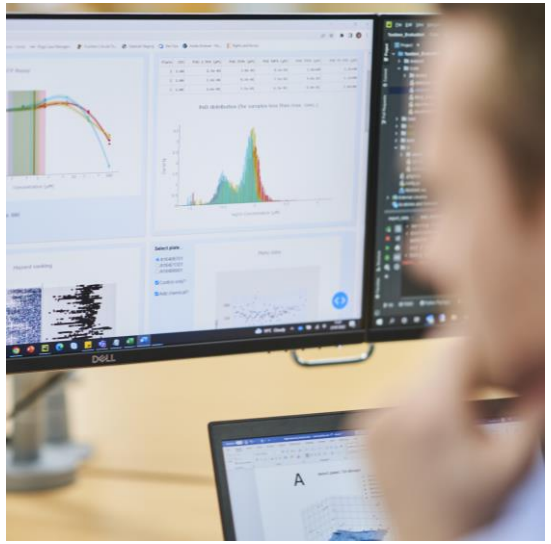
Accelerating the Transition to Animal-Free Safety Assessment

What can we learn from the Cosmetics Animal Testing bans?

Gavin Maxwell, Julia Fentem, Ian Malcomber & Carl Westmoreland - SEAC, Unilever



Unilever

Unilever Policy & Approach
Safe & Sustainable Products without Animal Testing

We say use science. Not animals.

What we believe

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

How we do it

40+ years of developing non-animal safety science

70+ collaborations

600+ publications





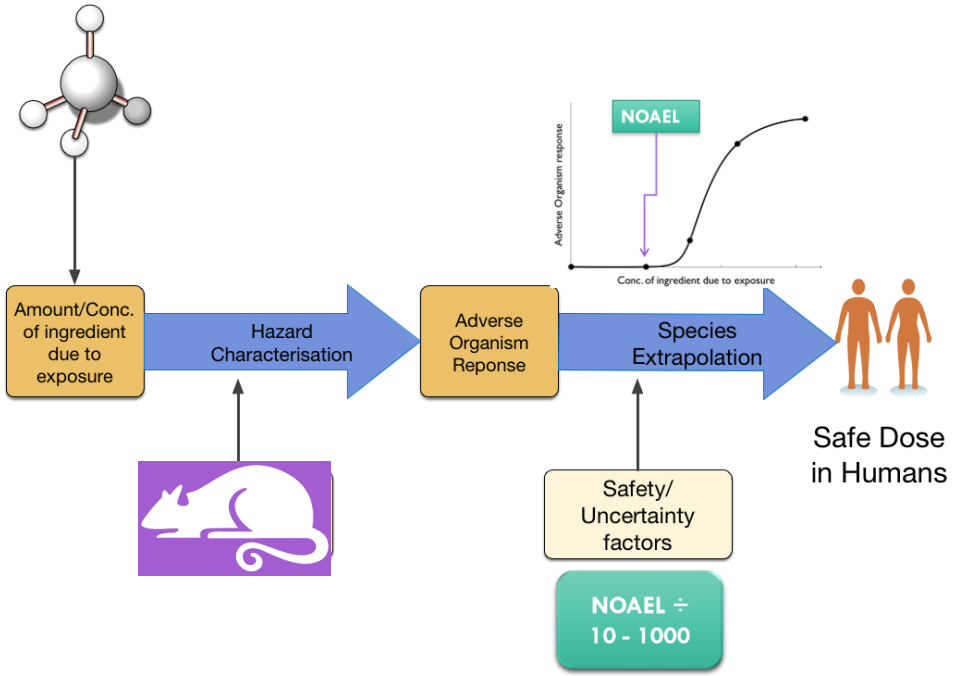

Unilever

44 countries have banned animal testing for Cosmetics so far...

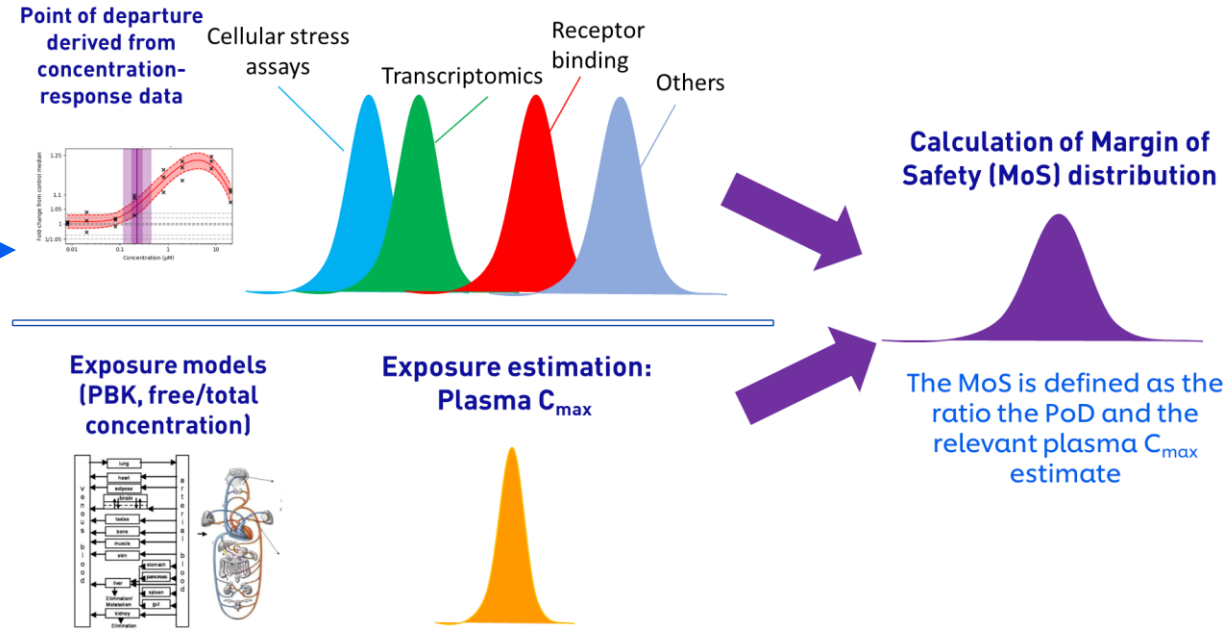
https://www.afsacollaboration.org/cosmetics-global-regulatory-alignment/

Transition to Animal-free Safety Assessment = implementing the NGRA paradigm shift in Regulatory frameworks, globally

'Traditional' Risk Assessment



'Next Generation' Risk Assessment



Unilever

Q: Have Cosmetic Animal Testing bans accelerated the transition to Animal-Free Safety Assessment?

A: ☑ **Collaborative Research (Academic, Industry, Govt, Regulator)**

SEURAT-1

COSMETICS EUROPE LRSS

Cosmetics Europe
the personal care association

EUTOXRISK

ASPIS

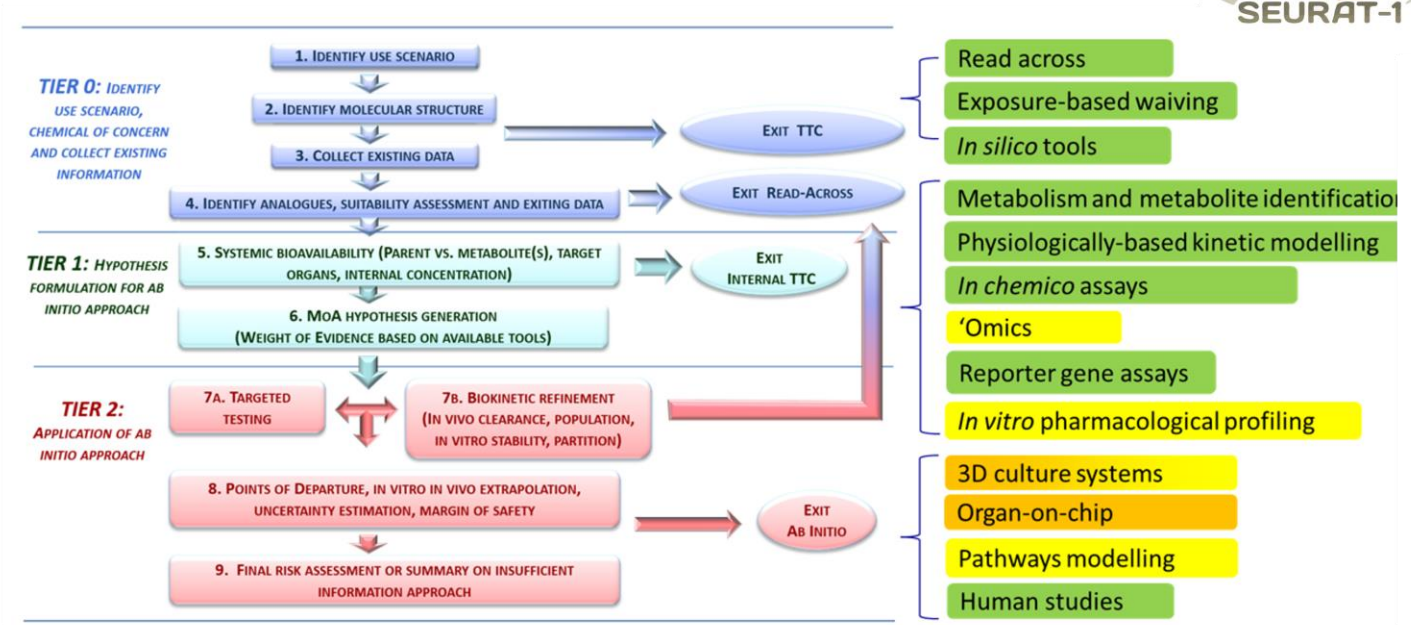
ONTOX

RISK HUNT3R

PRECISION TOX

ICCS INTERNATIONAL COLLABORATION ON COSMETICS SAFETY

SEURAT-1 NGRA framework: tiered testing to support human health safety assessment



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

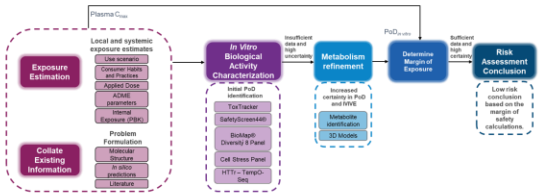
Unilever

Q: Have Cosmetic Animal Testing bans accelerated the transition to Animal-Free Safety Assessment?

A: ☑ **Internal Company Investment (capability-build, governance, upskilling, recruitment)**

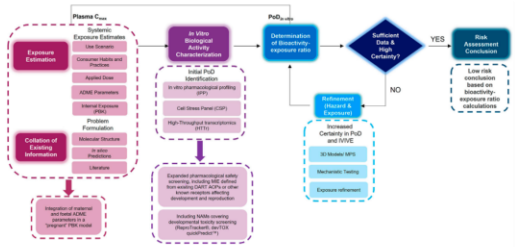
Unilever NGRA frameworks for Consumer Safety decisions

Systemic



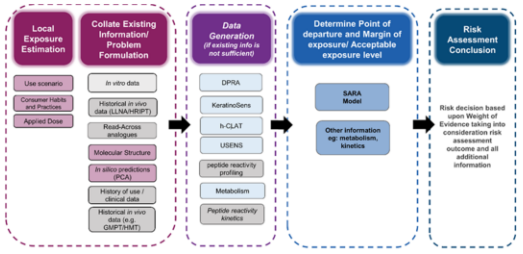
Baltazar et al (2020) *Toxicol Sci*, 176, 236-252

Developmental & Reproductive



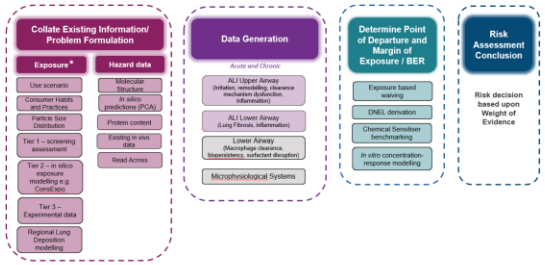
Rajagopal et al (2022) *Frontiers in Toxicology*, doi: 10.3389/ftox.2022.838466

Skin Sensitisation

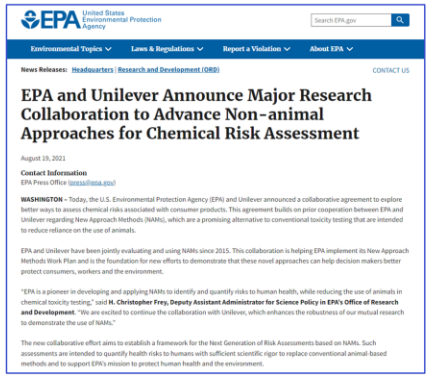


Reynolds et al (2021) *Reg Tox Pharmacol*, **127**, 105075

Inhalation



Ongoing Evaluations



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

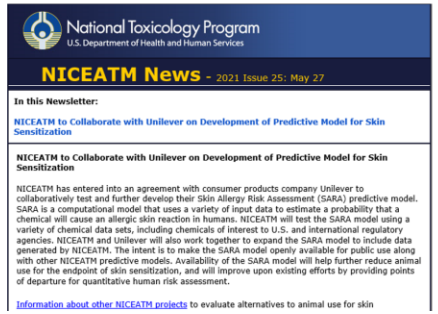
August 19, 2021

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

EPA and Unilever have been jointly evaluating and using NAMs since 2015. This collaboration is helping EPA implement its New Approach Methods Work Plan and is the foundation for new efforts to demonstrate that these novel approaches can help decision makers better protect consumers, workers and the environment.

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

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



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

Modern safety team is truly multi-disciplinary:

- Cell Biology
- Chemistry
- Computational Modelling
- Environmental Safety
- Exposure Science
- Informatics & Data Science
- Mathematics
- Microbiology
- Molecular Biology
- Process Safety
- Statistics
- Toxicology

Unilever

Q: Have Cosmetic Animal Testing bans accelerated the transition to Animal-Free Safety Assessment?

A: ☑ Regulatory Acceptance – Cosmetics (exposure-based use of NAMs for NGRA)

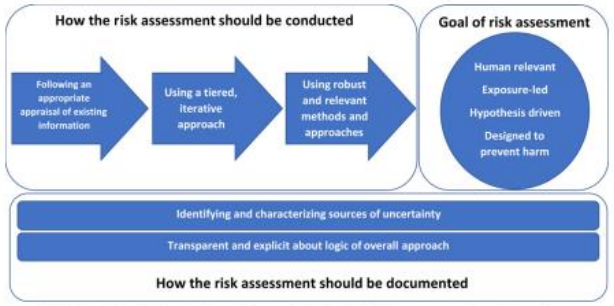


Fig. 1. Principles underpinning the use of new methodologies in the risk assessment of cosmetic ingredients.

4 Main overriding principles:

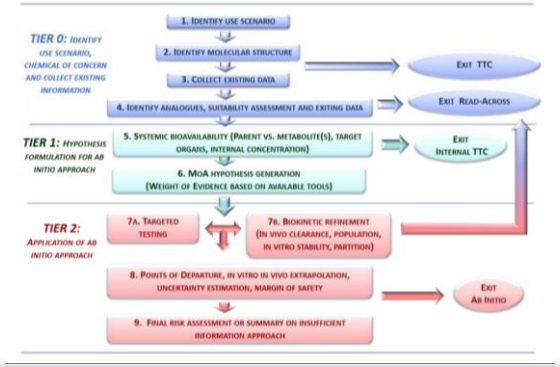
- The overall goal is a human safety risk assessment
- The assessment is exposure led
- The assessment is hypothesis driven
- The assessment is designed to prevent harm

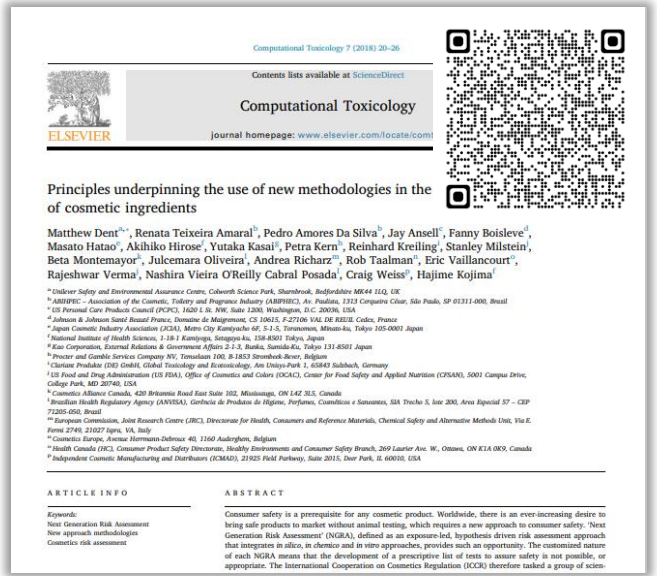
3 Principles describe how a NGRA should be conducted:

- Following an appropriate appraisal of existing information
- Using a tiered and iterative approach
- Using robust and relevant methods and strategies

2 Principles for documenting NGRA:

- Sources of uncertainty should be characterized and documented
- The logic of the approach should be transparent and documented





Computational Toxicology 7 (2018) 20–26

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Computational Toxicology

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ELSEVIER

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

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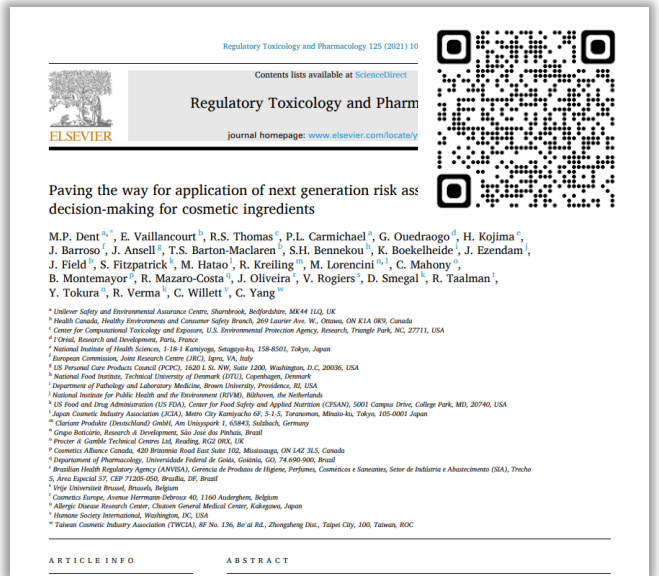
ARTICLE INFO

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

ABSTRACT

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



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ELSEVIER

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

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[l] Japan Cosmetic Industry Association (JCIA), Metro City Kamiyacho 6F, 5-1-5, Toranomon, Minato-ku, Tokyo, 105-0001 Japan
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ARTICLE INFO

ABSTRACT

European Commission

Scientific Committee on Consumer Safety

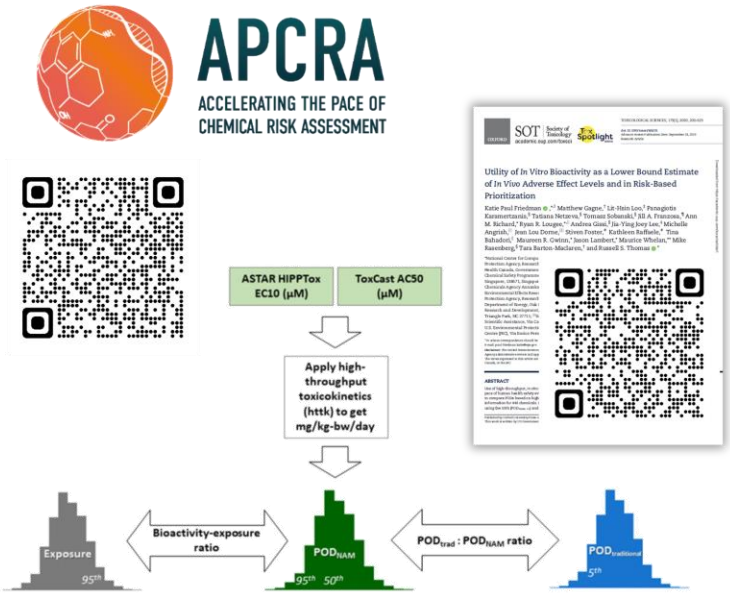
SCCS

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

12TH REVISION

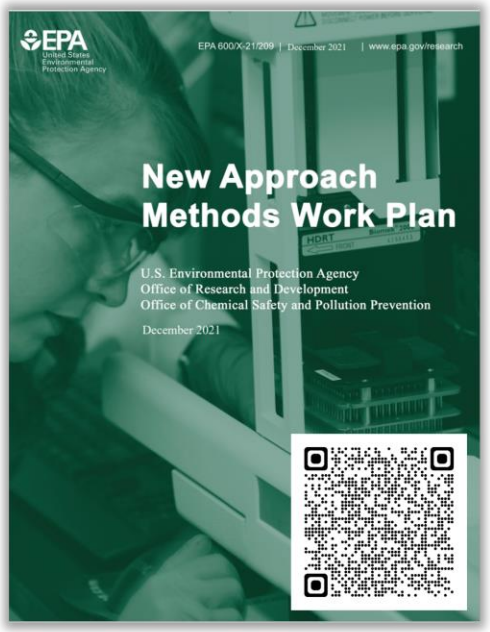
Q: Have Cosmetic Animal Testing bans accelerated the transition to Animal-Free Safety Assessment?

A: ☐ Regulatory Acceptance – Chemicals (OECD TGs, UN GHS, Chemical Regulations)

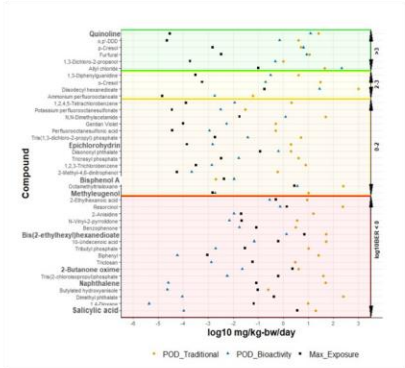


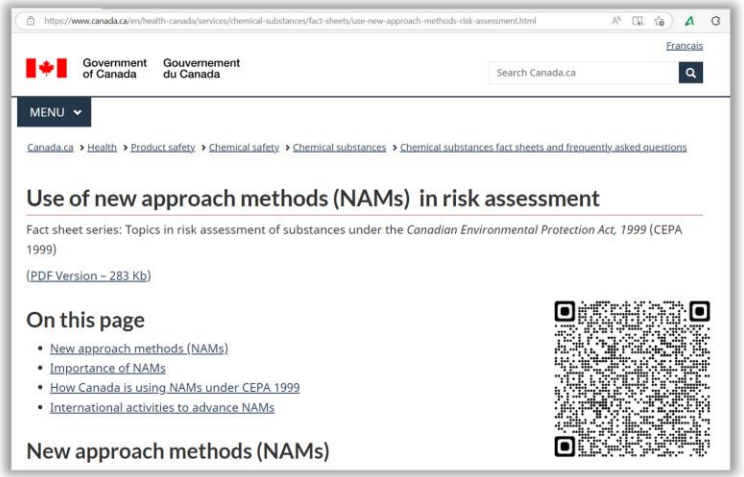
Paul Friedman et al. 2020

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



New Approach Methods Work Plan (epa.gov)





Q: So, what's the impact of Cosmetics regulations transitioning faster than Chemical regulations?

A: For example, in Europe …

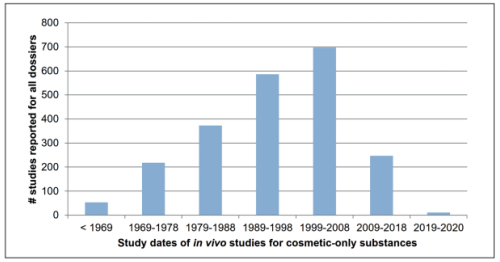


Fig. 1: All *in vivo* studies reported in cosmetic-only dossiers by study or report date as indicated in the ECHA database
Includes studies reported in publications; most of these pre-date 2009. The interval was selected to be consistent with the period when REACH was implemented in the EU. REACH was published in 2006 and entered into force in 2008. Companies started implementing it in 2009, and the first registration deadline was in 2010.

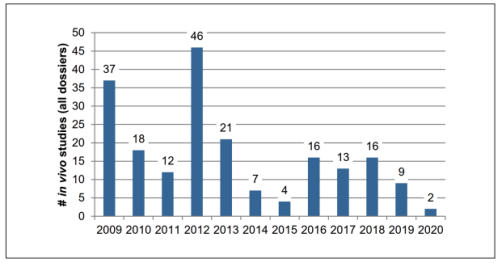
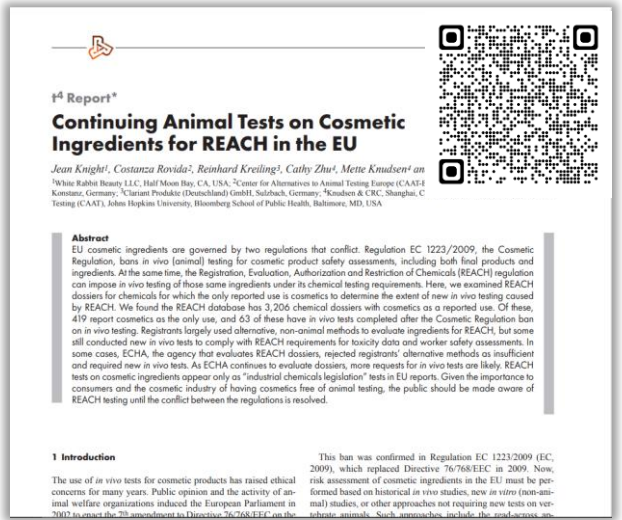


Fig. 2: Number of unique *in vivo* tests for cosmetic-only substances in 2009-2020 extracted from the ECHA database
The total number shown, 201, excludes 16 studies reported in dossiers or by registrants as being for a non-REACH purpose, indicating either a dual use or compliance with a non-EU country.



t4 Report*

Continuing Animal Tests on Cosmetic Ingredients for REACH in the EU

Jean Knight[1], Costanza Rovida[2], Reinhard Kreiling[3], Cathy Zhu[4], Mette Knudsen[4] an

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Abstract

EU cosmetic ingredients are governed by two regulations that conflict. Regulation EC 1223/2009, the Cosmetic Regulation, bans *in vivo* (animal) testing for cosmetic product safety assessments, including both final products and ingredients. At the same time, the Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) regulation can impose *in vivo* testing of those same ingredients under its chemical testing requirements. Here, we examined REACH dossiers for chemicals for which the only reported use is cosmetics to determine the extent of new *in vivo* testing caused by REACH. We found the REACH database has 3,206 chemical dossiers with cosmetics as a reported use. Of these, 419 report cosmetics as the only use, and 63 of these have *in vivo* tests completed after the Cosmetic Regulation ban on *in vivo* testing. Registrants largely used alternative, non-animal methods to evaluate ingredients for REACH, but some still conducted new *in vivo* tests to comply with REACH requirements for toxicity data and worker safety assessments. In some cases, ECHA, the agency that evaluates REACH dossiers, rejected registrants' alternative methods as insufficient and required new *in vivo* tests. As ECHA continues to evaluate dossiers, more requests for *in vivo* tests are likely. REACH tests on cosmetic ingredients appear only as "industrial chemicals legislation" tests in EU reports. Given the importance to consumers and the cosmetic industry of having cosmetics free of animal testing, the public should be made aware of REACH testing until the conflict between the regulations is resolved.

1 Introduction

The use of *in vivo* tests for cosmetic products has raised ethical concerns for many years. Public opinion and the activity of animal welfare organizations induced the European Parliament in 2002 to enact the 7th amendment to Directive 76/768/EEC on the

This ban was confirmed in Regulation EC 1223/2009 (EC, 2009), which replaced Directive 76/768/EEC in 2009. Now, risk assessment of cosmetic ingredients in the EU must be performed based on historical *in vivo* studies, new *in vitro* (non-animal) studies, or other approaches not requiring new tests on vertebrate animals. Such approaches include the read-across ap-

Save Cruelty Free Cosmetics

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

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

European Commission - Press release

Commission acts to accelerate phasing out of animal testing in response to a European Citizens' Initiative

Brussels, 25 July 2023

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

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

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

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

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

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

Q: So… what can we learn?

A: We need multi-stakeholder, multi-sector roadmaps to transition to Animal-Free Safety Assessment, globally to…

Regulators **CROs & Consultants**

Industry **Academics**

NGOs

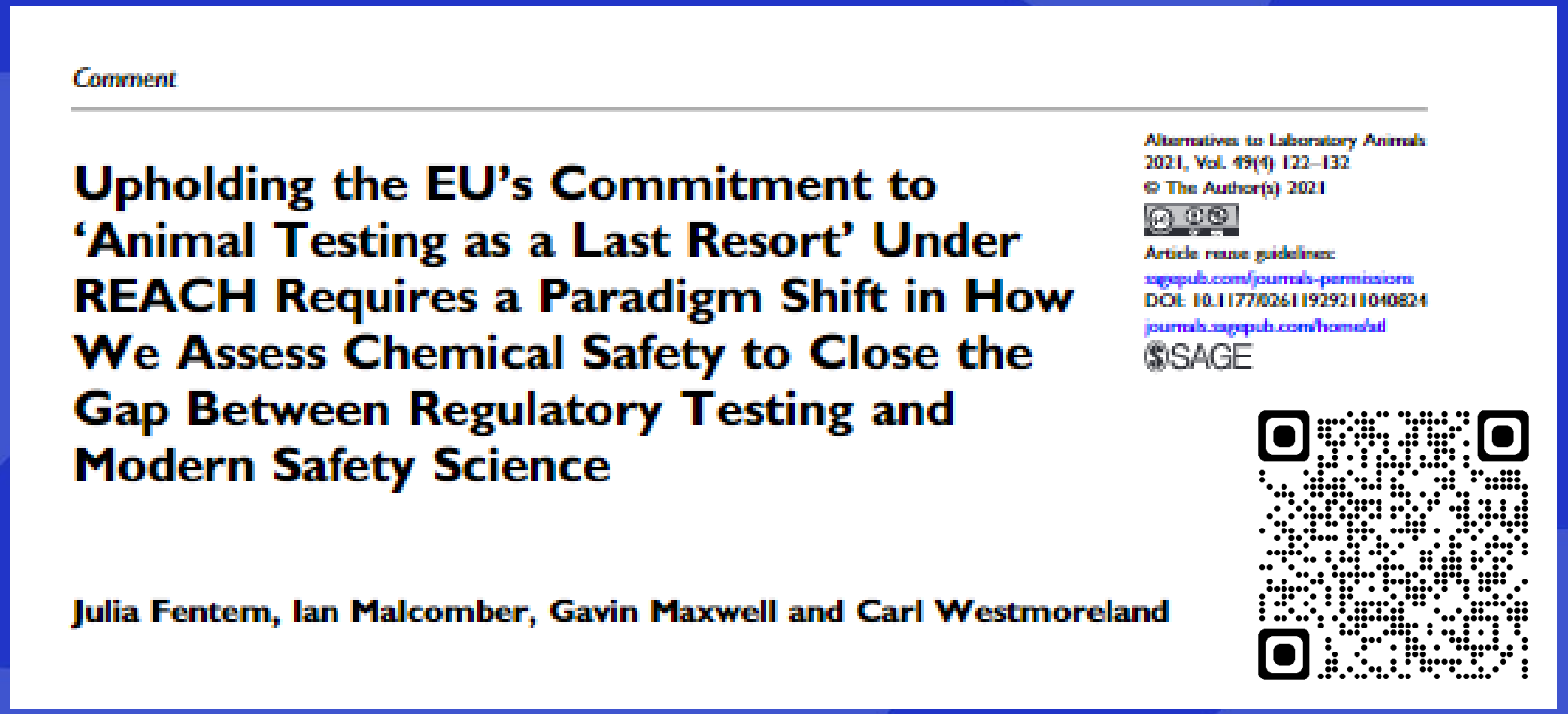
1. **Facilitate scientific dialogue** on NAM use between industry & regulatory scientists using **NGRA/IATA case studies to accelerate knowledge exchange**
2. **Re-focus validation** on building confidence in regulatory use of NAMs, using **NGRA/IATA case studies to ensure NAMs are fit for purpose & protective in use**
3. **Drive investment in Next-Gen Education** to help existing and future industry safety assessors & regulators **build Next Gen Safety Science skills & knowledge**

Unilever

Thank You for your attention!

Acknowledgements:

Julia Fentem, Ian Malcomber & Carl Westmoreland



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

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