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

Julia Fentem, Ian Malcomber, Gavin Maxwell and Carl Westmoreland

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

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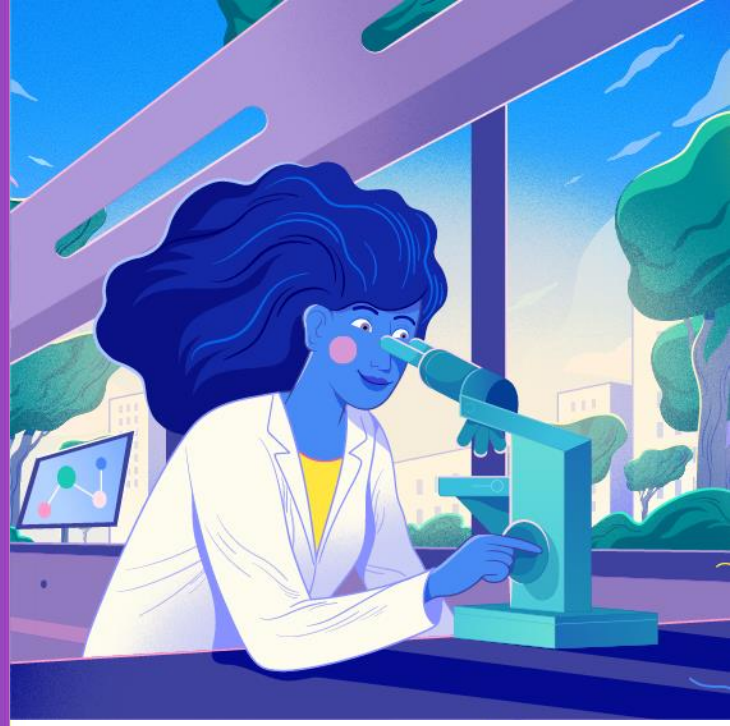
Advocating for changes in chemicals policy and regulations to enable use of advanced safety science in place of animal testing for protecting human health and our environment

Dr Julia Fentem
Head of Unilever Safety & Environmental Assurance Centre (SEAC)

Acknowledgements: Gavin Maxwell, Carl Westmoreland



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Overview

1. broader societal & regulatory context for using innovative safety science approaches to replace animal tests
   - translating our investigative research tools into regulatory application

2. how we apply NAMs in a tiered and integrated way to make decisions on ingredient safety for consumer products
   - introducing a conceptual approach and specific focus

3. why as scientists we need to champion policy & regulatory changes
   - how we can influence broader use of our advanced scientific tools & knowledge

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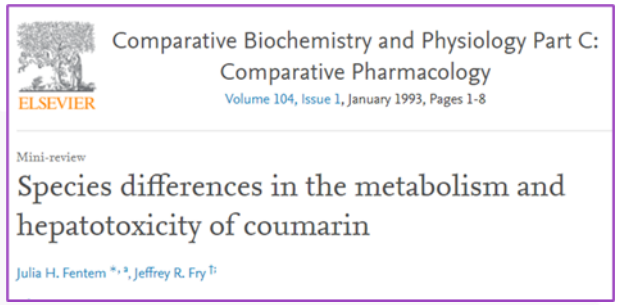
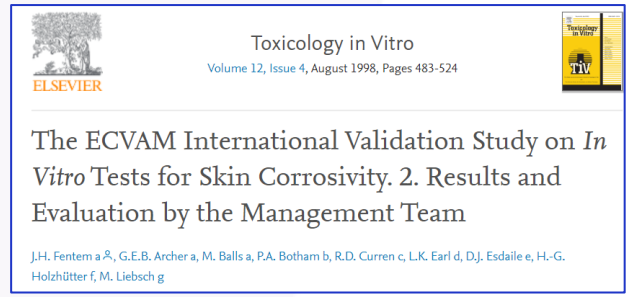
My Background

- PhD - Biochemical Toxicology



- Science Lead for a scientific animal welfare charity *(FRAME, UK)*

- Toxicology Section Lead for ECVAM *(European Commission JRC, Italy)*



- Toxicologist / Head of Product Safety *(SEAC, Unilever)*

SEAC SAFETY & ENVIRONMENTAL ASSURANCE CENTRE
Scientific Excellence And Collaboration

Unilever

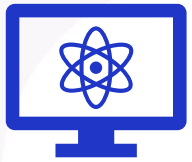
We say use science.
Not animals.

Unilever's Approach
Safe & Sustainable Ingredients & Products without Animal Testing

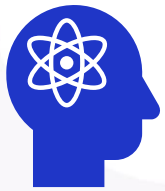
What we believe

- Every Unilever product must be safe for people and our environment
- Animal testing is not needed to assess product safety – there are a **wide range of non-animal alternatives grounded in modern science and new technology**

How we do it



40+ years of developing non-animal safety science



70+ collaborations

600+ publications

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.

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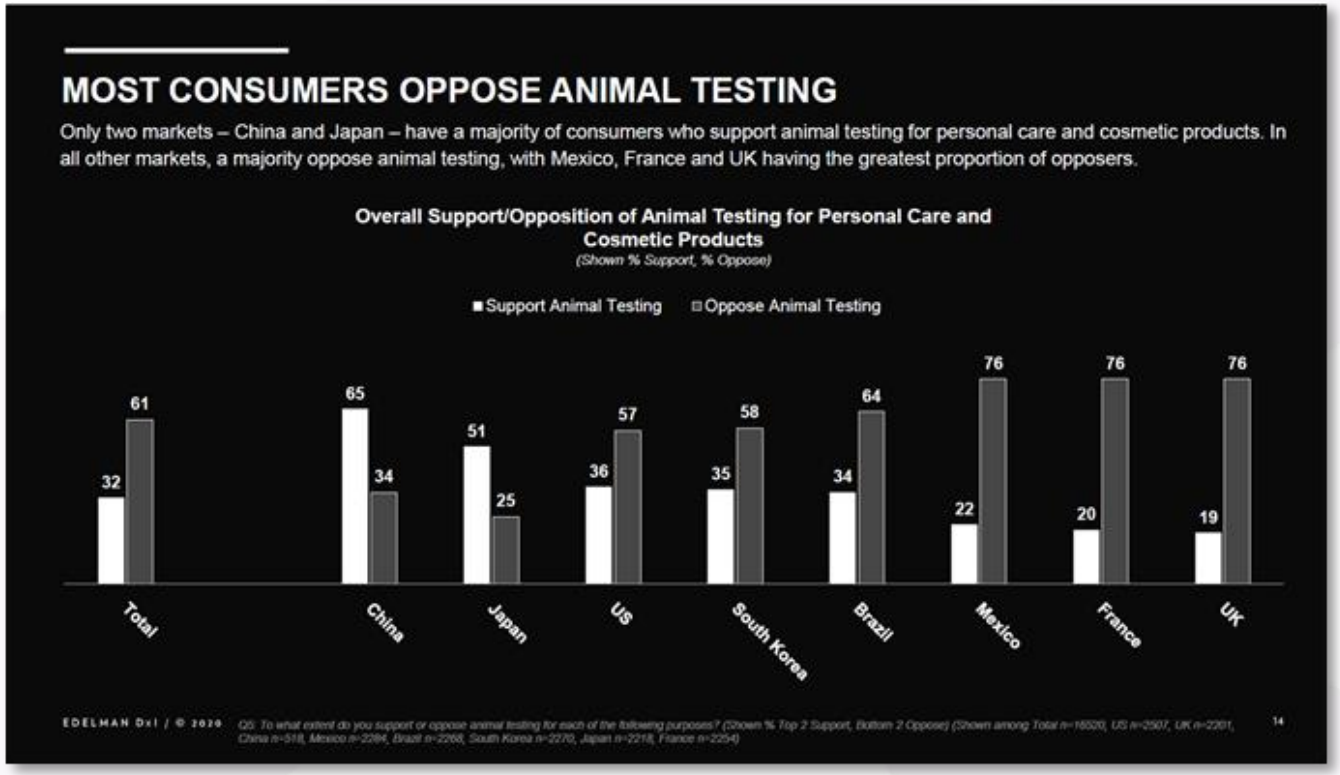
Consumer perspective on animal testing



United Kingdom		United States		Brazil	
Reducing waste and pollution	30%	Reducing and eliminating plastic	28%	Reducing and eliminating plastic	29%
Reducing and eliminating plastic	27%	Reducing waste and pollution	25%	Ending animal testing	25%
Ending animal testing	24%	Ending animal testing	19%	Reducing waste and pollution	24%
Paying a fairer share of tax	24%	Transparent on product ingredients	19%	Transparent on product ingredients	18%
Tackling climate change	19%	Making products affordable for all	19%	Making products affordable for all	16%

Top 5 Global Issues

- Reducing Waste & Pollution
- Reducing Plastic Packaging
- Ending Animal Testing
- Ingredient Transparency
- Tackling Climate Change (CO_2)

EU

76% of EU adults think testing for household cleaning products should be banned

74% of EU adults think testing for cosmetics products and their ingredients should be banned

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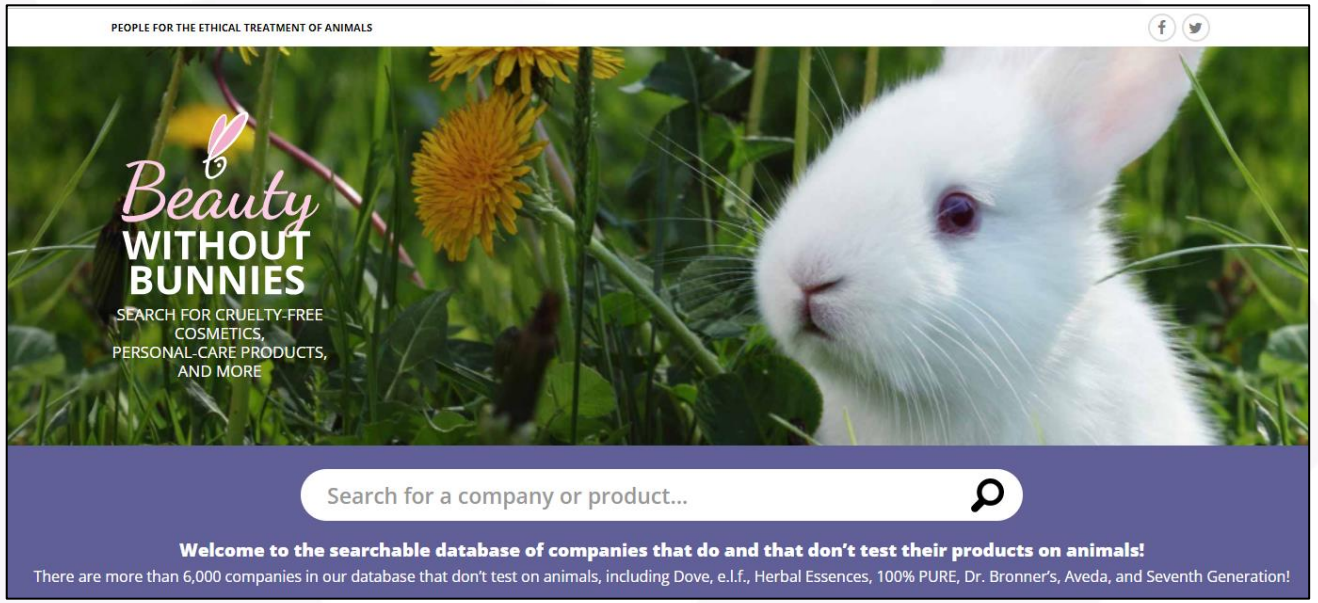
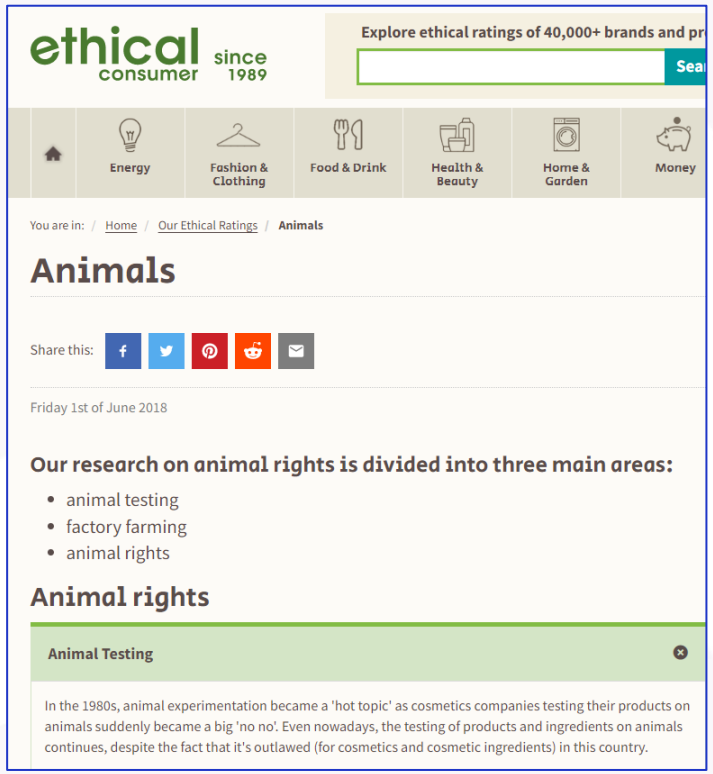
Ethical concerns from many sectors of society

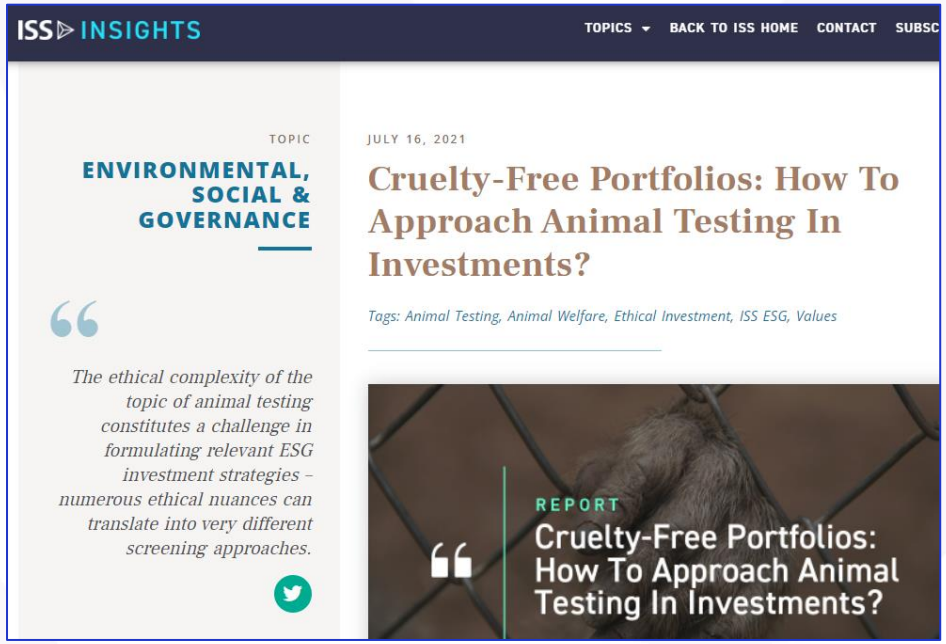
Cruelty-free

In the animal rights movement, cruelty-free is a label for products or activities that do not harm or kill animals anywhere in the world. Products tested on animals or made from animals are not considered cruelty-free, since these tests are often painful and cause the suffering and death of millions of animals every year.

Wikipedia







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Laboratory animal protection legislation

The guiding principles for ethical treatment of animals in testing and experimentation were first introduced by Russell and Burch in 1959 and are known as **the three Rs**: **Replacement, Reduction and Refinement.**

Introduction: Global Laws, Regulations, and Standards for Animals in Research

FREE

Mary Ann Vasbinder ✉, Paul Locke

ILAR Journal, Volume 57, Issue 3, 2016, Pages 261–265,
https://doi.org/10.1093/ilar/ilw039
Published: 04 May 2017 **Article history** ▾

DIRECTIVE 2010/63/EU OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL

of 22 September 2010

on the protection of animals used for scientific purposes

(Text with EEA relevance)

THE EUROPEAN PARLIAMENT AND THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty on the Functioning of the European Union, and in particular Article 114 thereof,

Having regard to the proposal from the European Commission,

Having regard to the opinion of the European Economic and Social Committee ([1]),

After consulting the Committee of the Regions,

Acting in accordance with the ordinary legislative procedure ([2]),

Whereas:

(1) On 24 November 1986 the Council adopted Directive 86/609/EEC ([3]) in order to eliminate disparities between laws, regulations and administrative provisions of the Member States regarding the protection of animals used for experimental and other scientific purposes. Since the adoption of that Directive, further disparities between Member States have emerged.

Animal Welfare Act

Last Modified: Jan 12, 2022 Print

USDA Animal Care, a unit within the Animal and Plant Health Inspection Service, administers the Animal Welfare Act (AWA). This federal law establishes requirements concerning the transportation, sale, and handling of certain animals and includes restrictions on the importation of live dogs for purposes of resale, prohibitions on animal fighting ventures, and provisions intended to prevent the theft of personal pets.

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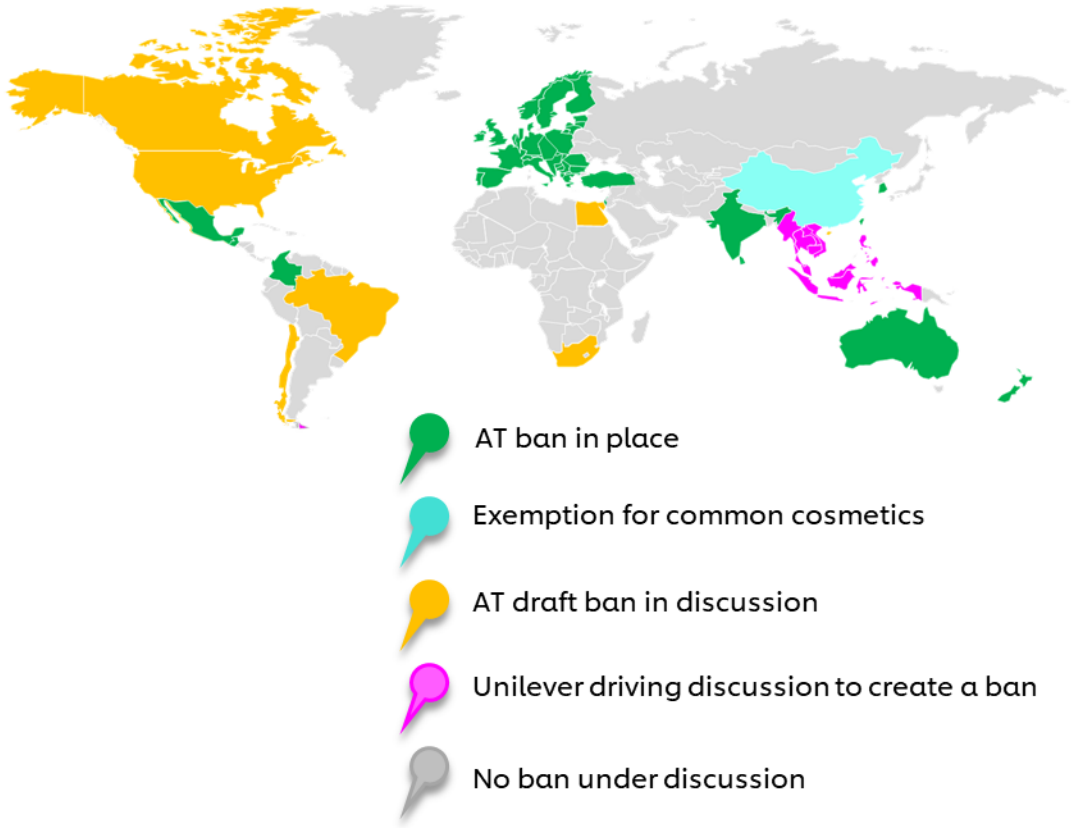
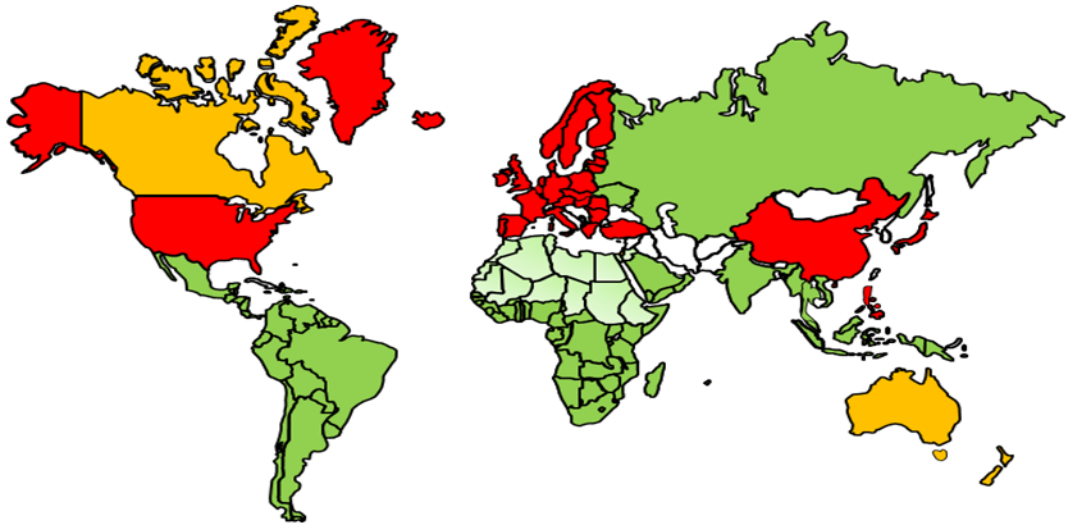
Regulatory context – cosmetics & chemicals
- some regulations ban animal testing, others require it

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

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Chemicals Regulations
- based on animal testing for characterising chemical hazards

The EU has enforced REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals), a comprehensive legal framework that address all chemicals in use, requiring companies marketing chemicals to present a set of test data.

The US equivalent, TSCA (Toxic Substances Control Act), set some basic requirements but is more limited in scope.

Korean REACH: The Act on the Registration and Evaluation of Chemicals (K-REACH)

China Publishes Amended New Chemical Regulation

Wednesday, May 13, 2020

On April 29, 2020, China's Ministry of Ecology and Environment (MEE) published the *Measures on Environmental Management Registration of New Chemical Substances* (hereinafter "MEE Order 12"),[1] to amend its new chemical regulation. This is the second revision of China's regulation on

UK registration, evaluation, authorisation and restriction of chemicals (REACH)

The Toxic Substances Control Act of 1976 (TSCA) is a federal regulation that allows the U.S. Environmental Protection Agency (EPA) to comprehensively manage chemicals in U.S. commerce. TCSA Compliance can require companies to restrict and remove substances from products to maintain U.S. market access.

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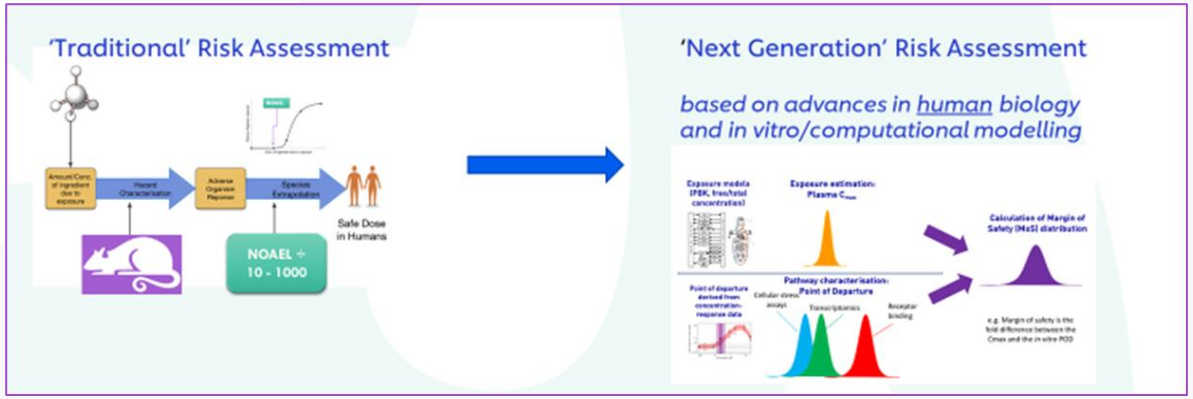
Applying innovative science not animal tests for safety decisions
- translating our investigative safety science for regulatory use



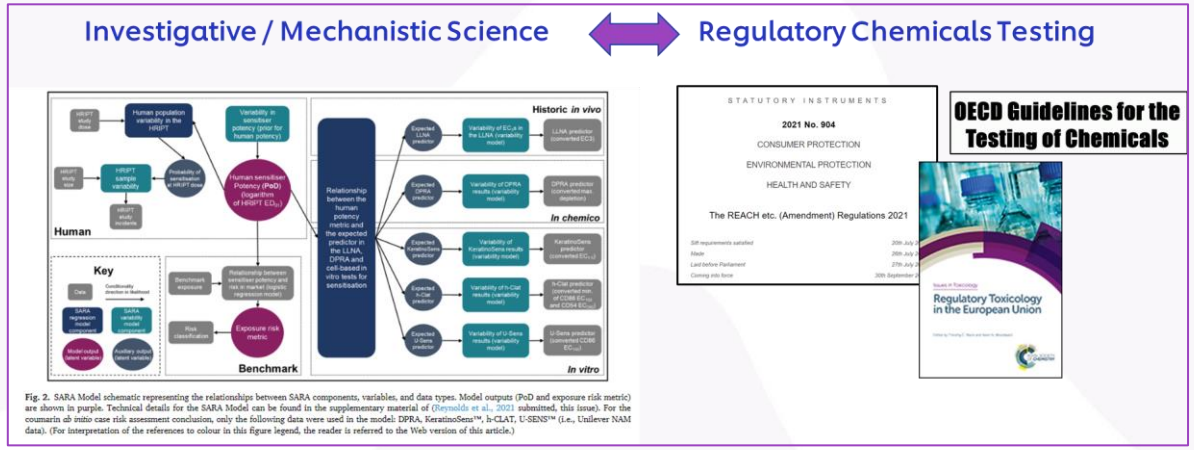
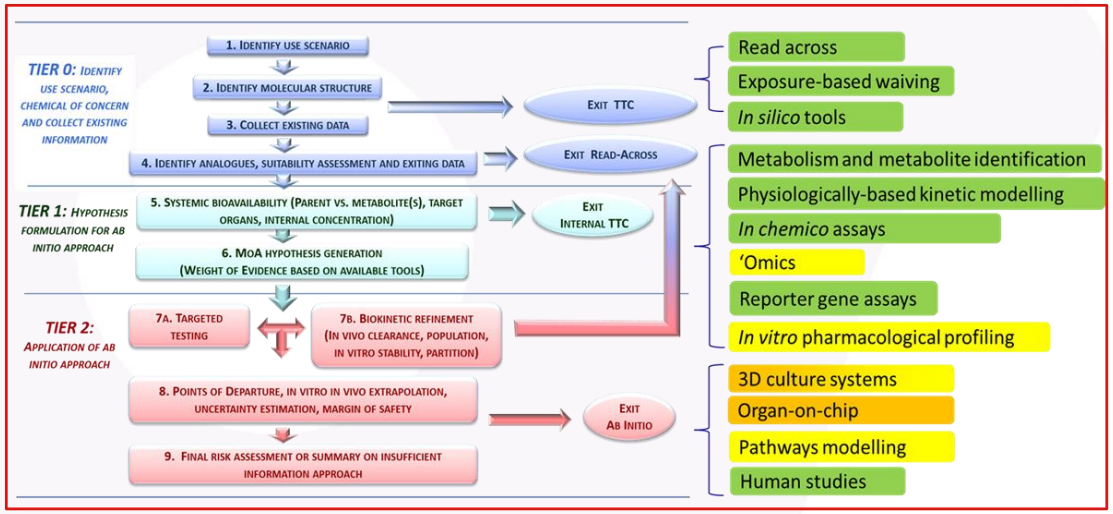


Fig. 2. SARA Model schematic representing the relationships between SARA components, variables, and data types. Model outputs (PoD and exposure risk metric) are shown in purple. Technical details for the SARA Model can be found in the supplementary material of (Reynolds et al., 2021 submitted, this issue). For the coumarin *ab initio* case risk assessment conclusion, only the following data were used in the model: DPRA, KeratinoSens™, h-CLAT, U-SENS™ (i.e., Unilever NAM data). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

EUTOXRISK



Comput Toxicol. 2017 Nov;4:31-44. doi: 10.1016/j.comtox.2017.10.001.

Ab initio chemical safety assessment: A workflow based on exposure considerations and non-animal methods.

Berggren E[1], White A[2], Ouedraogo G[3], Paini A[1], Richarz AN[1], Bois FY[4], Exner T[5], Leite S[6], Grunsven LAV[6], Worth A[1], Mahony C[7].

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Legal context – European Court of Justice cases
- upholding the principle of "animal testing as a last resort"

Facts

C-471/18 P - 21 January 2021 Federal Republic of Germany v Esso Raffinage

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.

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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.

Decision of the European Ombudsman closing the inquiry into complaint 1568/2012/(FOR)AN against the European Chemicals Agency (ECHA)

Decision
Case 1568/2012/AN - **Opened on** 19/09/2012 - **Decision on** 11/12/2014 - **Institution concerned** European Chemicals Agency (Settled by the institution) |

The case, lodged by the PETA Foundation, concerned the scope of the European Chemicals Agency's (ECHA's) powers and duties under the REACH Regulation. The complainant considered that ECHA does not do enough to ensure that registrants of chemical substances refrain from performing unnecessary animal tests in order to demonstrate their substances' safety.

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.

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

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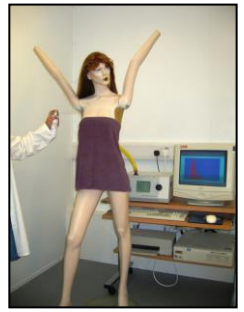
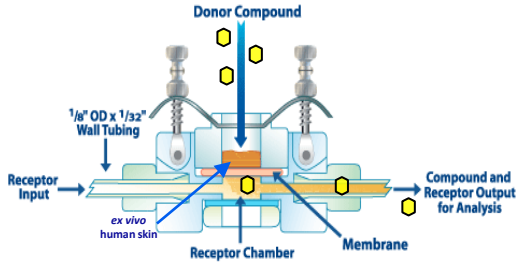
Assuring consumer safety without animal testing
- maximising use of existing information and animal-free approaches

- All our risk assessments are exposure-led

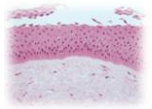
Table 2: Estimated daily exposure levels for different cosmetic product types according to Cosmetics Europe data (SCCNFP/0321/00; Hall *et al.*, 2007, 2011).

Product type	Estimated daily amount applied	Relative amount applied (mg/kg bw/d)	Retention factor [1]	Calculated daily exposure (g/d)	Calculated relative daily exposure (mg/kg bw/d)
Bathing, showering					
Shower gel	18.67 g	279.20	0.01	0.19	2.79
Hand wash soap [2]	20.00 g	-	0.01	0.20 [3]	3.33
Hair care					
Shampoo	10.46 g	150.49	0.01	0.11	1.51
Hair conditioner [2]	3.92 g	-	0.01	0.04	0.60
Hair styling products	4.00 g	57.40	0.1	0.40	5.74



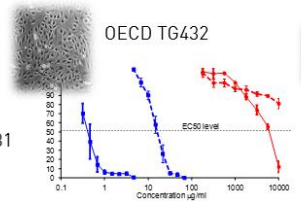


- Use all available safety data on the ingredient
  - clinical, epidemiological, animal (if dates permit), *in vitro*, etc.
- Exposure-based waiving approaches (e.g. toxicological threshold of concern)
- *In silico* predictions
- History of safe use
- Read-across
- Use of existing OECD *in vitro* approaches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

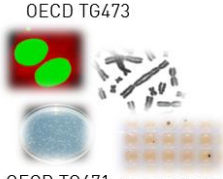


OECD TG437

OECD TG430/431
OECD TG439



OECD TG432



OECD TG473
OECD TG471
OECD TG476

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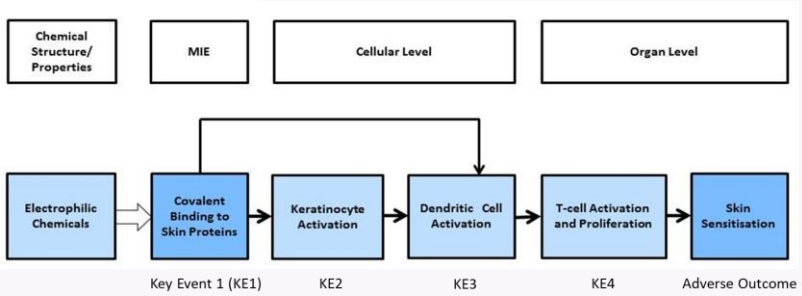
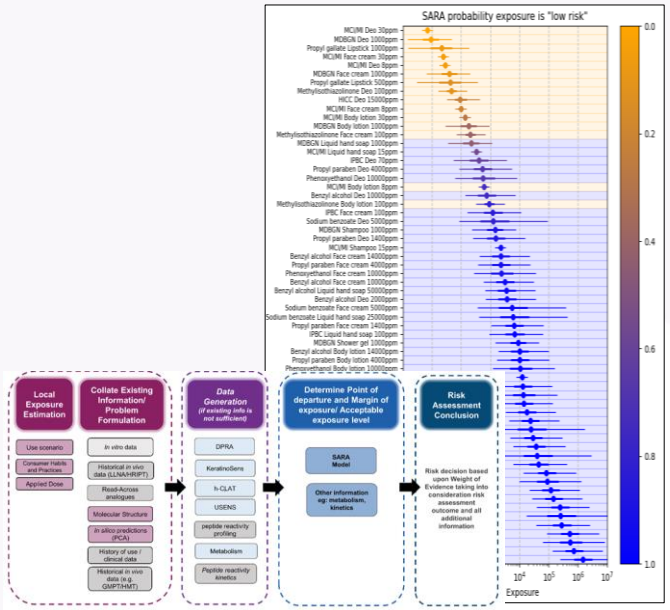
Non-Animal Methods for Skin Allergy Risk Assessment (SARA)

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

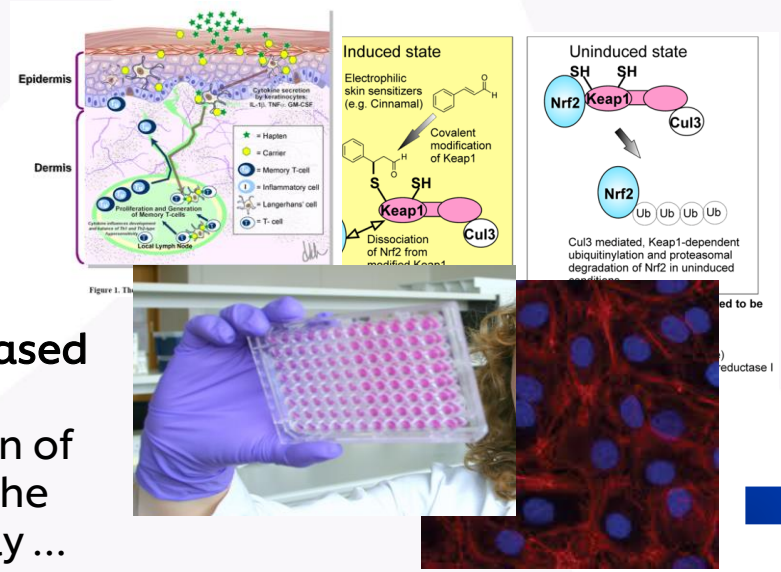




Unilever's **SARA Model** – developed as a computational approach to integrate information from the historical data and various cell-based experiments …

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

Developing a **risk assessment framework** …



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


Contents lists available at ScienceDirect
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journal homepage: www.elsevier.com/locate/yrtph

A hypothetical skin sensitisation next generation risk assessment for coumarin in cosmetic products

G. Reynolds *, J. Reynolds, N. Gilmour, R. Cubberley, S. Spriggs, A. Aptula, K. Przybylak, S. Windebank, G. Maxwell, M.T. Baltazar **
Unilever Safety and Environmental Assurance Centre, Colworth Science Park, Sharnbrook, Bedfordshire, MK44 1LQ, UK


Regulatory Toxicology and Pharmacology
Volume 131, June 2022, 105159

Next generation risk assessment for skin allergy: Decision making using new approach methodologies

N. Gilmour, J. Reynolds, K. Przybylak, M. Aleksic, N. Aptula, M.T. Baltazar, R. Cubberley, R. Rajagopal, G. Reynolds, S. Spriggs, C. Thorpe, S. Windebank, G. Maxwell

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https://doi.org/10.1016/j.yrtph.2022.105159

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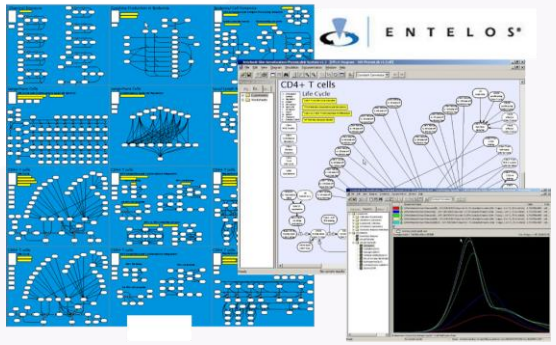
Highlights

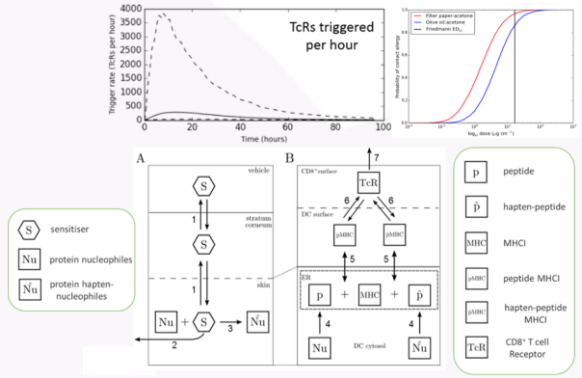
- Application of new approach methodologies in a next generation risk assessment framework for skin allergy.
- Use of the skin allergy risk assessment (SARA) model, a defined approach for potency and risk assessment of skin sensitisers.
- Skin sensitisation risk assessment case studies using new approach methodologies.

Skin Allergy Risk Assessment



Entelos model

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



SARA TKTD qAOP model

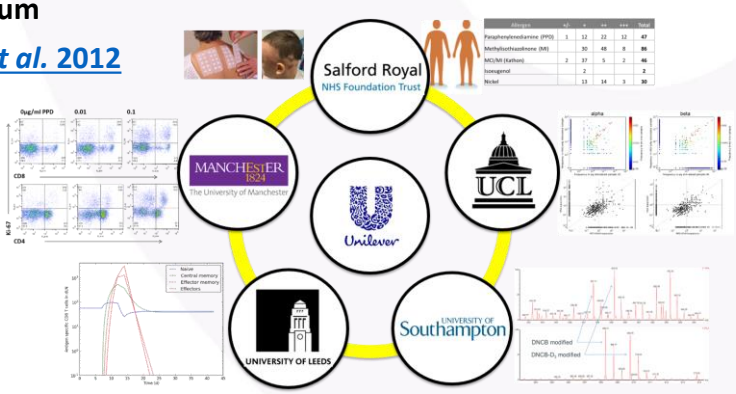
[Mackay et al. 2013](#)

SARA Bayesian Model

[Reynolds *et al.* 2019](#)

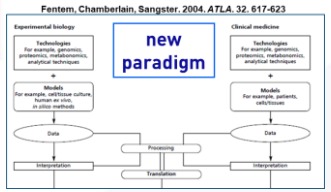
T cell Forum

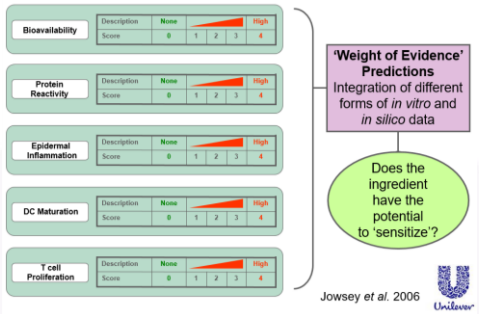
[Kimber et *al.* 2012](#)



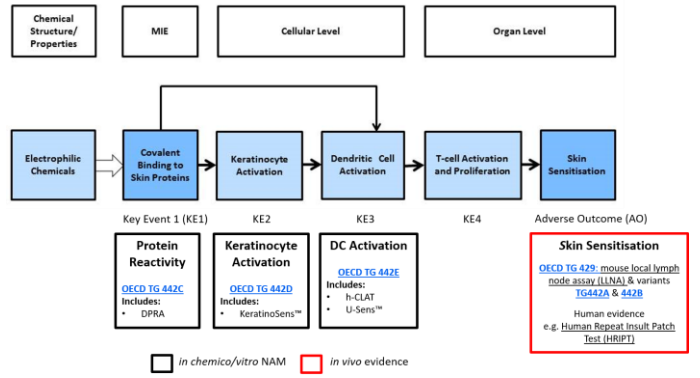
Integration of non-animal data

[Jowsey *et al.* 2006](#)

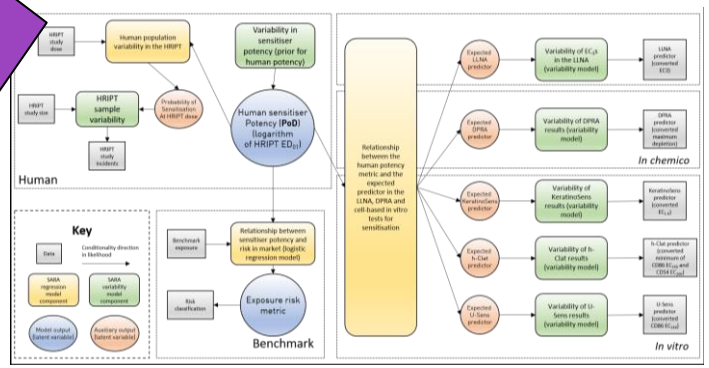




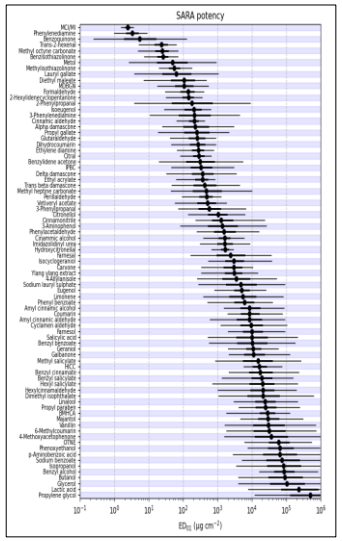
Skin Allergy AOP and SARA inputs



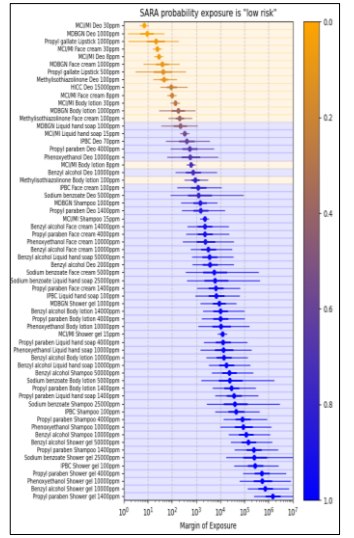
SARA Model Structure



SARA Human Potency

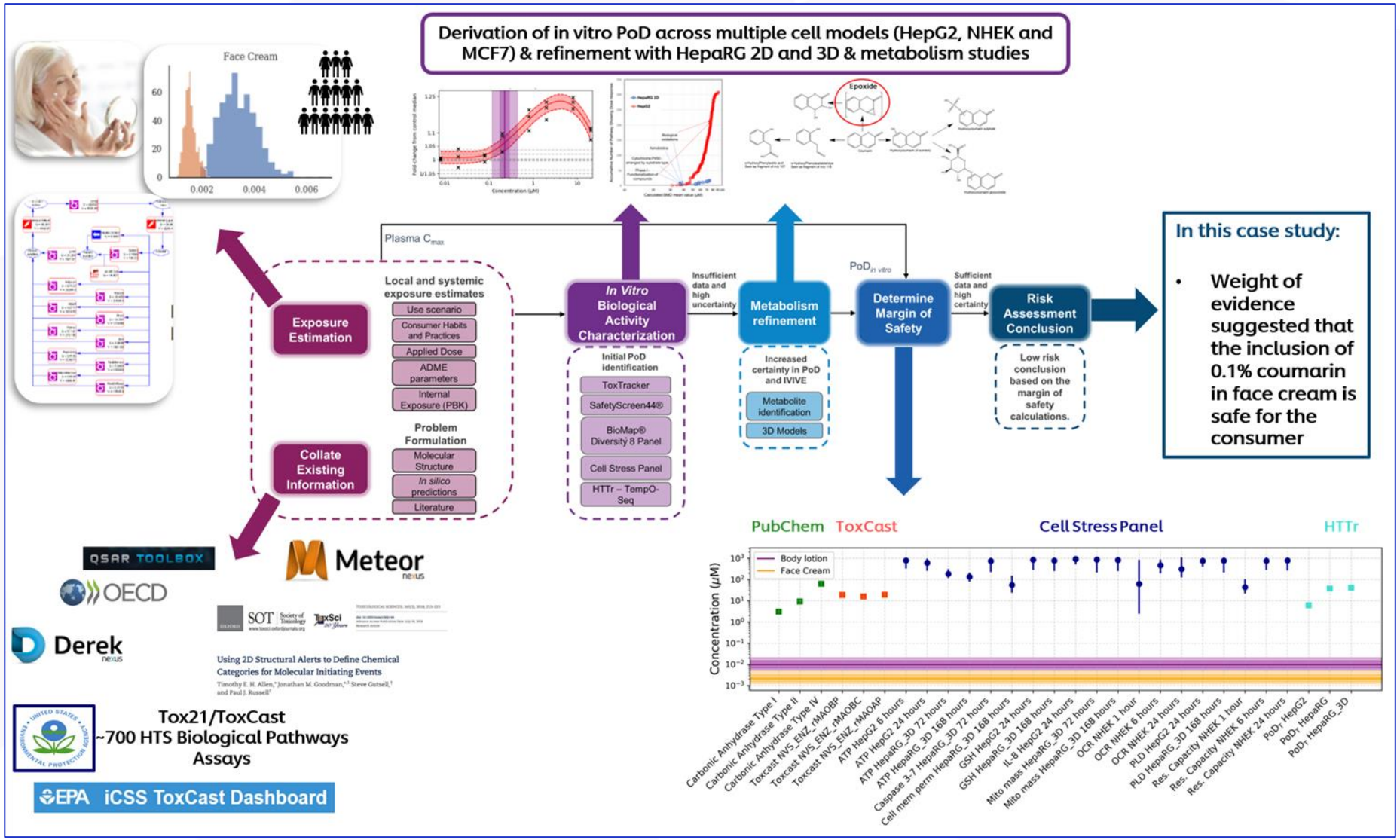


SARA Consumer Risk



Unilever

A large toolbox of modern scientific methods (NAMs) is used



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

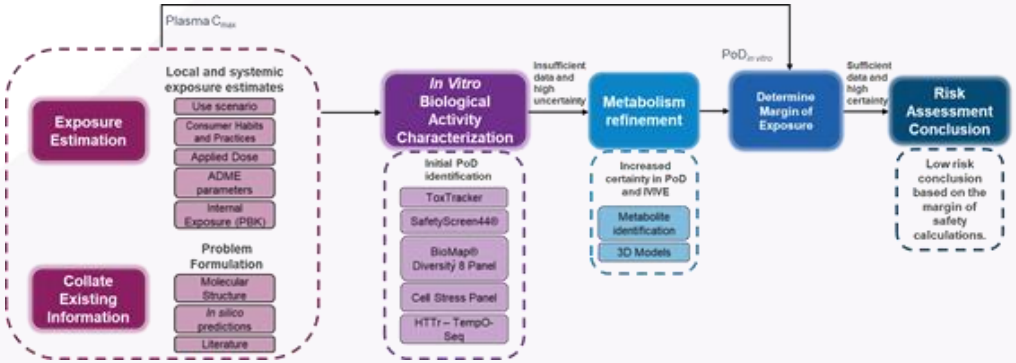
Hatherell *et al* (2020) Toxicological Sciences, **176,** 11-33

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

Unilever

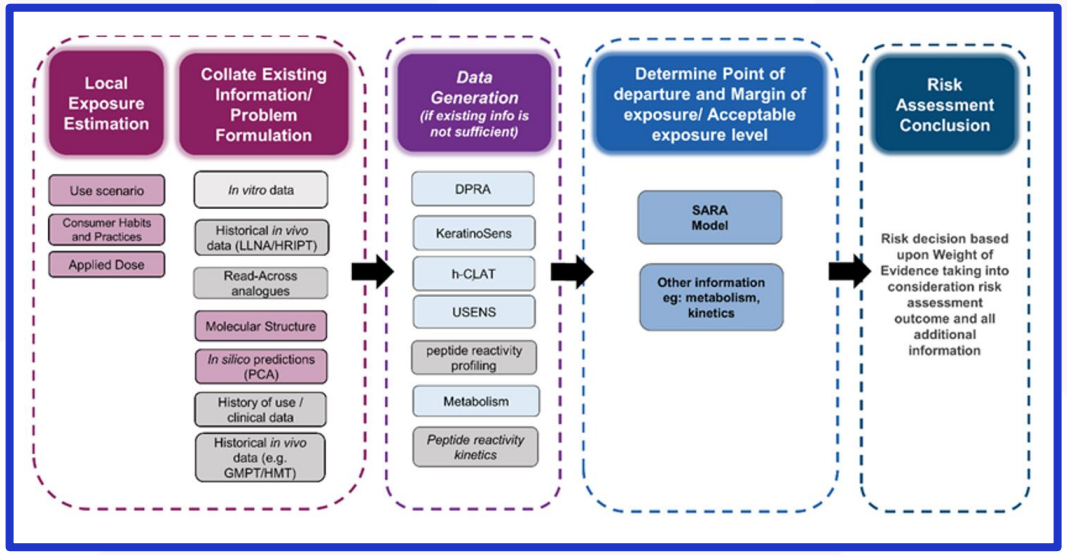
Unilever Frameworks for using NAMs to make Human Safety Decisions

Systemic



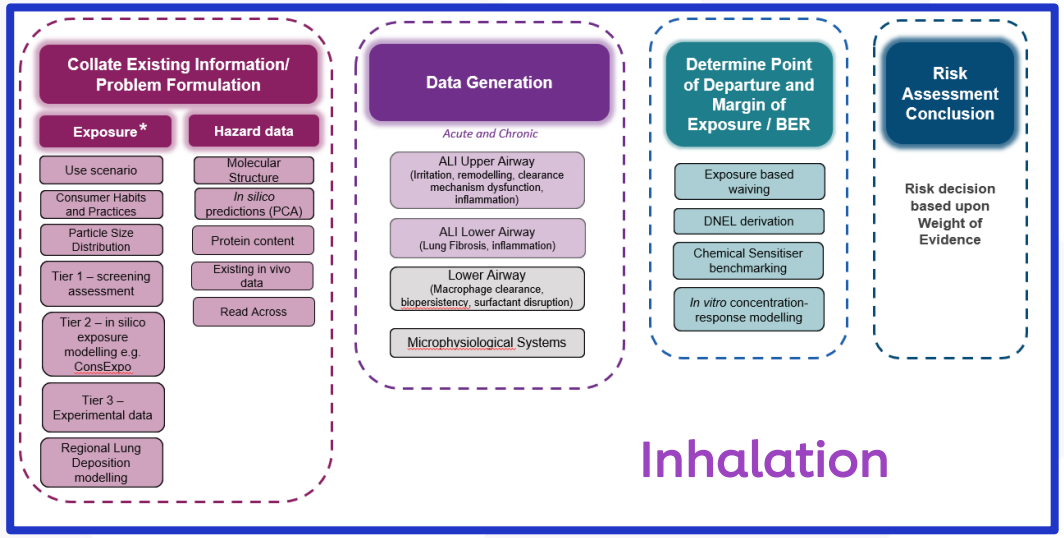
Baltazar et al (2020) *Toxicol Sci*, 176, 236-252

Skin Sensitisation

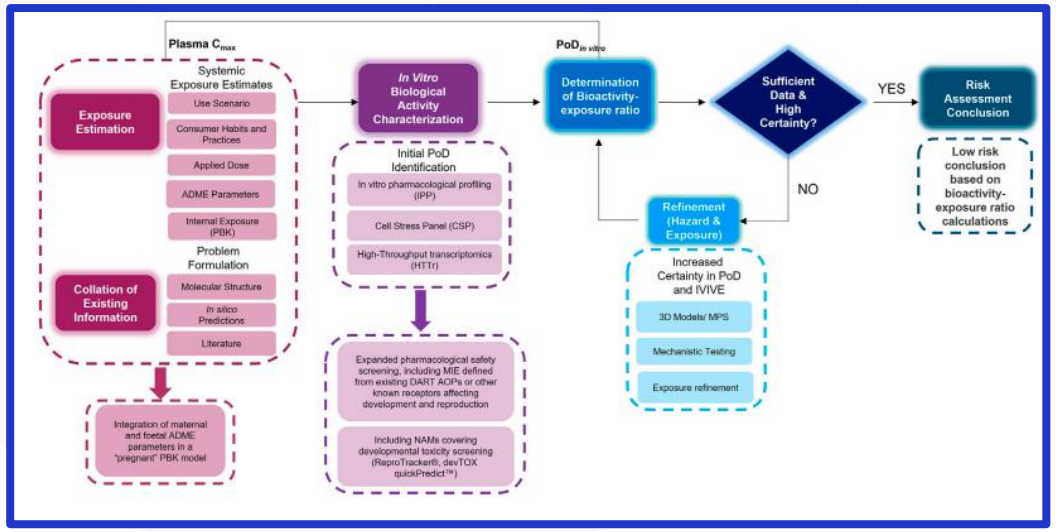


Reynolds et al (2021) *Reg Tox Pharmacol*, **127**, 105075

Inhalation



Developmental & Reproductive (DART)



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

Unilever

Use of NAMs in assessing safety risks of cosmetics ingredients

Computational Toxicology 7 (2018) 20–26

Contents lists available at ScienceDirect

Computational Toxicology

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

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

Matthew Dent[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[p], Nashira Vieira O'Reilly Cabral Posada[l], Craig Weiss[p], Hajime Kojima[f]

ARTICLE INFO

ABSTRACT

SCCS/1628/21

Scientific Committee on Consumer Safety

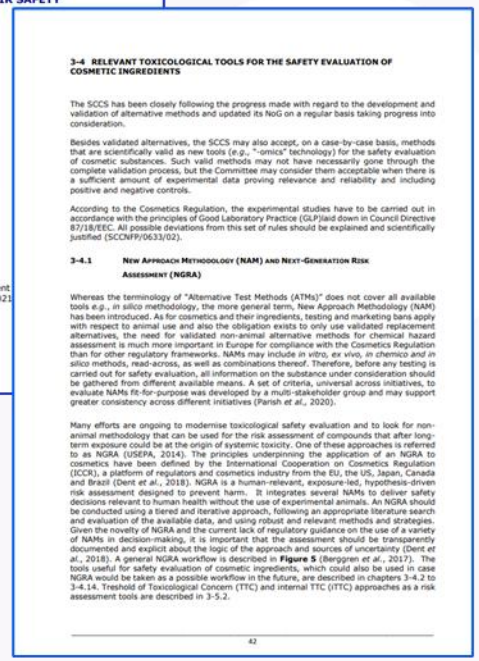
SCCS

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



3-4 RELEVANT TOXICOLOGICAL TOOLS FOR THE SAFETY EVALUATION OF COSMETIC INGREDIENTS

The SCCS has been closely following the progress made with regard to the development and validation of alternative methods and updated its NoG on a regular basis taking progress into consideration.

Besides validated alternatives, the SCCS may also accept, on a case-by-case basis, methods that are scientifically valid as new tools (e.g., "-omics" technology) for the safety evaluation of cosmetic substances. Such valid methods may not have necessarily gone through the complete validation process, but the Committee may consider them acceptable when there is a sufficient amount of experimental data proving relevance and reliability and including positive and negative controls.

According to the Cosmetics Regulation, the experimental studies have to be carried out in accordance with the principles of Good Laboratory Practice (GLP)laid down in Council Directive 87/18/EEC. All possible deviations from this set of rules should be explained and scientifically justified (SCCNFP/0633/02).

3-4.1 NEW APPROACH METHODOLOGY (NAM) AND NEXT-GENERATION RISK ASSESSMENT (NGRA)

Whereas the terminology of "Alternative Test Methods (ATMs)" does not cover all available tools e.g., in silico methodology, the more general term, New Approach Methodology (NAM) has been introduced. As for cosmetics and their ingredients, testing and marketing bans apply with respect to animal use and also the obligation exists to only use validated replacement alternatives, the need for validated non-animal alternative methods for chemical hazard assessment is much more important in Europe for compliance with the Cosmetics Regulation than for other regulatory frameworks. NAMs may include in vitro, ex vivo, in chemico and in silico methods, read-across, as well as combinations thereof. Therefore, before any testing is carried out for safety evaluation, all information on the substance under consideration should be gathered from different available means. A set of criteria, universal across initiatives, to evaluate NAMs fit-for-purpose was developed by a multi-stakeholder group and may support greater consistency across different initiatives (Parish et al., 2020).

Many efforts are ongoing to modernise toxicological safety evaluation and to look for non-animal methodology that can be used for the risk assessment of compounds that after long-term exposure could be at the origin of systemic toxicity. One of these approaches is referred to as NGRA (USEPA, 2014). The principles underpinning the application of an NGRA to cosmetics have been defined by the International Cooperation on Cosmetics Regulation (ICCR), a platform of regulators and cosmetics industry from the EU, the US, Japan, Canada and Brazil (Dent et al., 2018). NGRA is a human-relevant, exposure-led, hypothesis-driven risk assessment designed to prevent harm. It integrates several NAMs to deliver safety decisions relevant to human health without the use of experimental animals. An NGRA should be conducted using a tiered and iterative approach, following an appropriate literature search and evaluation of the available data, and using robust and relevant methods and strategies. Given the novelty of NGRA and the current lack of regulatory guidance on the use of a variety of NAMs in decision-making, it is important that the assessment should be transparently documented and explicit about the logic of the approach and sources of uncertainty (Dent et al., 2018). A general NGRA workflow is described in **Figure 5** (Berggren et al., 2017). The tools useful for safety evaluation of cosmetic ingredients, which could also be used in case NGRA would be taken as a possible workflow in the future, are described in chapters 3-4.2 to 3-4.14. Treshold of Toxicological Concern (TTC) and internal TTC (iTTC) approaches as a risk assessment tools are described in 3-5.2.

42

OECD

Organisation for Economic Co-operation and Development

ENV/CBC/MONO(2021)35

Unclassified

English - Or. English

27 October 2021

ENVIRONMENT DIRECTORATE
CHEMICALS AND BIOTECHNOLOGY COMMITTEE

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

Series on Testing and Assessment, No. 349

JT03483903

This document, as well as any data and map included herein, are without prejudice to the status of or sovereignty over any territory, to the delimitation of international frontiers and boundaries and to the name of any territory, city or area.

ICCR International Cooperation on Cosmetics Regulation

International Cooperation on Cosmetics Regulation (2018)

European Commission

European Commission: Scientific Committee on Consumer Safety (2021)

OECD

OECD (2021)

Unilever

Use of NAMs in evaluating food ingredients
EFSA investing in NAMs for regulatory assessments

Finally, the development of scientific methodologies and tools, and the opportunity to refine existing ones, will offer new approaches for risk assessment in line with the 3Rs principle (Replacement, Refinement, and Reduction) to animal testing. EFSA must continue to invest in harvesting data and information to stay abreast of evolving scientific methodologies and research and develop adequate methodologies to assess new sources of potential food/feed risks such as new production technologies.

Expected Operational Result 2.1.3

The quality of scientific guidance and methodologies, with the necessary risk assessment capabilities, is improved to address future challenges

KEY ACTIONS

- Ensure forward looking engagement with partners and stakeholders to achieve synergies on Risk Assessment topics of mutual interest and facilitate the development and implementation of harmonised risk assessment methodologies
- Prepare to address risk assessment challenges associated with food and feed system innovations
- Develop risk benefit approaches for chemical and biological hazards in human and environmental risk assessment
- Develop and implement systems-based approaches for regulatory environmental risk assessment
- Establish criteria and scientific assessment options to support the application of tiered approaches of methodological complexity to deliver fit for purpose assessments
- Develop and integrate new approach methodologies (NAMs) and omics for regulatory risk assessment
- Develop risk assessment of combined exposure to multiple chemicals, across regulatory domains
- Integrate, bioinformatic and cheminformatics approaches, technologies and data into next generation risk assessment
- Consider how microbiomes could be included in risk assessment, and develop tools to enable this
- Keep EFSA's risk assessment processes updated in line with evolving regulatory, policy and quality drivers (TR)

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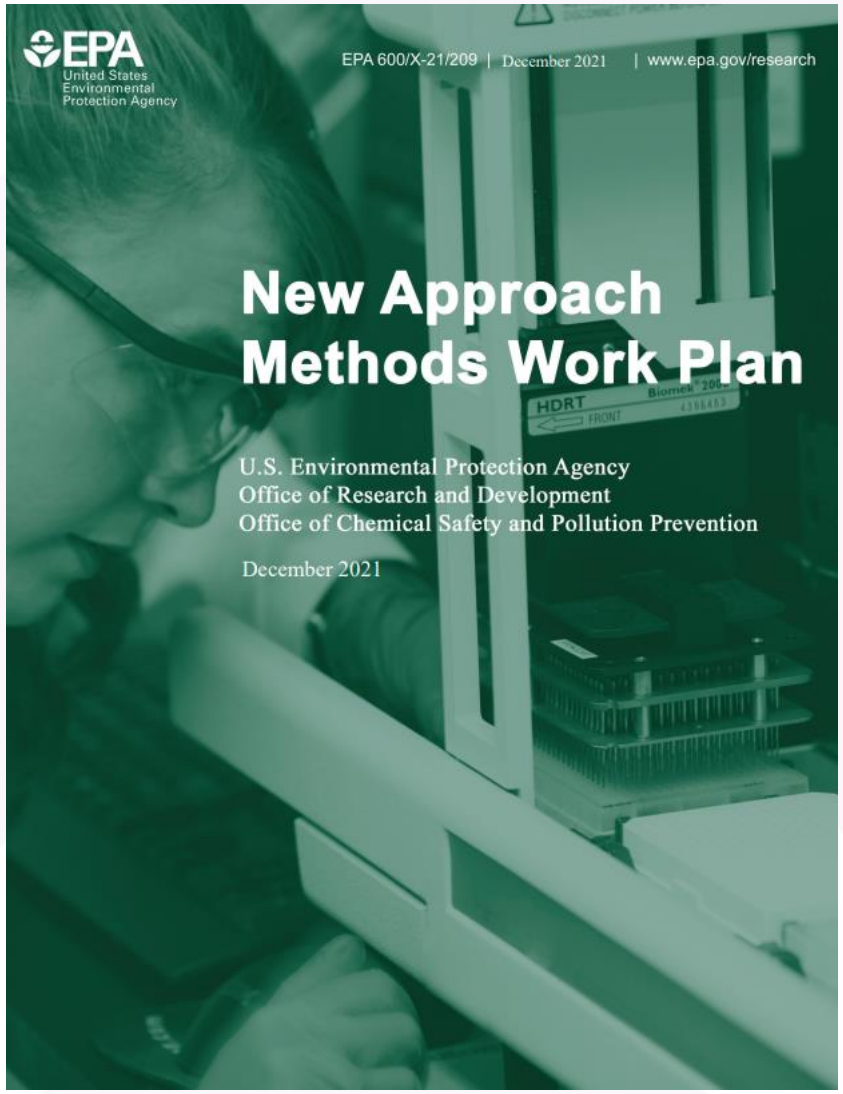
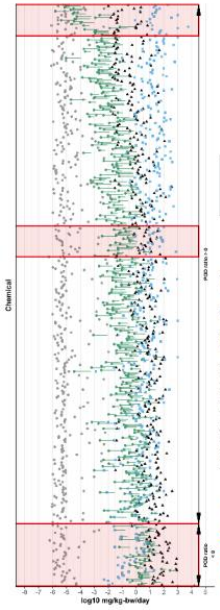
US EPA is leading on application of NAMs for chemicals safety





APCRA
ACCELERATING THE PACE OF CHEMICAL RISK ASSESSMENT

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*

"The primary objective of this work was to compare PODs based on high-throughput predictions of bioactivity, exposure predictions, and traditional hazard information for 448 chemicals"

Unilever

Overview

1. broader societal & regulatory context for using innovative safety science approaches to replace animal tests
   - translating our investigative research tools into regulatory application

2. how we apply NAMs in a tiered and integrated way to make decisions on ingredient safety for consumer products
   - introducing a conceptual approach and specific focus

3. **why as scientists we need to champion policy & regulatory changes**
   - how we can influence broader use of our advanced scientific tools & knowledge

Unilever

Advocating for regulatory change around the world

Unilever supports calls for a global ban on animal testing for cosmetics by 2023

Product testing

Hygiene products & disinfectants

Home care products

Ingredient testing – existing ingredients

ECHA
EUROPEAN CHEMICALS AGENCY

The EU's ban on animal testing for cosmetics helped change the world.

Now all that progress is at risk.

We say use science.
Not animals.

Unilever

Ingredient testing – new ingredients

Partner With Purpose

Unilever

Working to change regulatory requirements for cosmetics testing

Product testing requirements are evolving in China
- promoting use of non-animal safety science & assessments

Unilever played a lead role in helping modernise China's cosmetics safety approach

Non-animal safety approaches in China

2011: Unilever-hosted symposium at our Shanghai laboratory

2014: Mandatory animal testing for locally manufactured Common cosmetics removed

2019: High level UK-China government collaboration

2021: No mandatory animal testing for imported Common cosmetics. Unilever - Shanghai government lab collaboration on safety of hygiene/disinfectant products without animal testing

2021 animal-testing exemptions

Product classification/ market access		AT exemption?
Imported	Common Cosmetics	Yes*
	Special Cosmetics	No
Made in China	Common Cosmetics	Yes*
	Special Cosmetics	No

AT exemption requires a Good Manufacturing Practice (GMP) certificate and a Cosmetic Product Safety Report (CPSR).
* AT still required for some products e.g. anti-wrinkle and anti-acne rinse off products, baby products or products with new ingredients in 3 year monitoring period

The EU and UK animal testing bans on cosmetics are at risk
- regulators requesting new animal tests on hundreds of chemicals

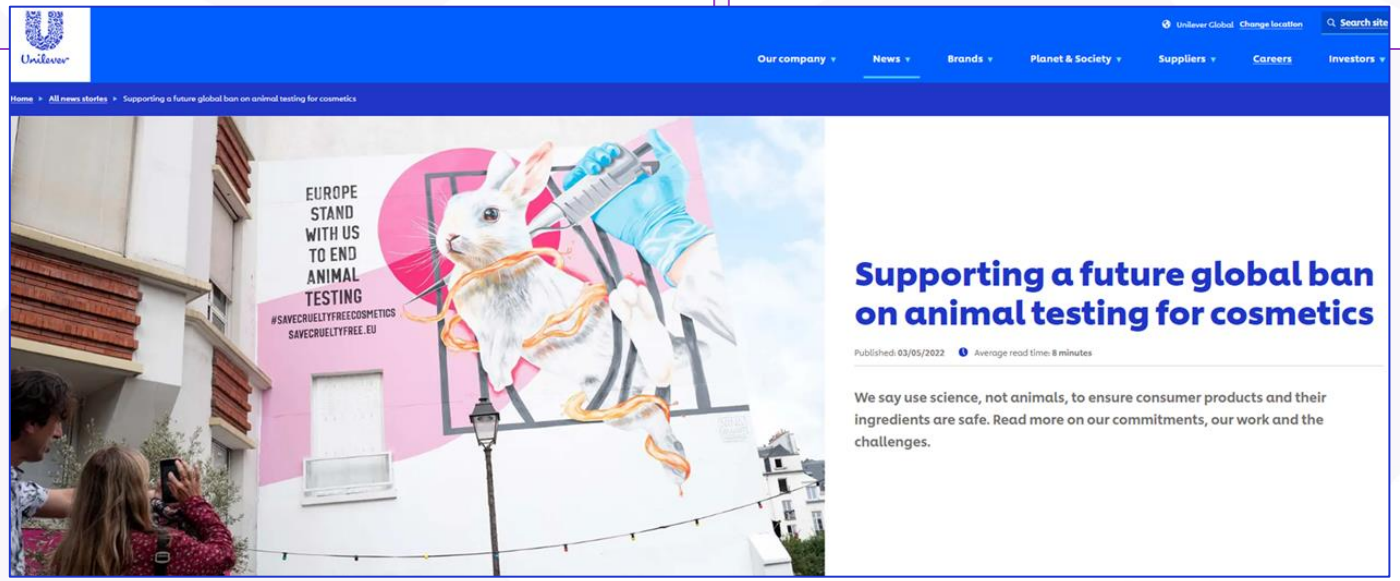
ECHA requesting more animal testing of existing ingredients

- EU ban on selling cosmetics including ingredients tested on animals was implemented in 2013 – ingredients cannot be used if they have been tested on animals anywhere in the world.
- Today, ECHA mandating new animal tests in the EU on hundreds of chemical ingredients in consumer products that have been used and manufactured safely for years – including those used solely in cosmetics.

Taking a stand …

- Along with animal protection NGOs, Unilever and other companies / brands have taken a very public stand against animal testing for cosmetic ingredients

Open Letter: Cosmetics Animal Testing Ban Effectively Shredded



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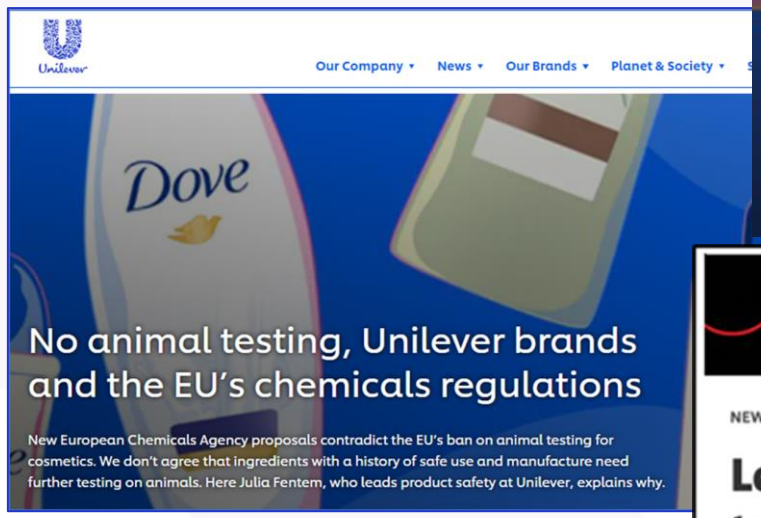
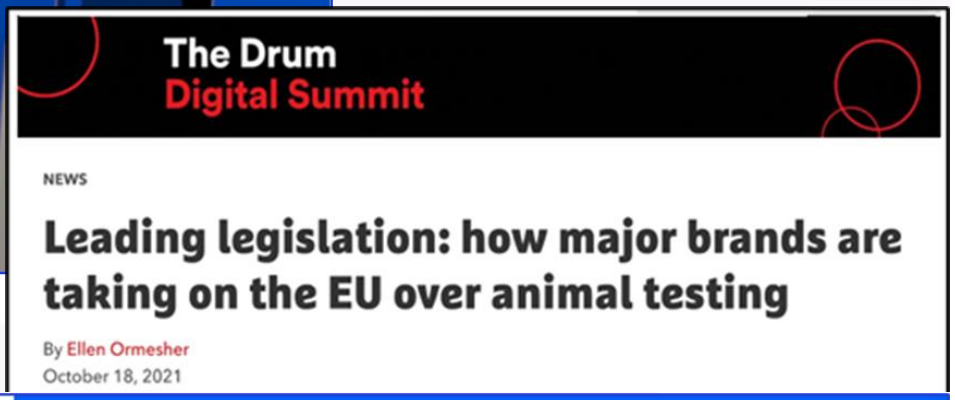
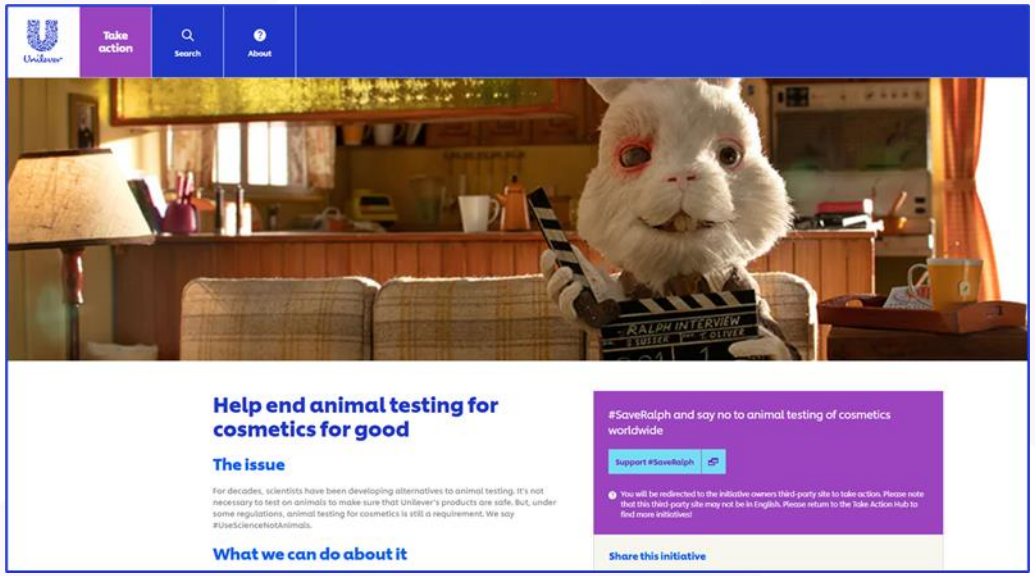
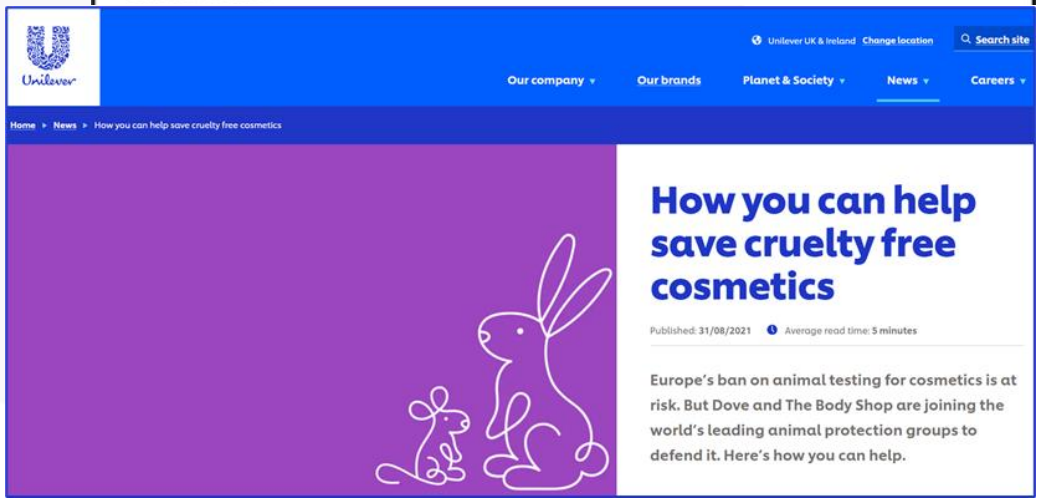
Transformational change requires activism & public engagement - scientists advocating with the animal protection NGOs & brands









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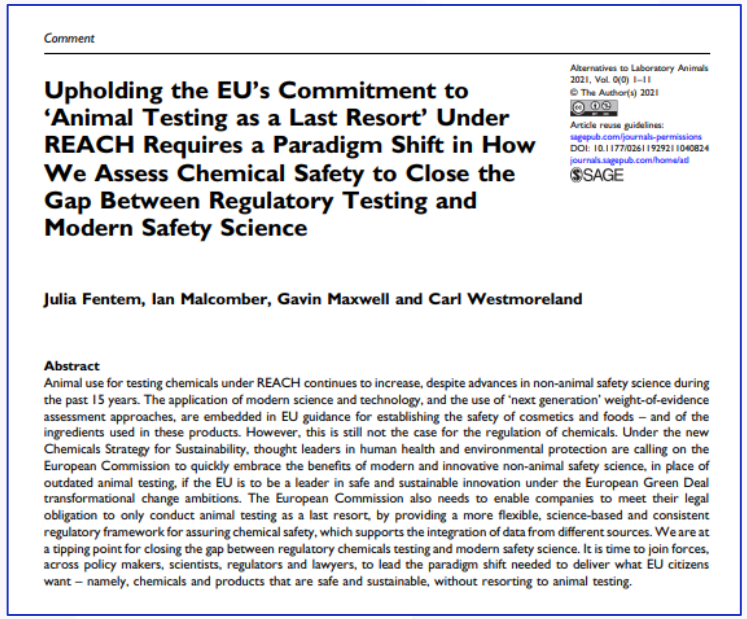
NAMs and REACH / EU Chemicals Strategy for Sustainability

- **Whilst NAMs are increasingly used for safety assessment purposes, their application in chemicals registration remains limited**
- Failure of ECHA to implement 'animal testing as a last resort'
- New animal testing requested for widely used existing chemicals under REACH
- Inconsistency in EU approaches for establishing product and ingredient (chemical) safety
- **Re-thinking the EU's approach to chemical safety**



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. 0(0) 1–11

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

Julia Fentem, Ian Malcomber, Gavin Maxwell and Carl Westmoreland

Abstract

Animal use for testing chemicals under REACH continues to increase, despite advances in non-animal safety science during the past 15 years. The application of modern science and technology, and the use of 'next generation' weight-of-evidence assessment approaches, are embedded in EU guidance for establishing the safety of cosmetics and foods – and of the ingredients used in these products. However, this is still not the case for the regulation of chemicals. Under the new Chemicals Strategy for Sustainability, thought leaders in human health and environmental protection are calling on the European Commission to quickly embrace the benefits of modern and innovative non-animal safety science, in place of outdated animal testing, if the EU is to be a leader in safe and sustainable innovation under the European Green Deal transformational change ambitions. The European Commission also needs to enable companies to meet their legal obligation to only conduct animal testing as a last resort, by providing a more flexible, science-based and consistent regulatory framework for assuring chemical safety, which supports the integration of data from different sources. We are at a tipping point for closing the gap between regulatory chemicals testing and modern safety science. It is time to join forces, across policy makers, scientists, regulators and lawyers, to lead the paradigm shift needed to deliver what EU citizens want – namely, chemicals and products that are safe and sustainable, without resorting to animal testing.

European Union

European Citizens' Initiative

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.

ECHA
EUROPEAN CHEMICALS AGENCY

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.

Unilever

Closing the Science – Regulatory Use Gap

Safety scientists are calling for paradigm shift & regulatory change - safe & sustainable ingredients without animal testing

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

Julia Fentem, Ian Malcomber, Gavin Maxwell and Carl Westmoreland

Archives of Toxicology
https://doi.org/10.1007/s00204-021-03215-9

REGULATORY TOXICOLOGY

A framework for chemical safety assessment incorporating new approach methodologies within REACH

Nicholas Ball[1] · Remi Bars[2] · Philip A. Botham[3] · Andreea Cuciureanu[4] · Mark T. D. Cronin[5] · John E. Doe[5] · Tatsiana Dudzina[6] · Timothy W. Gant[7] · Marcel Leist[8] · Bennard van Ravenzwaay[9]

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Cosmetics

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

By Kacey Culliney

Cosmetics

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

By Kacey Culliney

Time to re-think & modernise our approach …

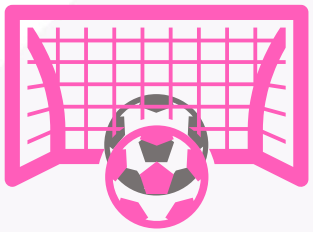
1. Conducting an animal test because it's a (perceived) regulatory requirement isn't adequate scientific justification

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

Unilever

Using advanced science to assess chemical (ingredient) safety
- action needed to accelerate changes to chemicals regulatory frameworks



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

Regulatory compliance
=
Best science to protect people & our environment

- ☑ get creative using relevant NAMs* / scientific data
- ☐ modernise Legal & Regulatory requirements
- ☐ develop NAM-based regulatory frameworks

*NAM = New Approach Methodology

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

Julia Fentem, Ian Malcomber, Gavin Maxwell and Carl Westmoreland

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

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

Some closing thoughts …

1. the NAMs scientific community continues to grow, producing some excellent scientific outputs – new methods, testing strategies, case studies, publications … innovative research & innovation

2. NAMs-based ingredient risk assessments enable decisions on safety, integrating relevant scientific data in weight-of-evidence approaches … leading scientists & influential scientific committees are promoting the use of NAMs & including in their guidance

3. most regulatory decision-makers & chemicals safety policy leaders are considerably less familiar with advanced safety science / NAMs … and are increasingly resistant to changing from traditional animal testing

→ if we want our safety science / NAMs to have impact in better protecting people & our environment and enabling safer use of chemicals, we need to play our part in closing the gap, building confidence in the use of NAMs and helping drive regulatory / policy change – outreach, training, guidance … **activist NAMs scientists advocating for change**

Unilever