
Save Cruelty Free Cosmetics

Objectives

With the EU ban on cosmetics tests on animals came the promise of a Europe in which animals no longer suffer and die for the sake of cosmetics. That promise has been broken. Authorities still demand animal tests on ingredients used in cosmetics, which goes against the expectations and wishes of the public and the intention of legislators.

Yet, never have we had such powerful non-animal tools for assuring safety or such a golden opportunity to revolutionise human and environmental protection. The European Commission must uphold and strengthen the ban and transition to animal-free safety assessment.

We call on the European Commission to do the following:

1. Protect and strengthen the cosmetics animal testing ban.
Initiate legislative change to achieve consumer, worker, and environmental protection for all cosmetics ingredients without testing on animals for any purpose at any time.

2. Transform EU chemicals regulation.
Ensure human health and the environment are protected by managing chemicals without the addition of new animal testing requirements.

3. Modernise science in the EU.
Commit to a legislative proposal plotting a roadmap to phase-out all animal testing in the EU before the end of the current legislative term.

Engaging politicians, policy-makers & regulators in phasing out animal testing and using modern non-animal safety science

INTERGROUP ON THE WELFARE & CONSERVATION OF ANIMALS

24 Oct 2022

The Revision of EU Chemicals Legislation as a step towards human-relevant, new approach methods

Read more >

13 Oct 2022

How can the European Union move away from animal testing?

Read more >

[The Revision of EU Chemicals Legislation as a step towards human-relevant, new approach methods | Intergroup (animalwelfareintergroup.eu)]

Cruelty Free EUROPE

TARGET ZERO

Routes to a toxic-free Europe without animal testing

27 October 2022 ONLINE EVENT

[Target Zero - 27 October 2022 (toxicfreeeuropewithoutanimaltesting.com)]

"Accelerating the Transition to Animal-Free, Sustainable Innovation"

European Partnership for Alternative Approaches to Animal Testing (EPAA)
Annual Conference 2022

15/11/2022
13:00-18:00
Brussels, Centre Broschette

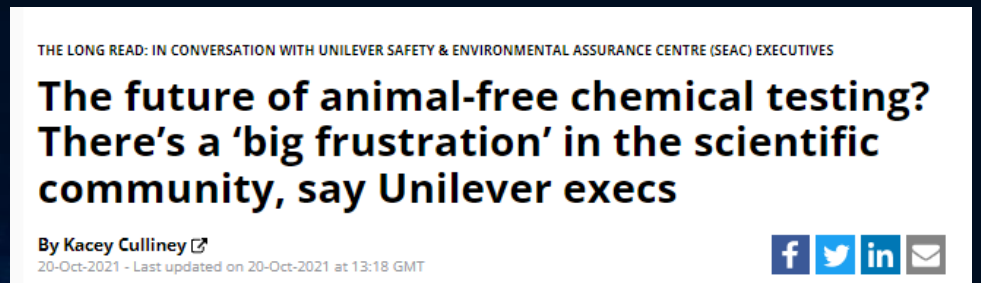
[European Partnership for Alternative Approaches to Animal Testing (europa.eu)]

We must persist in speaking up to drive change

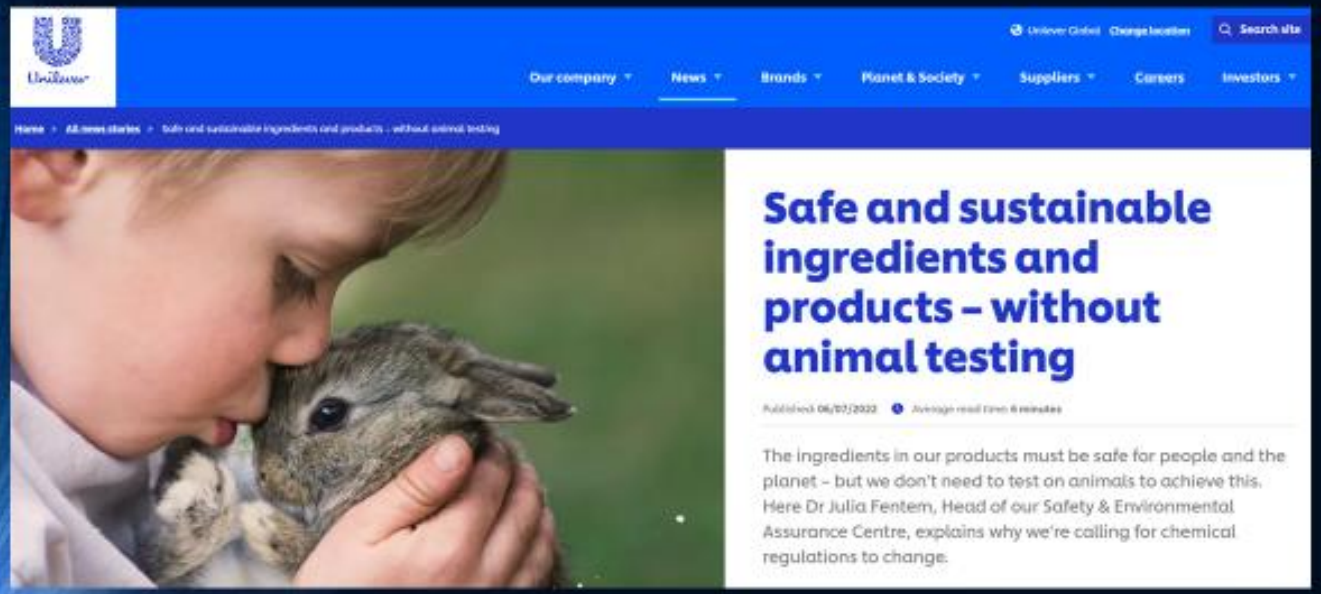
- NAMs scientific community continues to grow, with increasing involvement of early career scientists producing some excellent scientific outputs – new methods, testing strategies, case studies, publications …
- NAMs-based chemical assessments enable decisions on safety - relevant scientific data combined in weight-of-evidence approaches …

➢ Must convince policy & regulatory decision-makers who are unfamiliar with advanced animal-free safety science and have responsibilities for chemical safety where reliance on animal testing is the norm

➢ If we want our modern science to have impact in enabling safer chemicals, we scientists must play our part in closing this gap, in building confidence in the use of NAMs and in helping drive policy & regulatory change – **& team-up with communications & policy experts!**



Our Ambition – Safe & Sustainable Chemicals without Animal Testing



> 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.

We say use science.
Not animals.

To turn our ambition into reality we now need a common Roadmap for Transformation, Transition & Translation …

THANK YOU

YOUR THOUGHTS & QUESTIONS?