Safe and Sustainable Innovation approaches and the role NAMs play – experience from Unilever

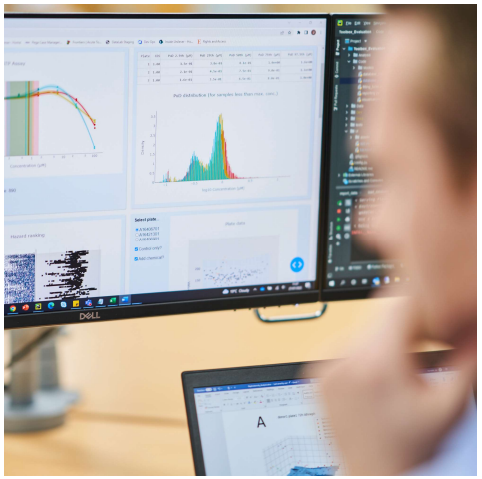
OECD SG SSIA, 24th Oct 23

Ian Malcomber

Head of Ingredient Stewardship

Safety & Environmental Assurance Centre

Unilever R&D



Unilever

Unilever: We make many of the world's favourite brands

Over **400** brands

13 of the top **50** consumer goods brands

14 brands with turnover over €1bn

Available in over **190** countries

3.4b people use our products every day

Unilever's Safety & Environmental Assurance Centre (SEAC)

SEAC is Unilever's global centre of excellence in Safety & Sustainability Sciences

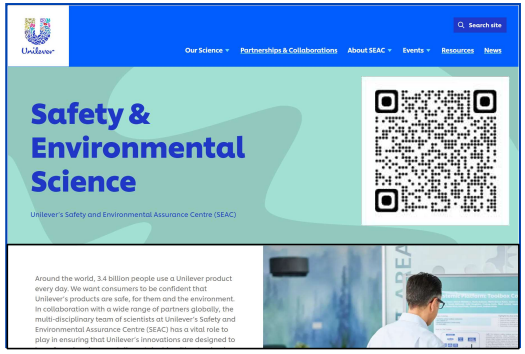
Diverse, multi-disciplinary team of ~150 scientists based at Colworth, UK; ~70 miles north of London

Highly collaborative, working with >70 academic, industry, government & NGO partners worldwide

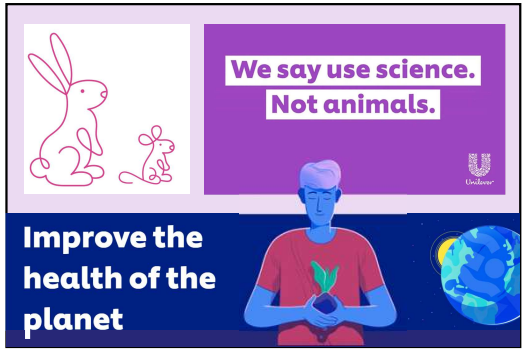
Our purpose is to protect people & the environment by ensuring:

1 Unilever's products & innovations are **Safe & Sustainable by Design without animal testing**

2 Our scientists & capabilities are **industry-leading & we apply this to Unilever's Products & Brands**



3 Safety & Env. Sustainability **policies & regulations are based on modern science**

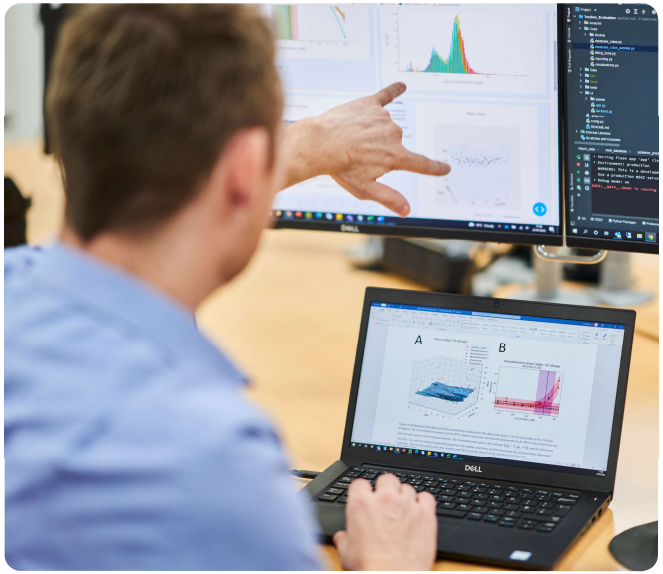


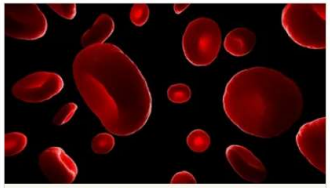
Unilever

Safety without Animal Testing:

- **Unilever is committed to ending animal testing globally**. We believe in using science, not animals, to assure the safety of our products and their ingredients.
- **Non-animal safety approaches are applied by our multi-disciplinary scientists** in collaboration with world-class researchers & experts.
- These partnerships, combined with our expertise, **enable us to protect people and the environment without animal testing**.

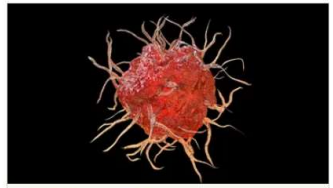
https://seac.unilever.com/our-science/safety-without-animal-testing/





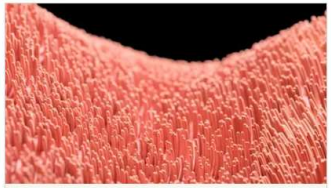
Systemic Safety

To understand the safety of ingredients if they are absorbed into the body (systemic safety), we do not use an animal study to...



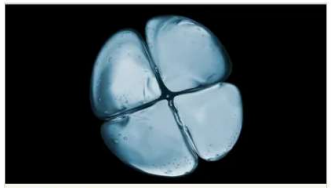
Skin Allergy Safety

Some ingredients used in consumer products have the potential to cause allergic contact dermatitis (ACD), a type of skin allergy. To...



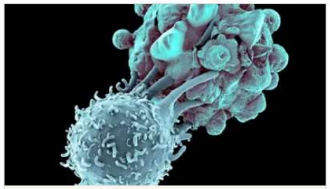
Inhalation Safety

A significant proportion of Unilever's products are aerosols and sprays which include underarm antiperspirants, hair sprays...



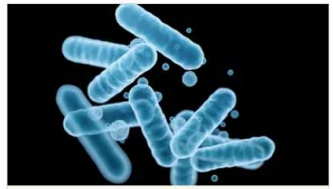
DART Safety

Developmental and reproductive toxicity (DART) refers to potential adverse effects that exposure to an ingredient may have on ...



Immune Effects Safety

We consider all potential adverse impacts on the human immune system resulting from exposure to an ingredient. These include...

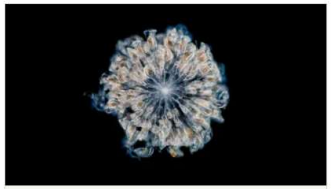


Microbiological Safety

Some of our consumer products have the potential to change the human microbiome or raise microbiological concerns...

Environmental Safety

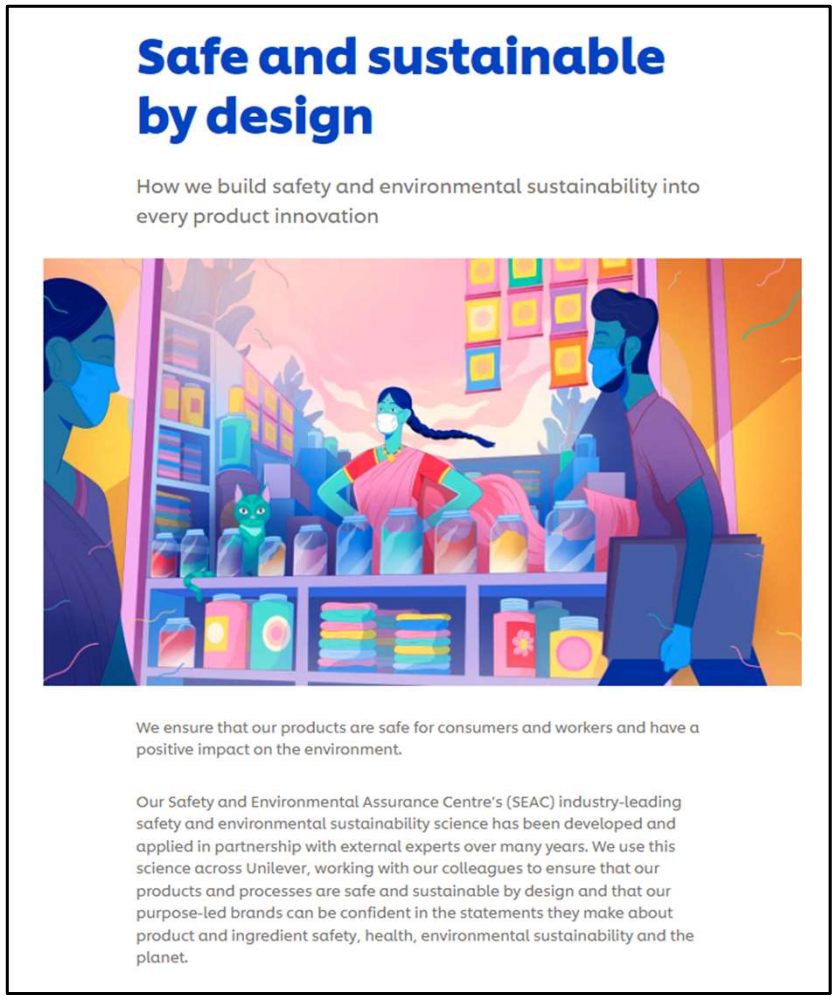
Unilever ingredients are often disposed of down the drain after use, so it is important for us to assess the environmental safety of...



Biodegradation

Biodegradation is the process in which an ingredient is broken down through natural processes by microorganisms into simple substances...

Safe & Sustainable Innovation has long been embedded into Unilever



Safe and sustainable by design

How we build safety and environmental sustainability into every product innovation

We ensure that our products are safe for consumers and workers and have a positive impact on the environment.

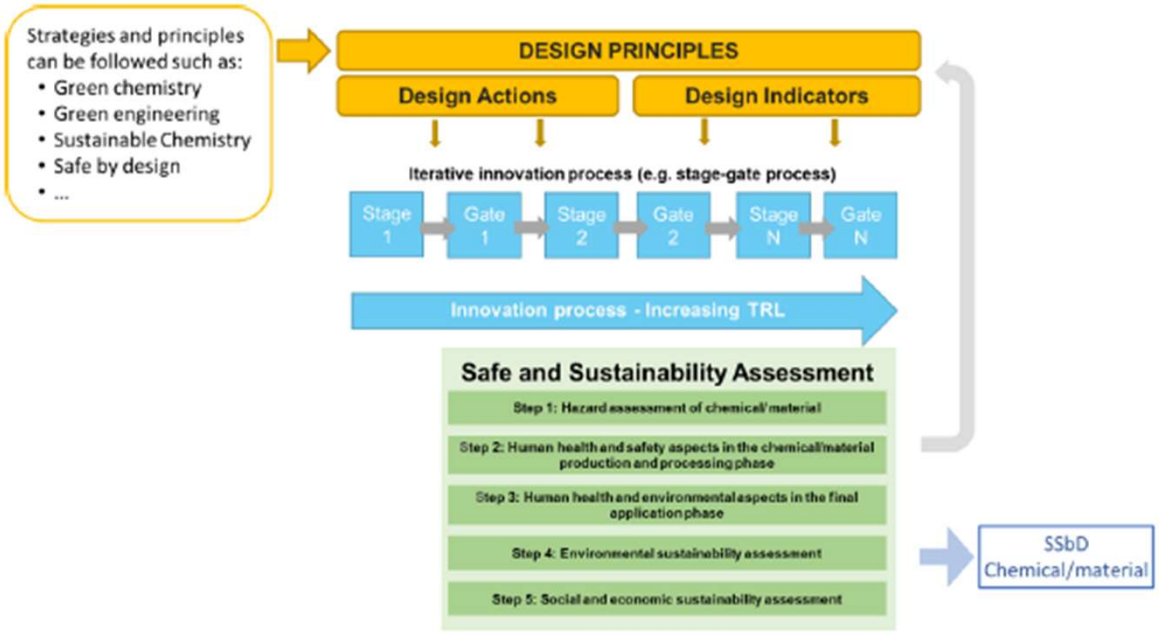
Our Safety and Environmental Assurance Centre's (SEAC) industry-leading safety and environmental sustainability science has been developed and applied in partnership with external experts over many years. We use this science across Unilever, working with our colleagues to ensure that our products and processes are safe and sustainable by design and that our purpose-led brands can be confident in the statements they make about product and ingredient safety, health, environmental sustainability and the planet.

https://www.unilever.com/planet-and-society/safety-and-environment/safe-and-sustainable-by-design/

- Corporate Strategy provides the 'North Star'
- Brand strategy engagement on long term innovation needs
- Innovation programme review & influence
- Early & ongoing involvement in innovation projects (concept ➔ post market launch)
- Guidance, digital systems & tools
- Corporate Code Policy (Responsible Innovation) & Standards

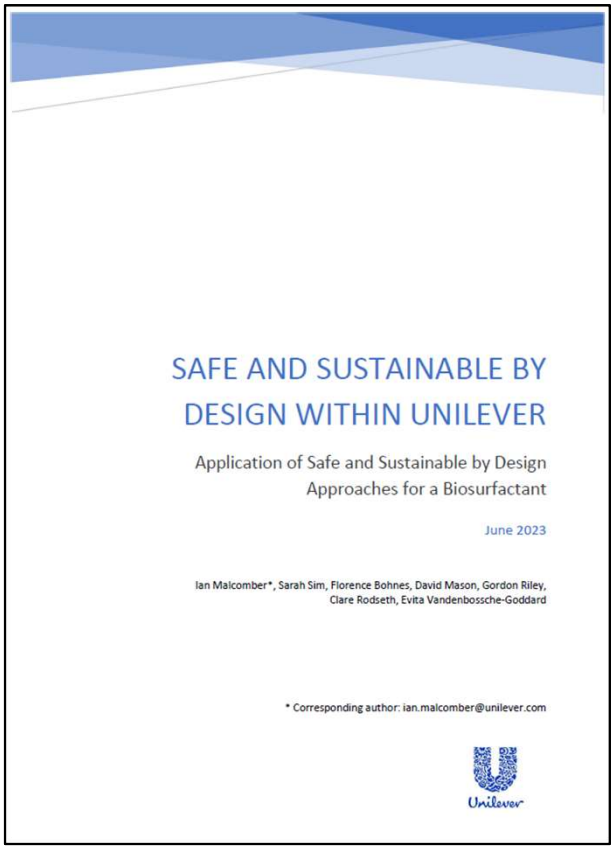
Unilever

SSbD Frameworks in Development: EU



From: https://research-and-innovation.ec.europa.eu/research-area/industrial-research-and-innovation/key-enabling-technologies/chemicals-and-advanced-materials/safe-and-sustainable-design_en

Unilever SSbD Case Study: Overview of typical safety and sustainability approaches used by Unilever throughout innovation stages for a biosurfactant



SAFE AND SUSTAINABLE BY DESIGN WITHIN UNILEVER

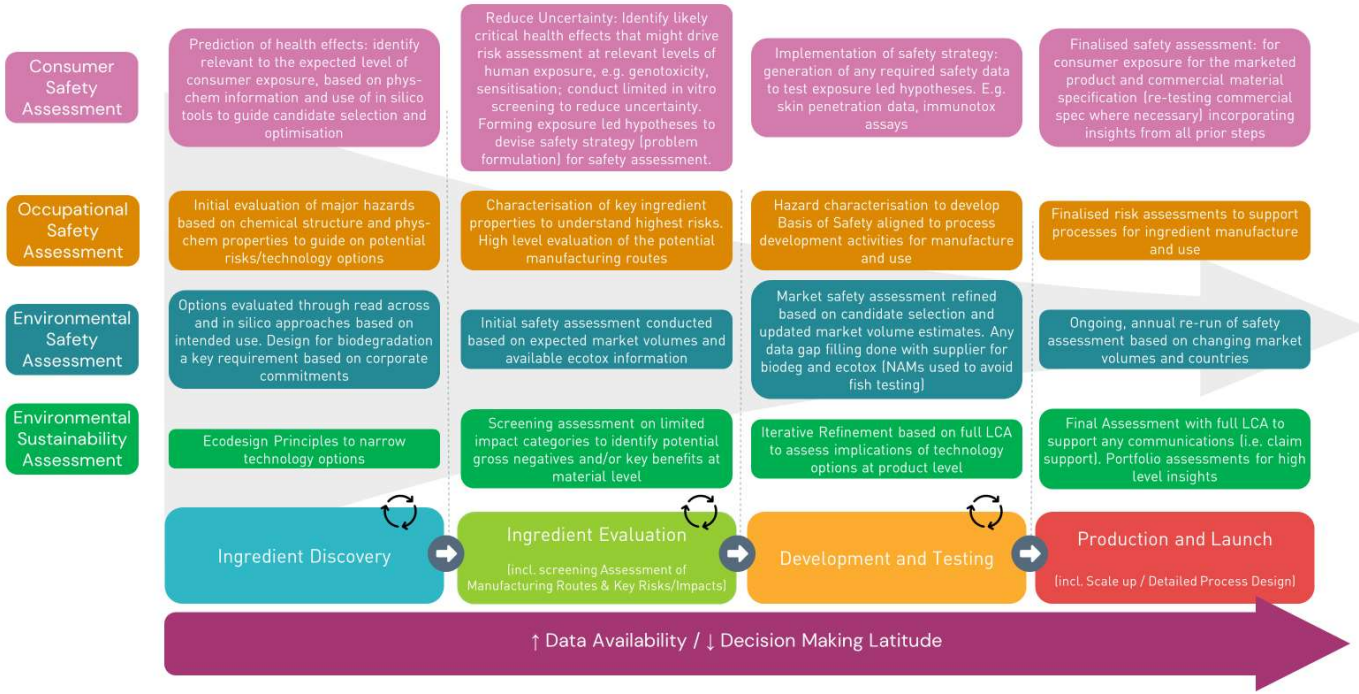
Application of Safe and Sustainable by Design Approaches for a Biosurfactant

June 2023

Ian Malcomber*, Sarah Sim, Florence Bohnes, David Mason, Gordon Riley, Clare Rodseth, Evita Vandenbossche-Goddard

* Corresponding author: ian.malcomber@unilever.com

Unilever



Unilever

https://seac.unilever.com/files/92ui5egz/production/6814727012110f78df6380f9d5d0f28c029218b4.pdf

Unilever supports the development of Safe & Sustainable Innovation frameworks that drives a paradigm shift in the use of non-animal safety science and embeds environmental sustainability in chemical innovation

Our view on the priority challenges on the implementation of a SSbD Framework:

1. Workability for all Industry: Build expertise; Develop tools, guidance & training
2. Data Availability: NAMs, Exposure Scenarios, Life Cycle Inventories
3. Staged Assessments: Framework reflecting innovation processes
4. Reconsider Conceptual Framing of Absolute Safety & Sustainability
5. Trade-offs: Approaches needed to manage them within the assessment
6. Priority Needs: Early stage screening (esp. NAMS), Mechanism for new approaches

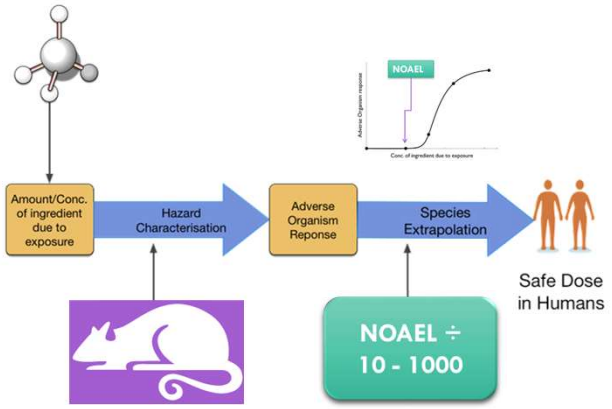
Unilever

A paradigm shift is underway as use of non-animal safety science increases & safety assessment frameworks evolve to embed NGRA

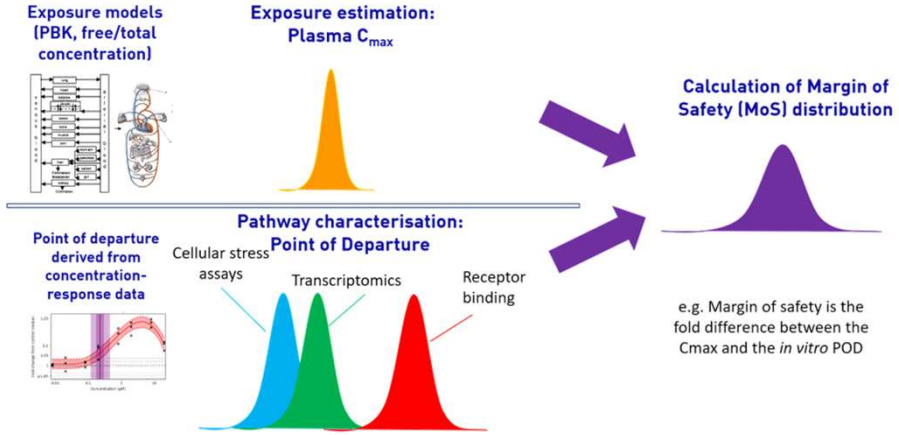
Non-animal safety science is increasingly being used to make decisions on:

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**

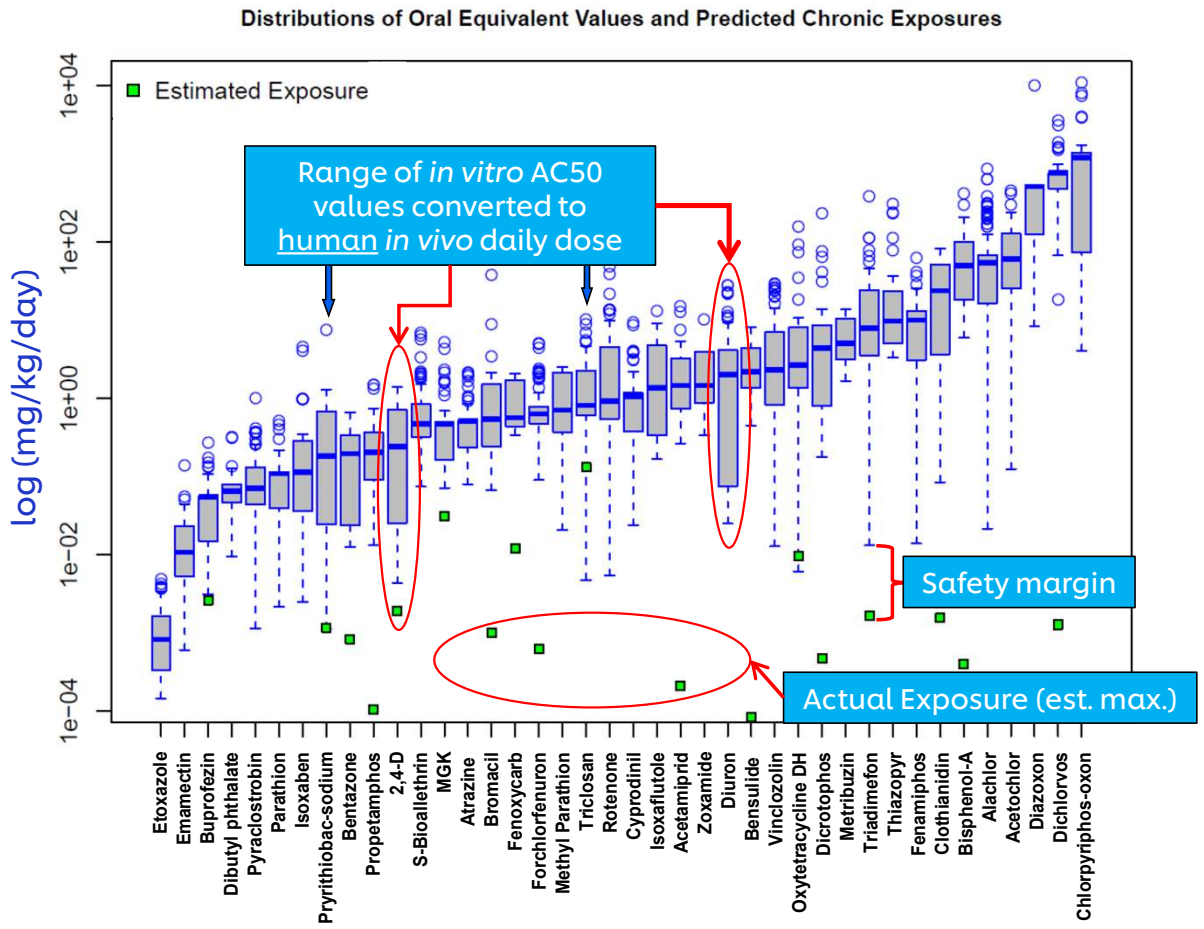
'Traditional' Risk Assessment



'Next Generation' Risk Assessment



Next Generation Risk Assessment (NGRA): aim is protection, not prediction of animal data



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

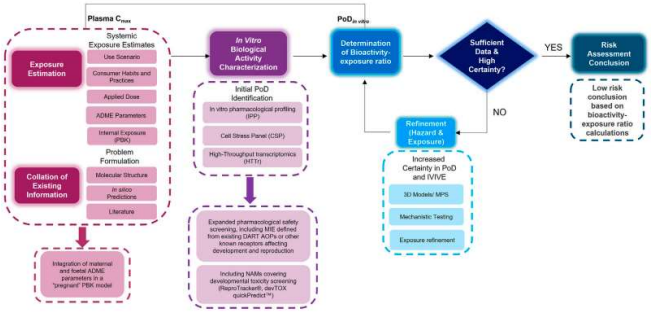
At no point does NGRA attempt to predict the results of high dose toxicology studies in animals.

NGRA **uses new exposure science and understanding of human biology.**

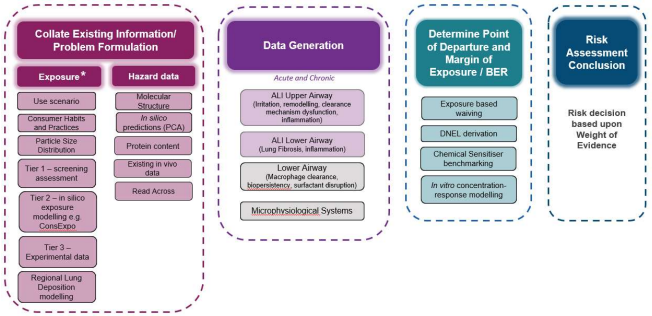
Graph from Rusty Thomas EPA, with thanks. Rotroff *et al* (2010) Toxicological Sciences , **117**, 348-358

Unilever NGRA frameworks for Consumer Safety decisions

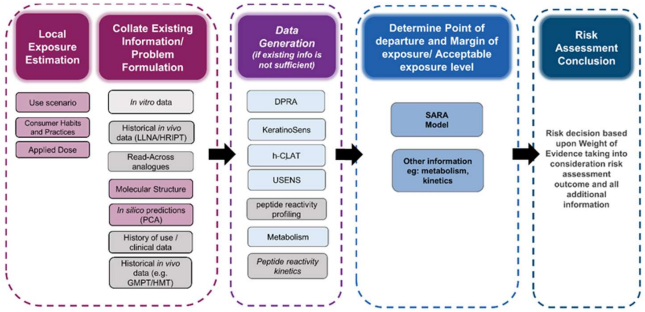
Developmental & Reproductive



Inhalation

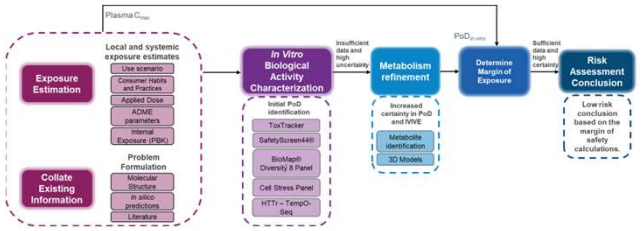


Skin Sensitisation



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

Systemic



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

Ongoing Evaluations

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

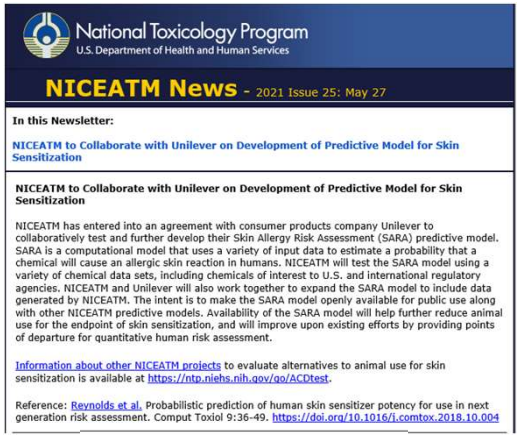
Contact Information
EPA Press Office (press@epa.gov)

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."

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.

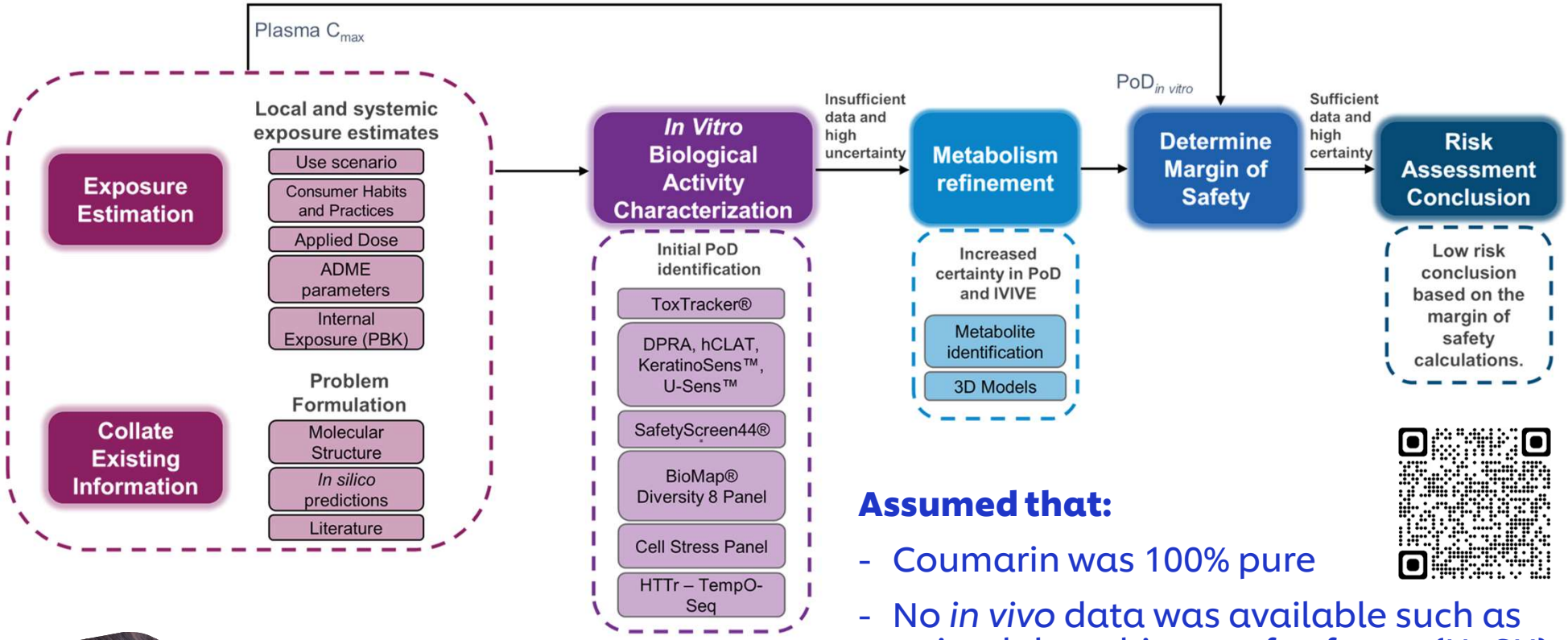
Information about other NICEATM projects to evaluate alternatives to animal use for skin sensitization is available at https://ntp.niehs.nih.gov/go/ACDtest.

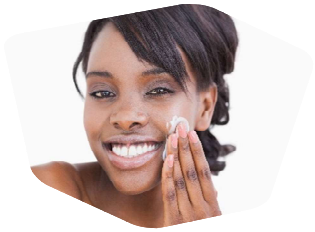
Reference: Reynolds et al. Probabilistic prediction of human skin sensitizer potency for use in next generation risk assessment. Comput Toxiol 9:36-49. https://doi.org/10.1016/j.comtox.2018.10.004

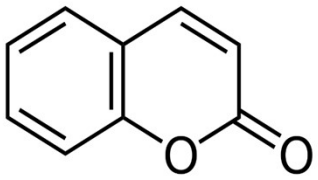
Unilever

OECD

NGRA for Systemic Exposure & Effects through a hypothetical case study:
0.1% coumarin in face cream







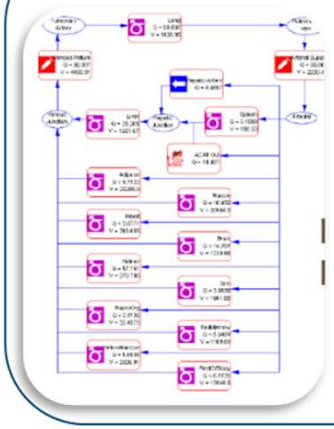
Assumed that:

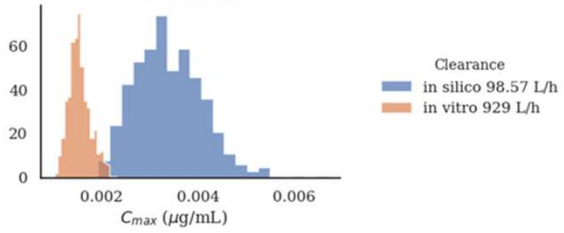
- Coumarin was 100% pure
- No *in vivo* data was available such as animal data, history of safe use (HoSU) or clinical data or use of animal data in read across

Baltazar *et al.*, (2020) *Tox Sci* Volume 176, Issue 1, 236–252

Key NAMs used in Coumarin case study

PBK Modelling





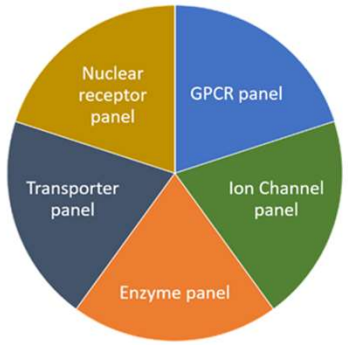
Toxicology in Vitro (2020), **63**, 104746

In vitro pharmacological profiling


PERSPECTIVES

A GUIDE TO DRUG DISCOVERY — OPINION

Reducing safety-related drug attrition: the use of *in vitro* pharmacological profiling

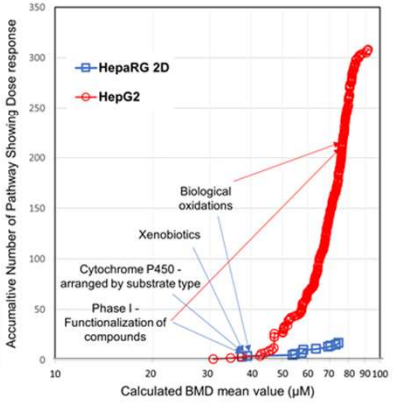


eurofins | Cerep

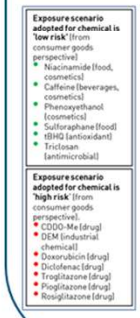
Transcriptomics

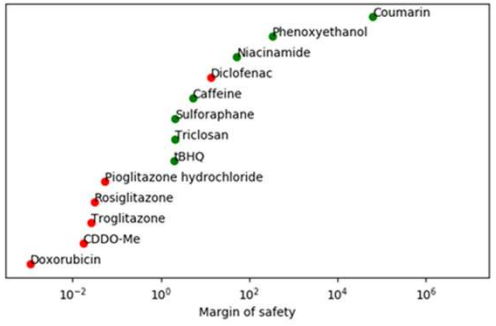
- Use of full human gene panel ~ 21k
- 24 hrs exposure
- 7 concentrations
- 3 cell lines HepG2/ HepaRG/ MCF7
- 3D HepaRG spheroid

BMDexpress 2

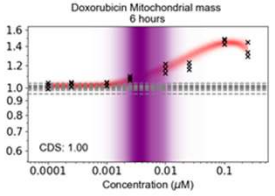


Cellular Stress Pathways





cyprotex AN EVOTEC COMPANY

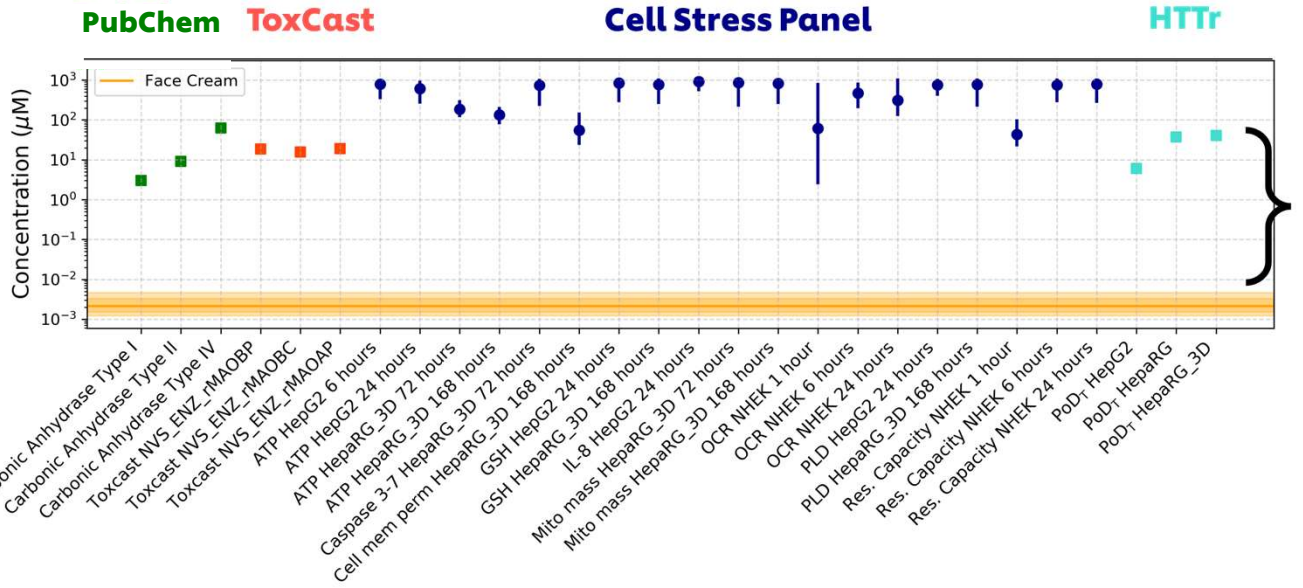


Toxicol Sci (2020), **176**, 11-33

Unilever

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

Determine Margin of Safety



Margin of safety

The 5th percentile of the MoS distribution ranged between 706 and 96738

In this case study:

- **Weight of evidence suggested that the inclusion of 0.1% coumarin in face cream is safe for the consumer**

Baltazar *et al.*, (2020) *Tox Sci* Volume 176, Issue 1, 236–252

What we would like to see in Safe & Sustainable Innovation frameworks

- Acceptance of NAMs tools & approaches allowing flexibility in their use to account for the specifics of the assessment being conducted
- Safety assessed for defined uses considering exposure & any risk management measures (not hazard alone)
  - Example: Enzymes in laundry detergents
- Approaches for considering Trade-offs

Challenge: How to use the latest human relevant safety science in Safe and Sustainable Innovation frameworks that rely on Classification & Labelling criteria based on traditional animal studies?

Unilever

Acknowledgements to many Unilever colleagues especially Carl Westmoreland and Gavin Maxwell

Thank You

seac.unilever.com

Unilever