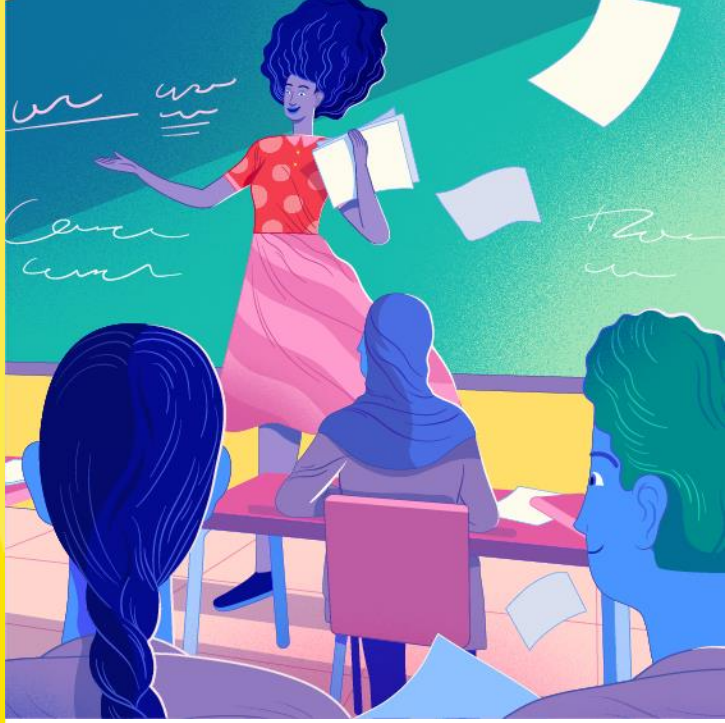
Application of a next generation risk assessment framework for skin sensitisation using new approach methodologies (NAMs)



Renato Ivan de Ávila, PhD

Scientist – Human Safety

Unilever Safety and Environmental Assurance Centre (SEAC)

Unilever

Agenda

1. Assessing ingredient & product safety without animal testing
2. Skin allergy risk assessment evolution
3. Use of Skin Sensitisation Adverse Outcome Pathway (AOP) to develop NAMs
4. Next generation risk assessment (NGRA) framework for skin allergy
5. Skin allergy Risk Assessment (SARA) model
6. Case study: 0.02% (200ppm) geraniol in a face cream
7. Conclusions & Next Steps

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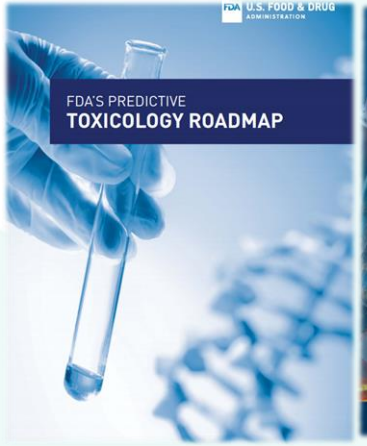
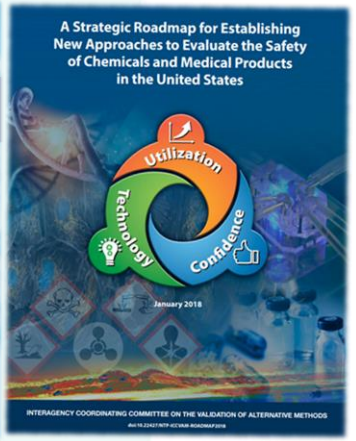
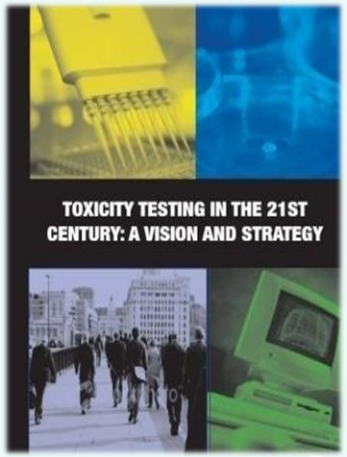
Assessing ingredient & product safety without animal testing

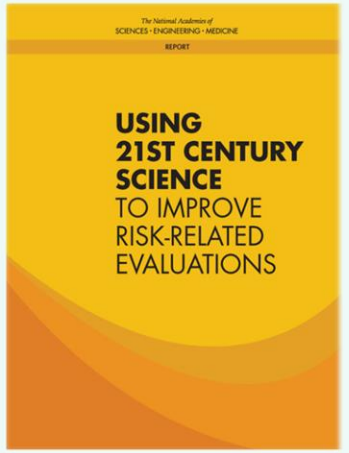
Next Generation Risk Assessment (NGRA)

Is it safe to include x% of chemical y in product z?









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Skin allergy risk assessment evolution

Increased mechanistic understanding

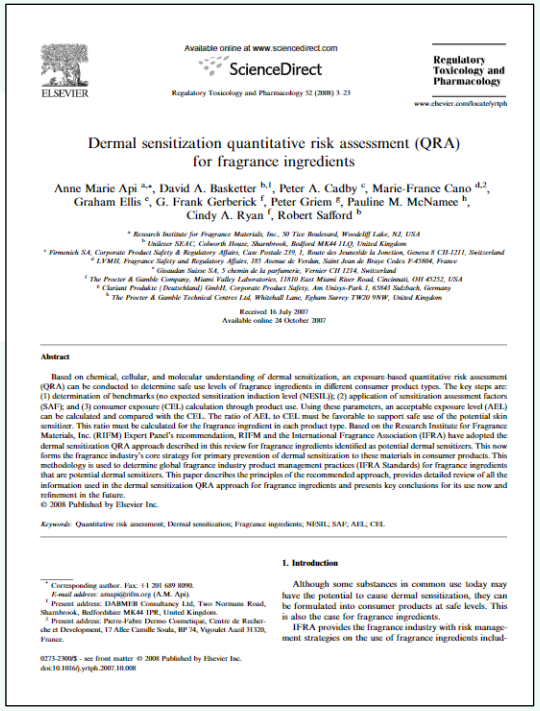
GPMT / Buehler → LLNA → Non-animal test methods

More accurate exposure assessments

Rinse off / Leave on → Individual Products → Aggregate exposure models; new exposure metrics

Increased transparency in risk assessment

Risk benchmarking → QRA (Quantitative Risk Assessment) → Computational / informatics approaches



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Regulatory Toxicology and Pharmacology 52 (2008) 3–23
www.elsevier.com/locate/yrtph

Dermal sensitization quantitative risk assessment (QRA) for fragrance ingredients

Anne Marie Api [a,*], David A. Basketter [b,1], Peter A. Cadby [c], Marie-France Cano [d,2], Graham Ellis [e], G. Frank Gerberick [f], Peter Griem [g], Pauline M. McNamee [h], Cindy A. Ryan [f], Robert Safford [h]

[a] Research Institute for Fragrance Materials, Inc., 50 Tice Boulevard, Woodcliff Lake, NJ, USA
[b] Unilever SEAC, Colworth House, Sharnbrook, Bedford MK44 1LQ, United Kingdom
[c] Firmenich SA, Corporate Product Safety & Regulatory Affairs, Case Postale 239, 1, Route des Jeunes, Geneva 8 CH-1211, Switzerland
[d] LVMH, Fragrance Safety and Regulatory Affairs, 185 Avenue de Verdun, Saint Jean de Braye Cedex F-45804, France
[e] Givaudan Suisse SA, 5 chemin de la parfumerie, Vernier CH 1214, Switzerland
[f] The Procter & Gamble Company, Miami Valley Laboratories, 11810 East Miami River Road, Cincinnati, OH 45252, USA
[g] Clariant Produkte (Deutschland) GmbH, Corporate Product Safety, Am Unisys-Park 1, 65843 Sulzbach, Germany
[h] The Procter & Gamble Technical Centres Ltd, Whitehall Lane, Egham Surrey TW20 9NW, United Kingdom

Received 16 July 2007
Available online 28 October 2007

Abstract

Based on chemical, cellular, and molecular understanding of dermal sensitization, an exposure-based quantitative risk assessment (QRA) can be conducted to determine safe use levels of fragrance ingredients in different consumer product types. The key steps are: (1) determination of benchmarks (no expected sensitization induction level (NESIL)); (2) application of sensitization assessment factors (SAF); and (3) consumer exposure (CEL) calculation through product use. Using these parameters, an acceptable exposure level (AEL) can be calculated and compared with the CEL. The ratio of AEL to CEL must be favorable to support safe use of the potential skin sensitizer. This ratio must be calculated for the fragrance ingredient in each product type. Based on the Research Institute for Fragrance Materials, Inc. (RIFM) Expert Panel's recommendation, RIFM and the International Fragrance Association (IFRA) have adopted the dermal sensitization QRA approach described in this review for fragrance ingredients identified as potential dermal sensitizers. This now forms the fragrance industry's core strategy for primary prevention of dermal sensitization to these materials in consumer products. This methodology is used to determine global fragrance industry product management practices (IFRA Standards) for fragrance ingredients that are potential dermal sensitizers. This paper describes the principles of the recommended approach, provides detailed review of all the information used in the dermal sensitization QRA approach for fragrance ingredients and presents key conclusions for its use now and refinement in the future.
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Keywords: Quantitative risk assessment; Dermal sensitization; Fragrance ingredients; NESIL; SAF; AEL; CEL

1. Introduction

Although some substances in common use today may have the potential to cause dermal sensitization, they can be formulated into consumer products at safe levels. This is also the case for fragrance ingredients.

IFRA provides the fragrance industry with risk management strategies on the use of fragrance ingredients includ-

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Updating exposure assessment for skin sensitization quantitative risk assessment for fragrance materials

Anne Marie Api [a,*], David Basketter [b], James Bridges [c], Peter Cadby [d], Graham Ellis [e], Nicola Gilmour [f], Helmut Greim [g], Peter Griem [h], Petra Kern [i], Alain Khaiat [j], John O'Brien [k], Thomas Rustemeyer [l], Cindy Ryan [m], Bob Safford [n], Benjamin Smith [o,p], Matthias Vey [q], Ian R. White [r]

ARTICLE INFO

Keywords:
Quantitative risk assessment (QRA)
Fragrance materials
Aggregate exposure
Skin sensitization

ABSTRACT

In 2008, a proposal for assessing the risk of induction of skin sensitization to fragrance materials Quantitative Risk Assessment 1 (QRA1) was published. This was implemented for setting maximum limits for fragrance materials in consumer products. However, there was no formal validation or empirical verification after implementation. Additionally, concerns remained that QRA1 did not incorporate aggregate exposure from multiple product use and included assumptions, e.g. safety assessment factors (SAFs), that had not been critically reviewed. Accordingly, a review was undertaken, including detailed re-evaluation of each SAF together with development of an approach for estimating aggregate exposure of the skin to a potential fragrance allergen. This revision of QRA1, termed QRA2, provides an improved method for establishing safe levels for sensitizing fragrance materials in multiple products to limit the risk of induction of contact allergy. The use of alternative non-animal methods is not within the scope of this paper. Ultimately, only longitudinal clinical studies can verify the utility of QRA2 as a tool for the prevention of contact allergy to fragrance materials.

1. Introduction

Contact allergy to fragrance materials[1] is a topic of considerable interest for consumers, clinicians, industry and regulatory authorities. Mixtures of fragrance materials are used in a wide variety of consumer products at varying levels, leading to a wide range of exposures. Some of these fragrance materials have been identified as contact allergens and

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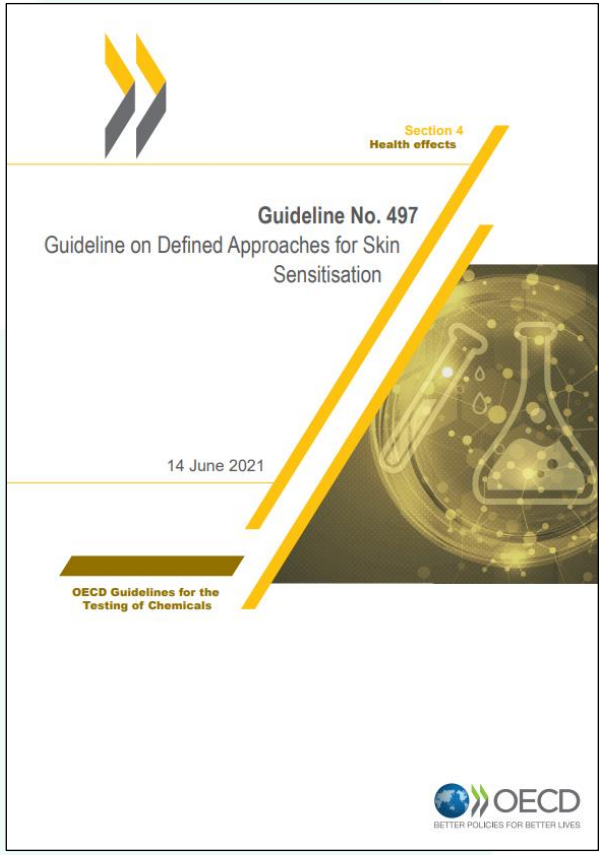
Development of a next generation risk assessment framework for the evaluation of skin sensitisation of cosmetic ingredients

Nicola Gilmour [a,1], Petra S. Kern [b,1], Nathalie Alépée [c], Fanny Boislève [d], Dagmar Bury [e], Elodie Clouet [a], Morihiko Hirota [f], Sebastian Hoffmann [g], Jochen Kühnl [h], Jon F. Lalko [i], Karsten Mewes [j], Masaaki Miyazawa [k], Hayato Nishida [l], Anne Osmani [i], Dirk Petersohn [b], Shuichi Sekine [f], Erwin van Vliet [m], Martina Klaric [b,*]

ABSTRACT

All cosmetic products placed onto the market must undergo a risk assessment for human health to ensure they are safe for consumers, including an assessment of skin sensitisation risk. Historically, in vivo animal test methods were used to identify and characterise skin sensitisation hazard, however non-animal and other new approach methodologies (NAMs) are now the preferred and mandated choice for use in risk assessment for cosmetic ingredients. The experience gained over the last three decades on how to conduct risk assessments based upon NAMs has allowed us to develop a non-animal, next generation risk assessment (NGRA) framework for the assessment of skin sensitisers. The framework presented here is based upon the principles published by the International Cooperation on Cosmetic Regulation (ICCR) and is human-relevant, exposure led, hypothesis driven and designed to prevent harm. It is structured in three tiers and integrates all relevant information using a weight of evidence (WoE) approach that can be iterated when new information becomes available. The initial tier (TIER 0) involves a thorough review of the existing information including; identification of the use scenario/consumer exposure; characterisation of the chemical purity and structure; in silico predictions; existing data pertaining to skin sensitisation hazard (historical or non-animal); the identification of suitable read-across candidates with supporting hazard identification/characterisation information and application of exposure-based waiving. Considering all information identified in TIER 0, the next step is the generation of a hypothesis (TIER 1). All data are considered in an exposure-led WoE approach, taking into account an initial view on whether a chemical is likely to be a skin sensitiser or not, choice of defined approach (DA) and availability of read-across candidates. If existing information is insufficient for concluding the risk assessment, the generation of additional information may be required to proceed (TIER 2). Such targeted testing could involve refinement of the exposure estimation or generation of data from in vitro or in chemico NAMs. Once sufficient information is available, the final stage of the NGRA framework is the determination of a point of departure (POD), characterising uncertainty and comparing to the consumer exposure in a WoE. Thorough evaluation of the sources of uncertainty is essential to ensure transparency and build trust in new risk assessment approaches. Although significant progress has been made, industry must continue to share its experience in skin sensitisation NGRA via case studies to demonstrate that this new risk assessment approach is protective for consumers. Dialogue and collaboration between key stakeholders, i.e. risk assessors, clinicians and regulators are important to gain mutual understanding and grow confidence in new approaches.



Defined Approaches (DAs):

- "2 out of 3" approach
- "Integrated Testing Strategy (ITS)" (v1-Derek Nexus and v2-OECD QSAR Toolbox)

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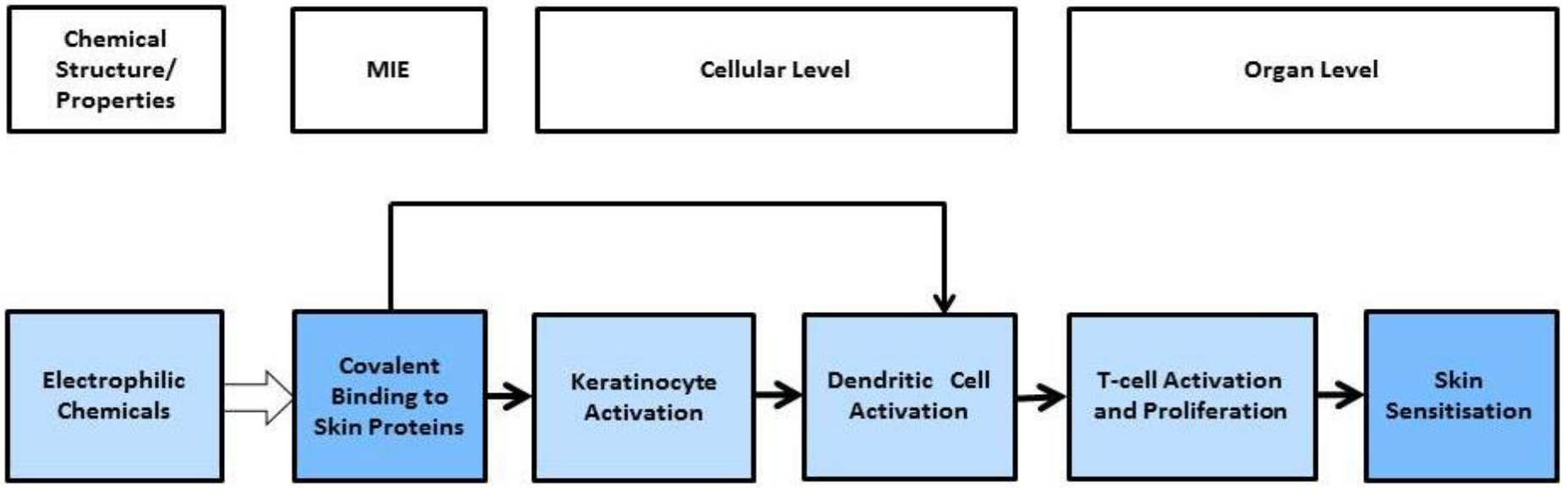
Success in skin allergy NGRA - NAMs aligned to skin sensitisation AOP



Key Event 1 (KE1) | KE2 | KE3 | KE4 | Adverse Outcome (AO)

Predictive Chemistry

For example:
- DEREK-NEXUS
- OECD QSAR Toolbox
- TIMES
- ToxTree

Protein Reactivity

OECD TG 442C
Includes:
- ADRA
- DPRA
- kDPRA

Keratinocyte Activation

OECD TG 442D
Includes:
- KeratinoSens™
- LuSens

DC Activation

OECD TG 442E
Includes:
- h-CLAT
- IL-8 Luc Assay
- U-Sens™
- GARD™skin

T Cell Proliferation

For Example:
- Human T cell proliferation assays (hTCPA)

Skin Sensitisation

OECD TG 429: mouse local lymph node assay (LLNA) & variants TG442A & 442B

OECD TG 406: Buehler & Guinea Pig Maximisation Test (GPMT)

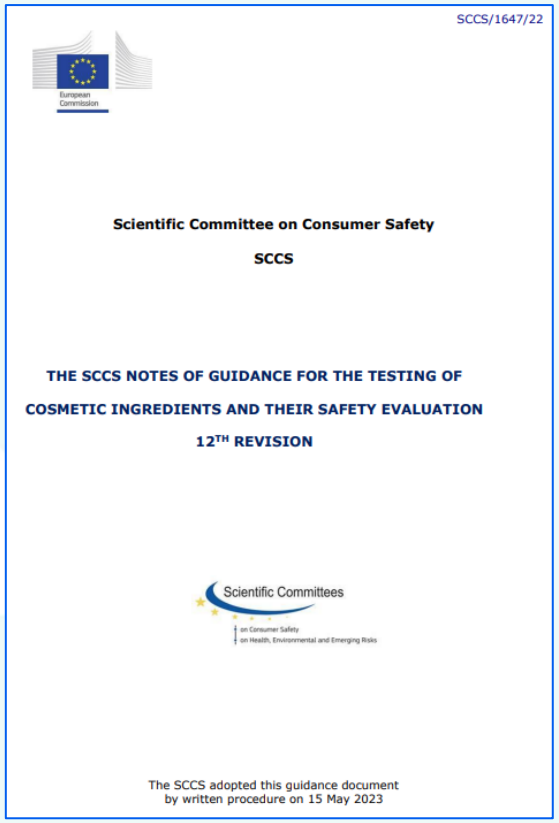
Human evidence
e.g. Human Repeat Insult Patch Test (HRIPT)

in silico NAM | *in chemico/vitro* NAM | *in vivo* evidence

OECD (2014), The Adverse Outcome Pathway for Skin Sensitisation Initiated by Covalent Binding to Proteins, OECD Series on Testing and Assessment, No. 168, OECD Publishing, Paris.

Skin allergy risk assessment evolution

SCCS
12th Notes of Guidance, 2023



SCCS/1647/22

European Commission

Scientific Committee on Consumer Safety

SCCS

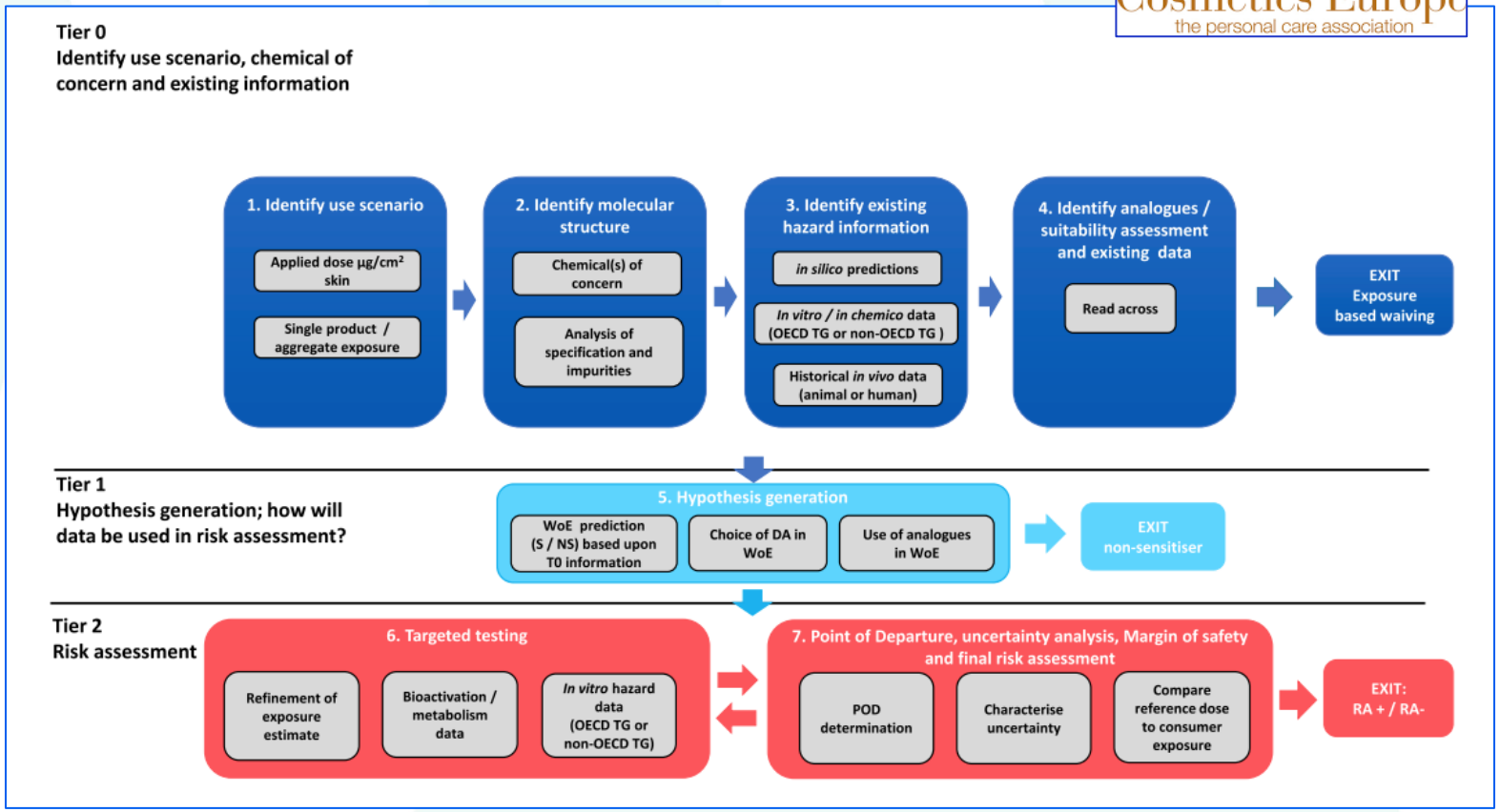
THE SCCS NOTES OF GUIDANCE FOR THE TESTING OF COSMETIC INGREDIENTS AND THEIR SAFETY EVALUATION 12TH REVISION

Scientific Committees on Consumer Safety on Health, Environmental and Emerging Risks

The SCCS adopted this guidance document by written procedure on 15 May 2023

Next generation risk assessment framework for skin sensitisation

Cosmetics Europe
the personal care association



Gilmour et al. Development of a next generation risk assessment framework for the evaluation of skin sensitisation of cosmetic ingredients. Regul. Toxicol. Pharmacol. 116, 2020.

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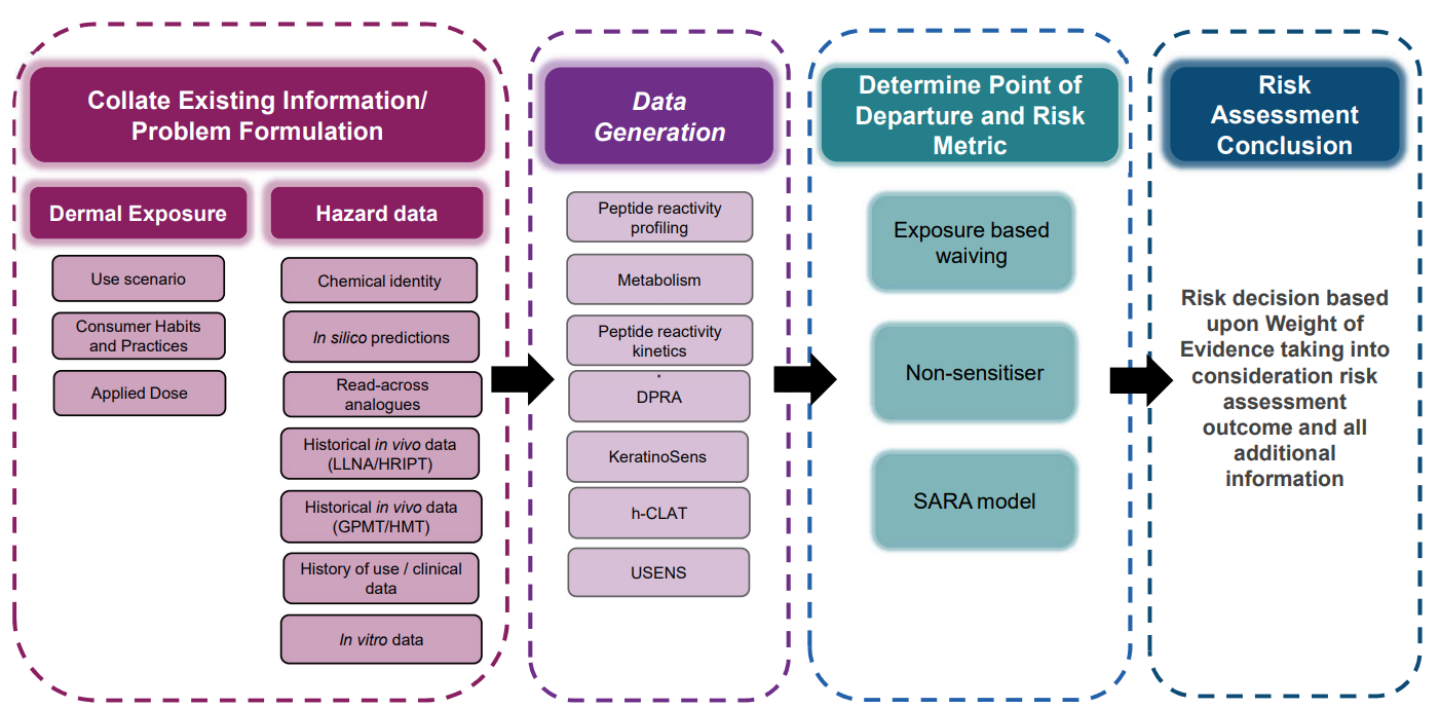
Next generation risk assessment (NGRA) framework for skin allergy



- Our NGRA framework for skin allergy is based upon the **International Cooperation on Cosmetics Regulation (ICCR) principles**[1] and the previously published **NGRA frameworks for systemic tox {Safety Evaluation Ultimately Replacing Animal Testing, SEURAT-1}**[2] and **skin allergy {Cosmetic Europe}**[3].
- Designed to use a WoE based upon all available information, accommodates range of consumer product exposure scenarios and can provide a quantitative point of departure (PoD) and risk metric:

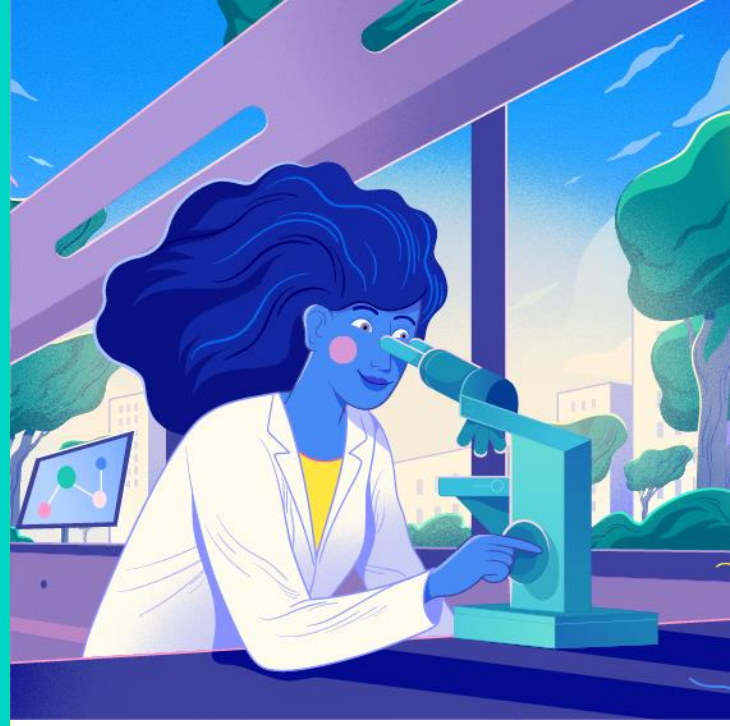
  → **Skin Allergy Risk Assessment (SARA) Model**

[1]Dent et al. Principles underpinning the use of new methodologies in the risk assessment of cosmetic ingredients. Comput. Toxicol. 7, 20–26, 2018.

[2]Berggren et al. Ab initio chemical safety assessment: A workflow based on exposure considerations and non-animal methods. Comput. Toxicol. 4, 31–44, 2017.

[3]Gilmour et al.. Development of a next generation risk assessment framework for the evaluation of skin sensitisation of cosmetic ingredients. Regul. Toxicol. Pharmacol. 116, 2020.

Introduction to the Skin allergy Risk Assessment (SARA) model



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Skin Allergy Risk Assessment (SARA) model

SARA Model Input Data Sources

- Historical Local Lymph Node Assay (LLNA) data
- Historical Human Repeated Insult Patch Test (HRIPT) data
- *In vitro* data: DPRA (OECD TG442C), KeratinoSens™ (OECD TG 442D), h-CLAT (OECD TG 442E), U-SENS™ (OECD TG 442E)

SARA Model Output Data Sources

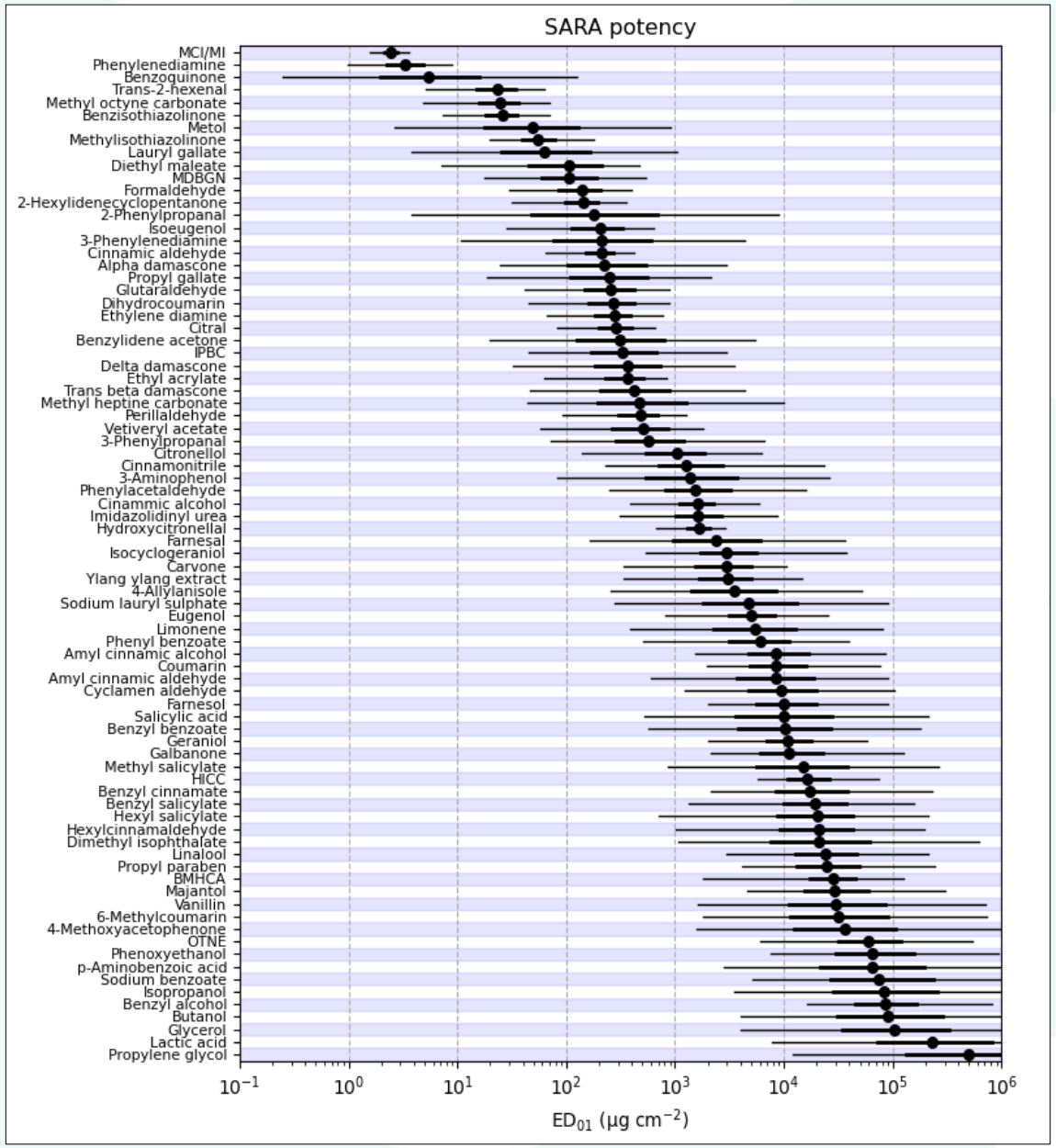
- Point of Departure (PoD) termed the ED_{01} – the expected dose at which there is a 1% chance of skin sensitisation in a human (HRIPT) population
- Risk metric – p(low risk) of a given chemical exposure

- **Defined approach (DA) to provide potency and risk information based upon NAMs**
- **A Bayesian statistical approach** which can make potency and risk predictions using any combination of **historical *in vivo* (LLNA, HRIPT) or NAMs (DPRA, KeratinoSens™, h-CLAT and U-SENS™) –** curated database of 81 chemicals
- **Skin sensitiser potency is expressed as the ED_{01},** the dose estimated to induce sensitisation in 1% of a HRIPT population. This is the **Point of Departure (PoD)** for the risk assessment.
- **Risk metric**: SARA model also makes use of **benchmark exposures to infer a probability that a consumer exposure to a chemical is 'low risk'**

Reynolds et al. Probabilistic prediction of human skin sensitiser potency for use in next generation risk assessment. Comput. Toxicol. 9, 36–49, 2019.

Reynolds et al. Decision making in next generation risk assessment for skin allergy: Using historical clinical experience to benchmark risk. Regul. Toxicol. Pharmacol. 134, 2022.

Potency across the SARA database - PoDs



This graph gives the ED_{01} and quantified uncertainty (the dot with the 50% and 95% confidence intervals denoted by the thick and thin lines either side)

Use of consumer exposure information and clinical evidence to develop skin allergy risk benchmarks

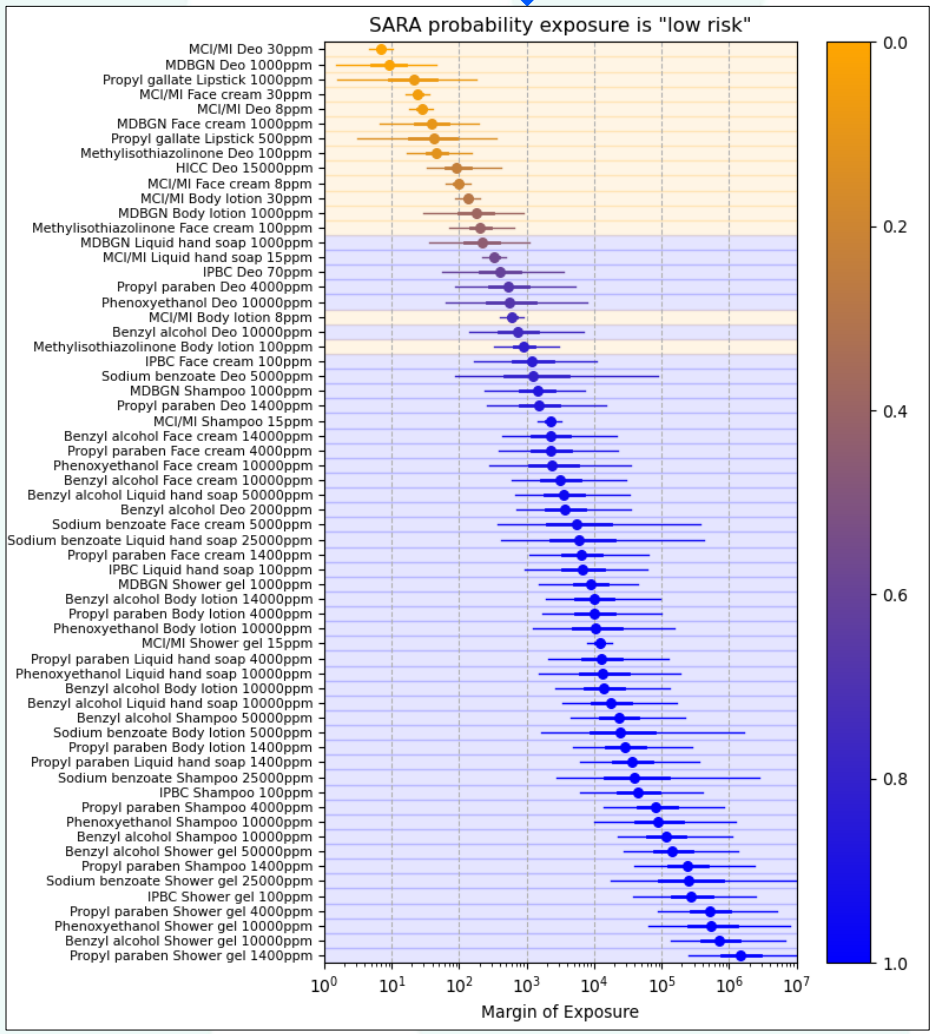
62 low or high risk benchmark exposures using 10 human skin allergens (e.g. MCI/MI) with an established history of use in 7 cosmetic product types.

Margin of exposure (MoE) calculation (PoD/Exposure)

Example

Material	Product type	Use level (ppm)	Consumer exposure to benchmark product (ng cm^{-2})	Induction risk
MCI/MI*	Deo	30	350	HIGH
		7.5	87.8	HIGH
	Face cream	30	100	HIGH
		7.5	25	HIGH
	Body lotion	30	18	HIGH
		7.5	4	HIGH
	Liquid hand soap	15	7.3	LOW
	Shampoo	15	1.1	LOW
	Shower gel	15	0.2	LOW

*MCI/MI = Methylisothiazolinone/methylchloroisothiazolinone



- Probabilistic estimates of the MoE corresponding to each benchmark exposure at specific exposure level.
- Background colours indicate assigned risk category:
  - blue: low risk,
  - orange: high risk
- Shaded colours indicate the model-inferred risk. Ranking based on the median margin of exposure.

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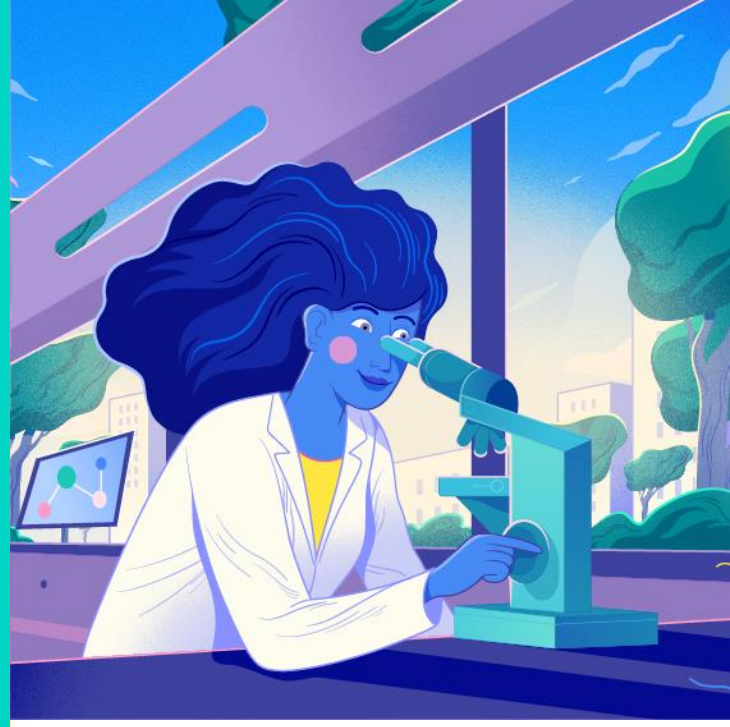
Skin Allergy Risk Assessment (SARA) Model Case Study

0.02% (200ppm) geraniol in a face cream



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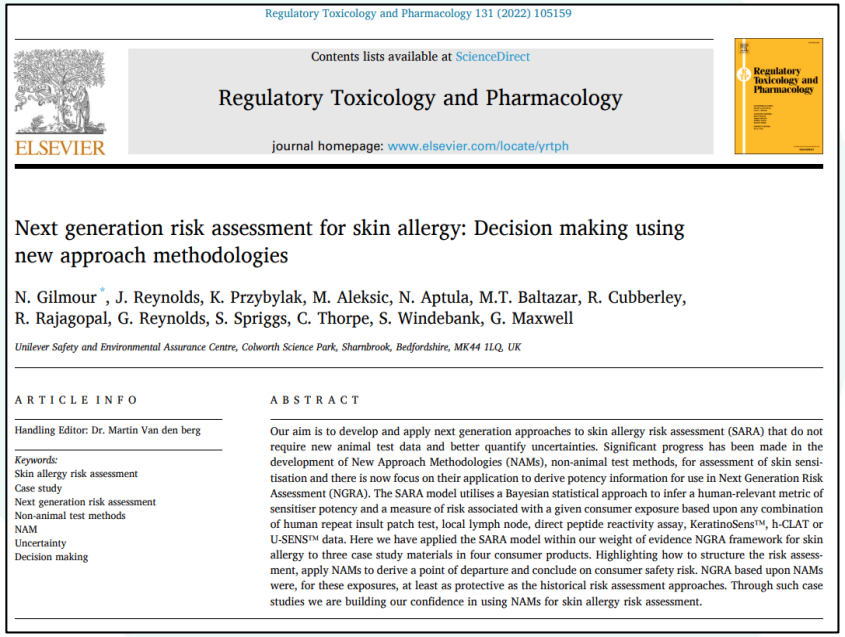
Application of the NGRA framework for Skin Allergy



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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

Unilever Safety and Environmental Assurance Centre, Colworth Science Park, Sharnbrook, Bedfordshire, MK44 1LQ, UK

ARTICLE INFO

Handling Editor: Dr. Martin Van den berg

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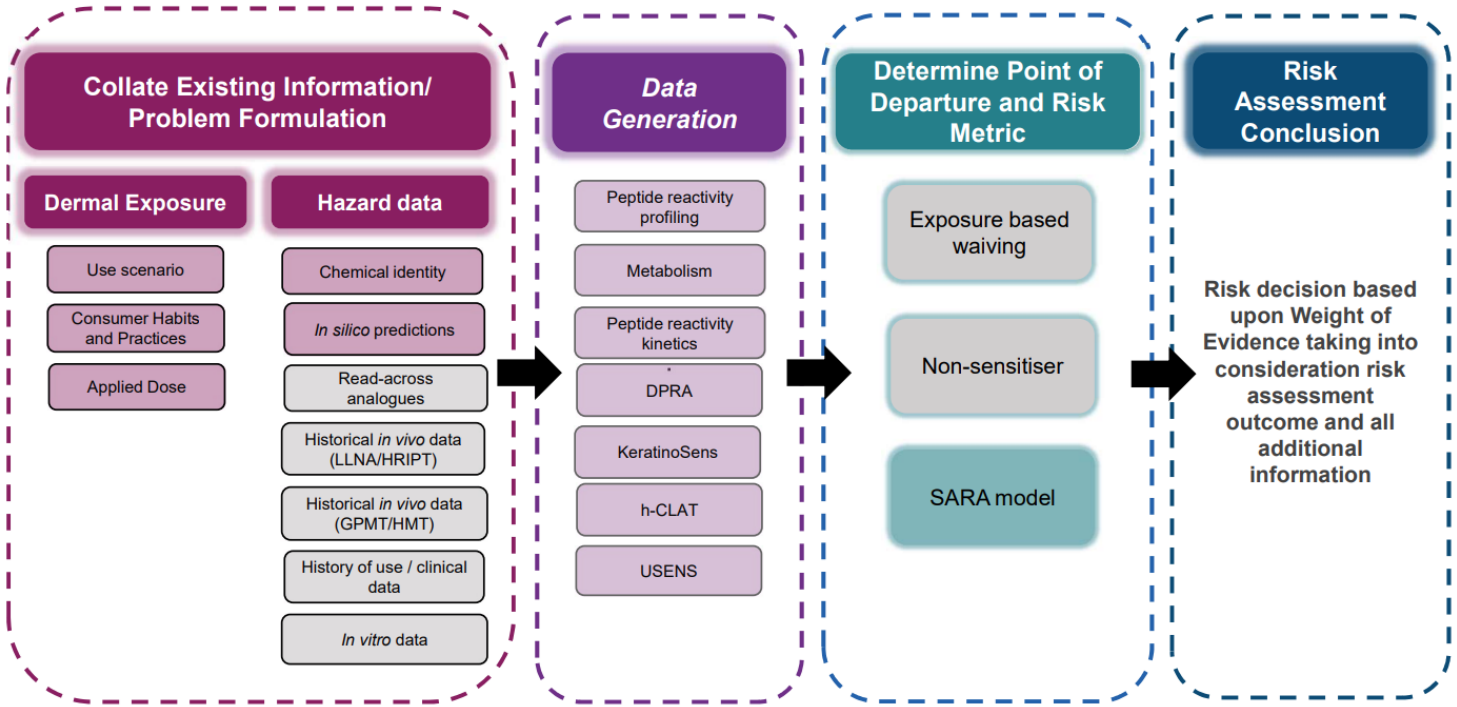
Skin allergy risk assessment
Case study
Next generation risk assessment
Non-animal test methods
NAM
Uncertainty
Decision making

ABSTRACT

Our aim is to develop and apply next generation approaches to skin allergy risk assessment (SARA) that do not require new animal test data and better quantify uncertainties. Significant progress has been made in the development of New Approach Methodologies (NAMs), non-animal test methods, for assessment of skin sensitisation and there is now focus on their application to derive potency information for use in Next Generation Risk Assessment (NGRA). The SARA model utilises a Bayesian statistical approach to infer a human-relevant metric of sensitiser potency and a measure of risk associated with a given consumer exposure based upon any combination of human repeat insult patch test, local lymph node, direct peptide reactivity assay, KeratinoSens™, h-CLAT or U-SENS™ data. Here we have applied the SARA model within our weight of evidence NGRA framework for skin allergy to three case study materials in four consumer products. Highlighting how to structure the risk assessment, apply NAMs to derive a point of departure and conclude on consumer safety risk. NGRA based upon NAMs were, for these exposures, at least as protective as the historical risk assessment approaches. Through such case studies we are building our confidence in using NAMs for skin allergy risk assessment.



- Our NGRA framework is applied to a hypothetical skin allergy assessment of a consumer product:
  → **0.02% (200ppm) geraniol in a face cream.**

- For the purposes of the case study, **historical *in vivo* data** and **read-across** were not used, and the use of **dermal sensitisation threshold** was not appropriate.

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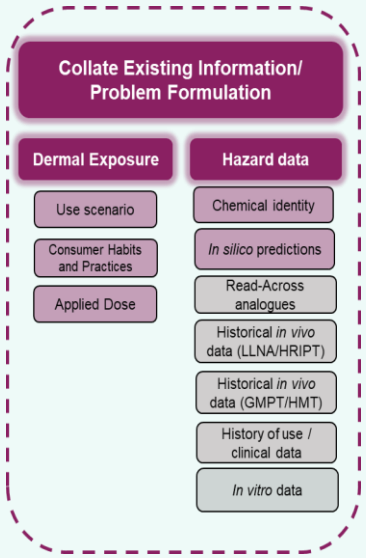
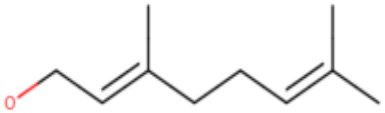
Local exposure + Collate Existing Information/ Problem Formulation



Geraniol

CAS 106-24-1



Product type	Face cream
Product used per day (90th percentile) (g/day)	1.54
Ingredient inclusion level (%)	0.02
Skin surface area face (cm^2)	565
Leave-on or Rinse-off	Leave-on
Local dermal exposure ($\mu g/cm^2$)	0.544

*Scientific Committee On Consumer Safety (SCCS), 2021. The SCCS Notes of Guidance for the Testing of Cosmetic Ingredients and Thier Safety Evaluation. 11th Revision.

DEREK NEXUS	Alert – terpenoid EC3 model – 20% (weak)
TIMES-SS v.2.30.1.11 **Skin Sensitisation model with autoxidation**	Parent – Non sensitiser (in domain) Metabolites – Strong sensitiser- after autoxidation to disubstituted a,b-unsaturated aldehydes, Weak sensitiser after autooxidation to hydroperoxides
ToxTree v.3.1.0	Alert for Schiff base formation
OECD QSAR Toolbox v.4.4	Protein binding by OECD Parent - No alert found Skin Metabolites (2) - Direct Acting Schiff Base Formers >> Di-substituted alpha, beta-unsaturated aldehydes

- Geraniol is a reactive chemical and likely to be a skin sensitiser due to activation to a chemical capable of forming a Schiff base.
- Confidence in this prediction is high based upon chemical prediction consensus from all applied *in silico* tools.
- Data generation needs:
  - Assuming an abiotic activation mechanism (autoxidation), peptide reactivity profiling data should be generated to test this hypothesis. An estimation of potency is required to enable risk assessment for this exposure.
  - To enable a potency prediction using the SARA model DPRA, KeratinoSens™, h-CLAT and U-SENS™ data should also be generated.

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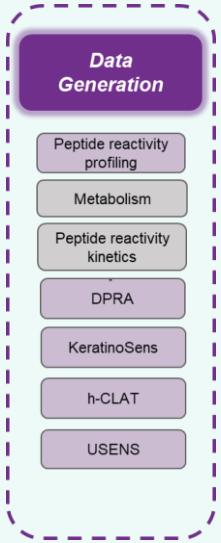
Data Generation



Reactivity Profiling (Aleksic et al., 2009*)	DPRA (OECD TG442C**)	KeratinoSens™ (OECD TG 442D**)	h-CLAT (OECD TG 442E**)	U-SENS™ (OECD TG 442E**)
Cys (no adducts, 73.7%) Lys (no adducts, 3.5%) His (no adducts, -11.1%) **Arg (double Schiff base, 15.2%)** Tyr (no adducts, 8.2%) **N-term (acylation, Schiff base, 40.2%)** Ala (no adducts, -2.1%)	**Negative** Cys depletion 0% Lys depletion 10%	**Positive** $EC_{1.5}$ 110 µM EC_3 >2000 µM IC_{50} 875 µM	**Positive** CD86 EC_{150} 123 µg ml^{-1} CD54 EC_{200} - µg ml^{-1} CV_{75} 140 µg ml^{-1}	**Positive** CD86 EC_{150} 53.6 µg ml^{-1} CV_{70} 113.9 µg ml^{-1}

- Geraniol was confirmed to be a **reactive chemical (Schiff base following autoxidation)** by peptide profiling where adducts consistent with formation of Schiff bases following oxidative activation were observed with the Arginine and N-terminus peptide.
- Geraniol demonstrated minimal depletion of Cys and Lys in the DPRA, which is consistent with the reactivity profiling data. Positive responses were evident in the KeratinoSens™, h-CLAT and U-SENS™.
- Thus, geraniol is a **skin sensitiser via Schiff base formation**.
- **Next step:** determination of the PoD, i.e. the human potency (ED_{01}) → SARA model

*Aleksic et al.. Reactivity profiling: covalent modification of single nucleophile peptides for skin sensitization risk assessment. Toxicol. Sci. 108, 401–411, 2009.

**DPRA, KeratinoSens™, h-CLAT and USENS™ data were sourced from the Cosmetics Europe database (Hoffmann et al. Non-animal methods to predict skin sensitization (I): the Cosmetics Europe database, Crit. Rev. Toxicol. 48, 344–358, 2018).

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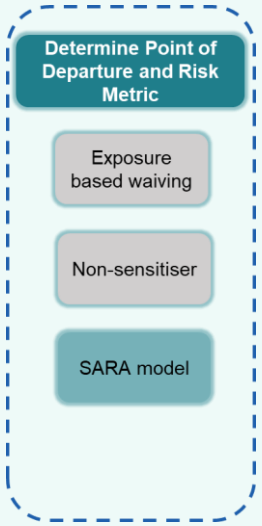
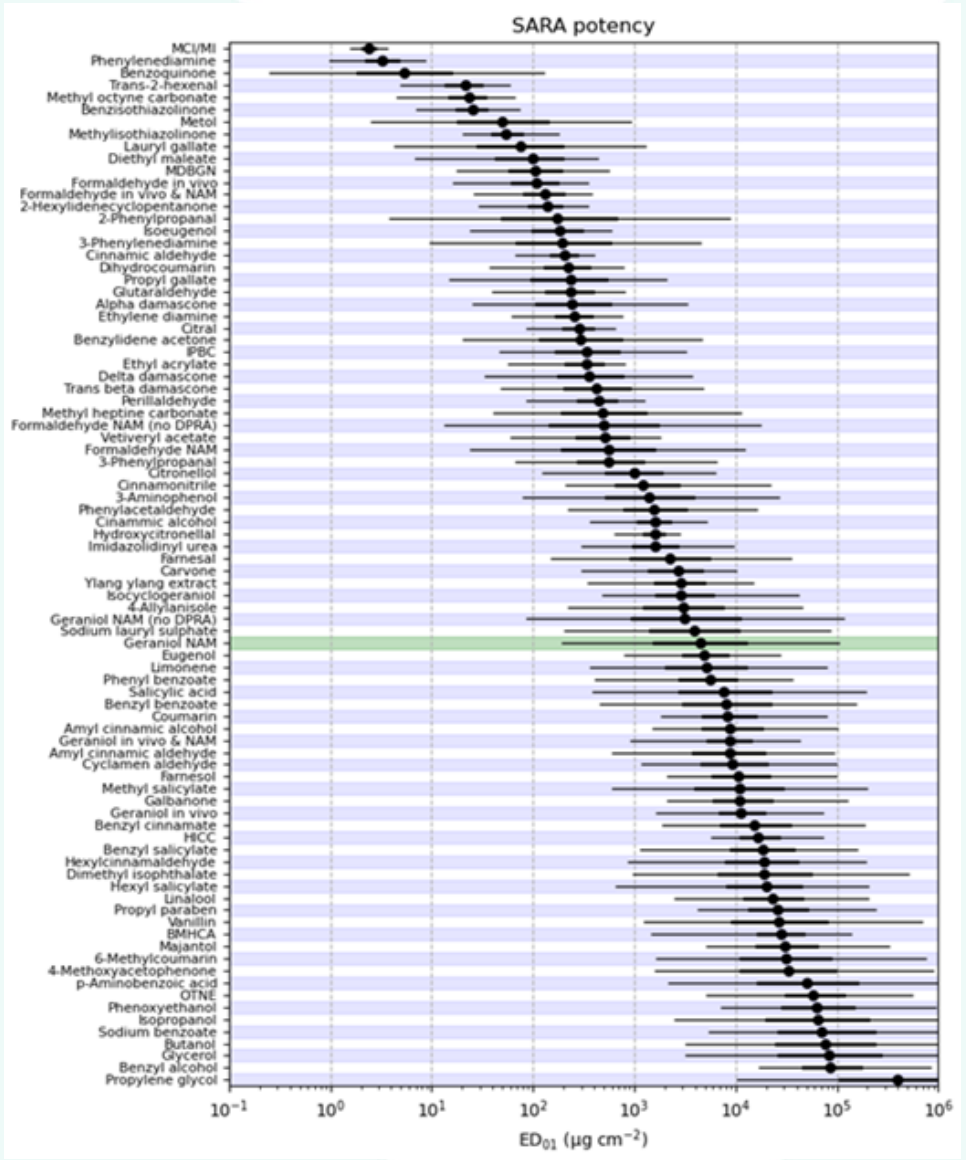
Determine Point of departure using SARA DA





- The generated DPRA, KeratinoSens™, h-CLAT and U-SENS™ data were used as inputs into the SARA model to define a **human relevant PoD (ED_{01} i.e the 1% sensitising dose for a HRIPT population)**.

- For geraniol (NAM data only), the expected **ED_{01} is 4,500 µg cm^{-2}** (2.5th percentile: 180 µg cm^{-2}, 97.5th percentile: 96,000 µg cm^{-2}).

- Geraniol ranks with eugenol, which at least based upon LLNA data is reported to be of moderate potency

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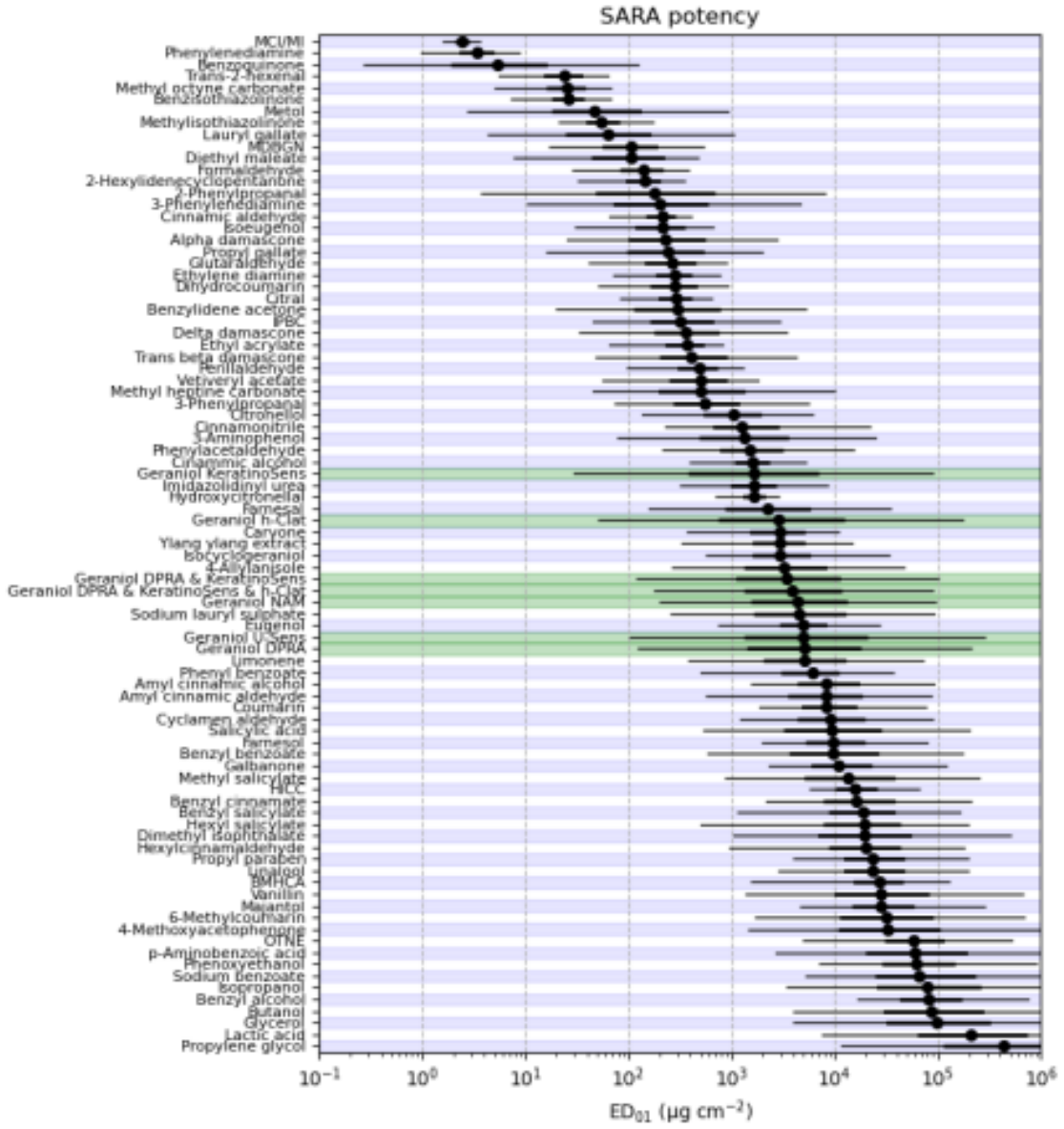
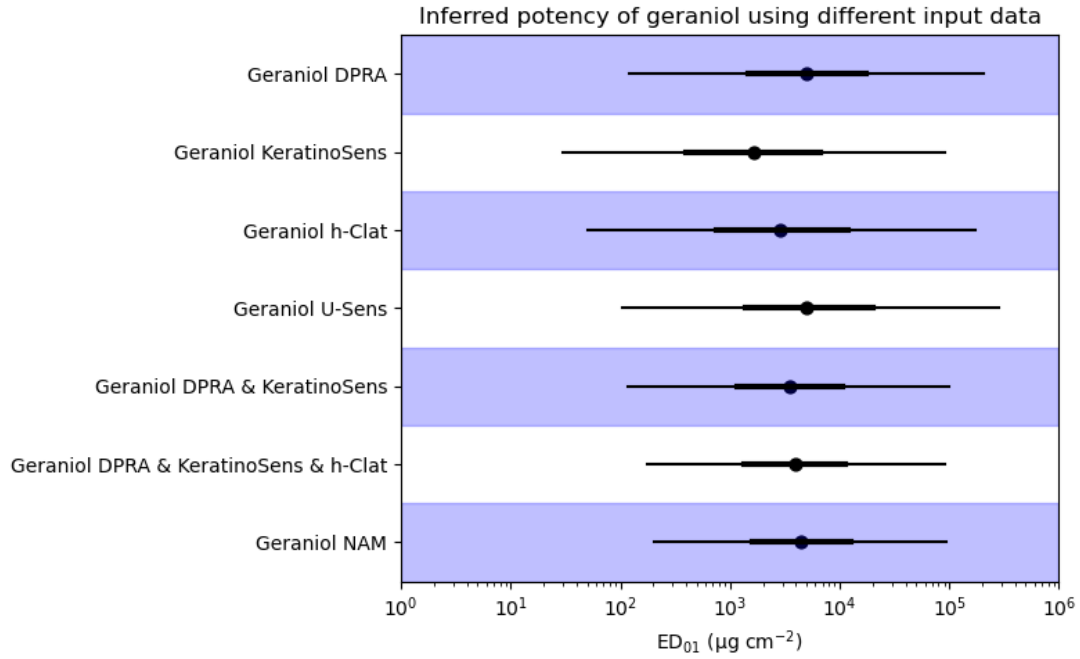
SARA model: partial datasets



- The SARA model can make predictions based upon **any combination** of the DPRA, KeratinoSens™, h-CLAT and U-SENS™ data.
- Predictions made using just KeratinoSens™ or h-CLAT data yielded a marginally higher expected potency (lower ED_{01}) compared with the predictions made using just DPRA or U-SENS™ data.
- Combining data increases the precision in the estimate of potency (reduced uncertainty).



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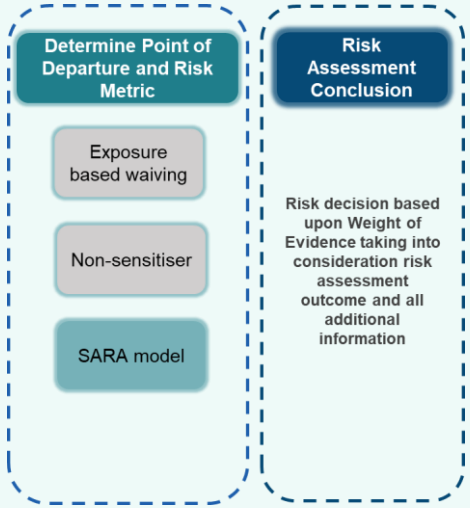
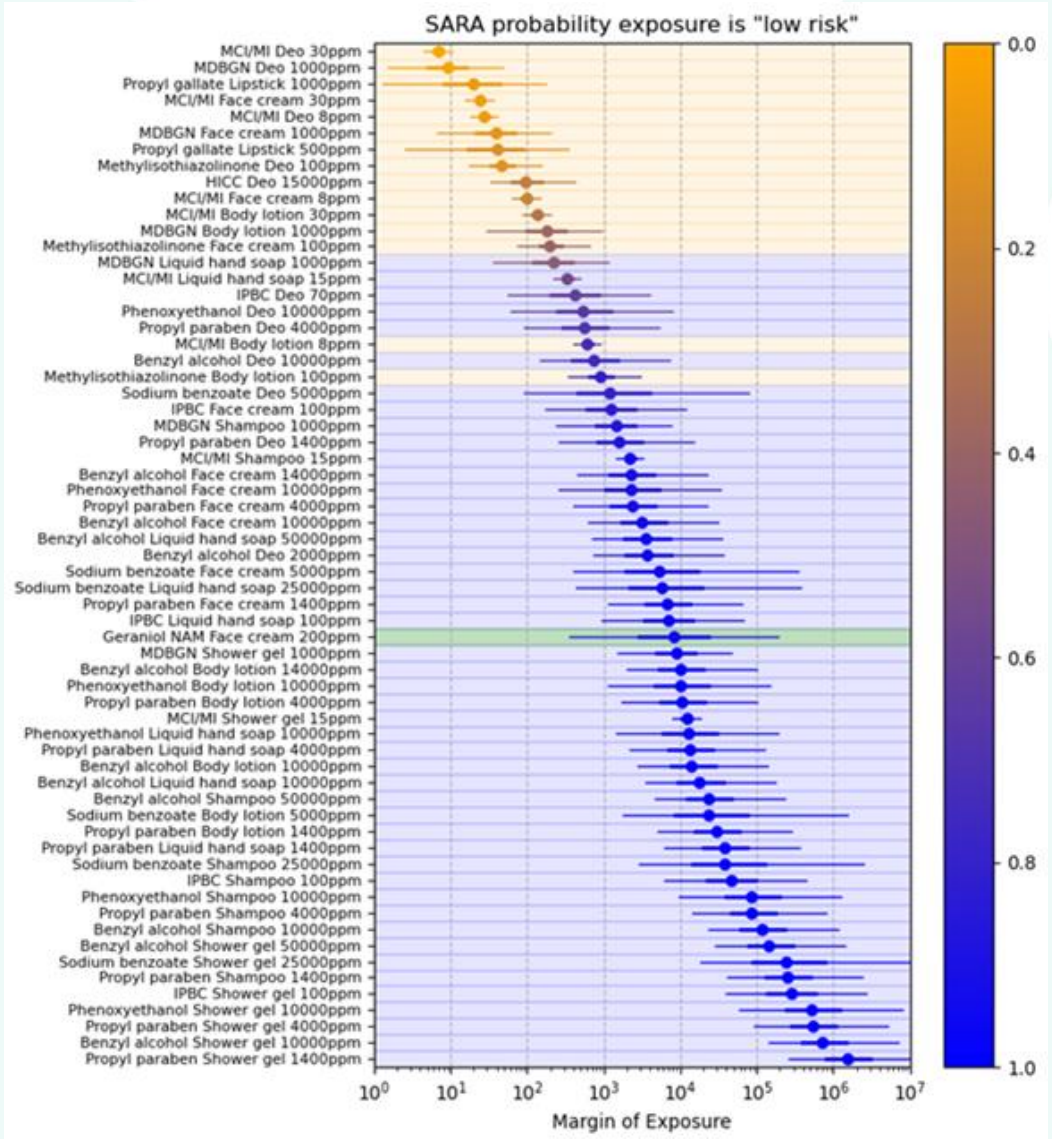
Determine MoE/Acceptable Exposure Level + NGRA conclusion





- The MoE was calculated from the ED_{01} for geraniol and the dermal exposure for 0.02% geraniol in a face cream using SARA DA
- The MoE for 0.02% geraniol face cream exposure ranks with the low-risk benchmarks.
- The SARA DA probability that this exposure is low risk is calculated to be 0.95. Thus, there is a 95% probability that this exposure is low risk.
- Geraniol used at 0.02% (200 ppm) in a face cream is low risk for induction of skin sensitisation

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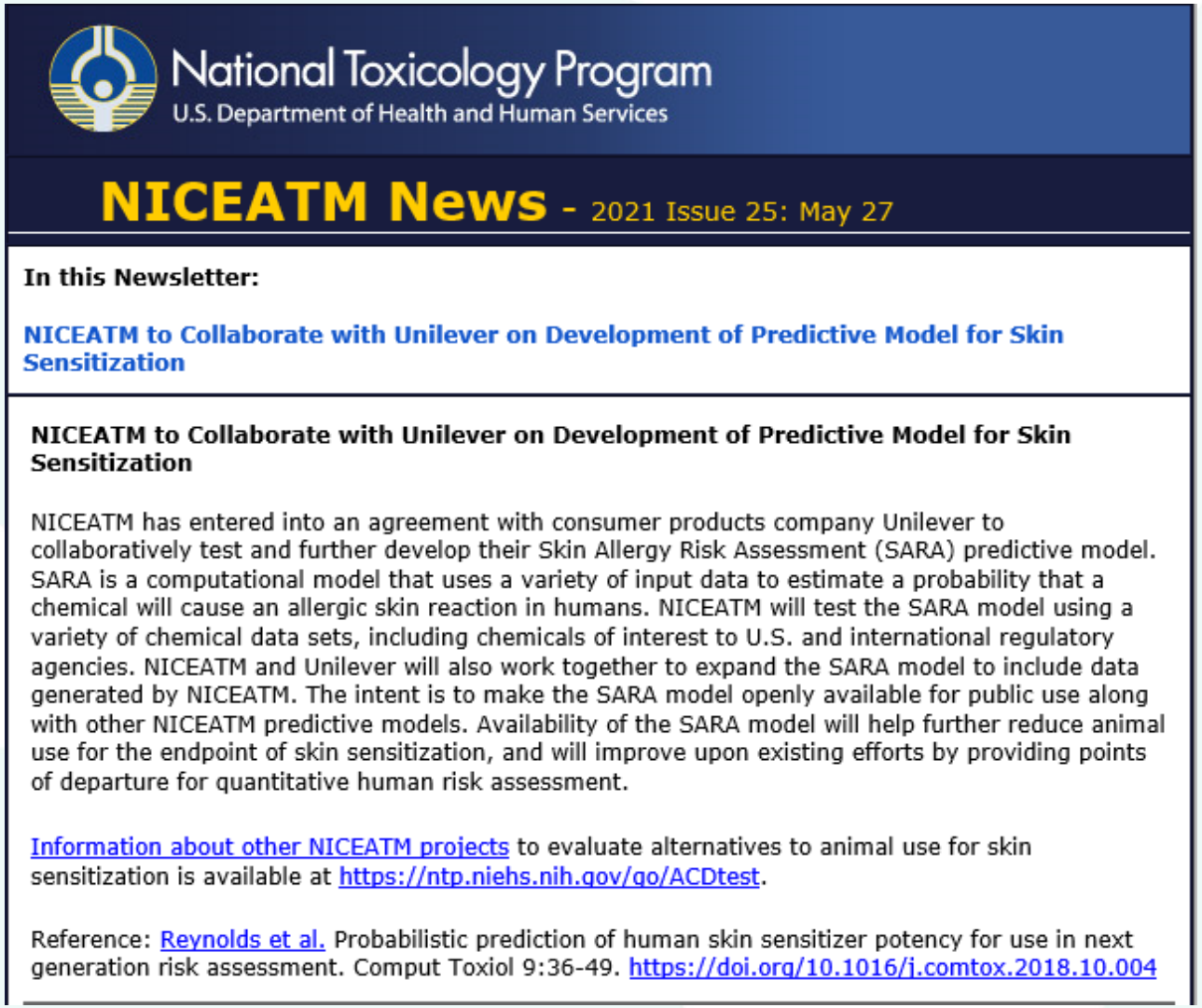
Conclusions & Next Steps

- Significant progress has been made in the last decade to apply non-animal experimental data using Defined Approaches (DAs) & tiered frameworks.
- Bayesian DAs enable experimental data variability to be modelled and uncertainty in PoDs & risk metrics to be factored into decision-making.
- Ongoing model development to expand the database, further incorporate mechanistic reactivity knowledge and explore new SARA inputs
- Recently published NGRA framework and case studies:
  - ✓ Cosmetic Europe NGRA framework (Gilmour et al., 2020)
  - ✓ Coumarin case study (Reynolds et al., 2021)
  - ✓ Unilever NGRA framework and other case studies (Gilmour et al., 2022; Gilmour et al., 2023)

NICEATM-Unilever CRADA



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.

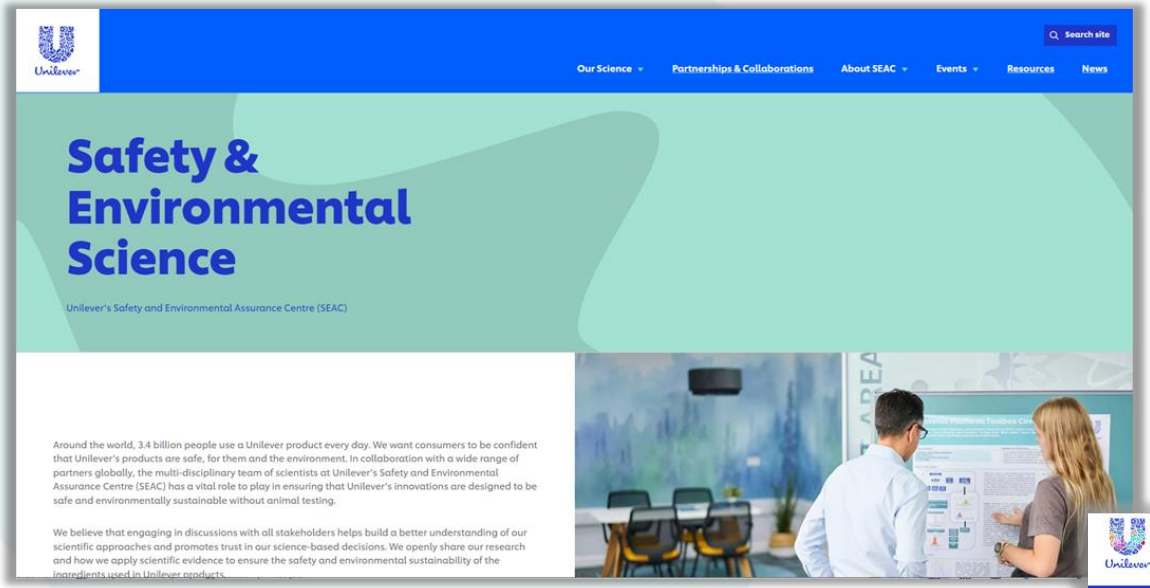
Information about other NICEATM projects to evaluate alternatives to animal use for skin sensitization is available at https://ntp.niehs.nih.gov/go/ACDtest.

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-NICEATM CRADA underway to develop a publicly available version of the SARA Model for evaluation as part of the OECD workplan for OECD DASS TG 497

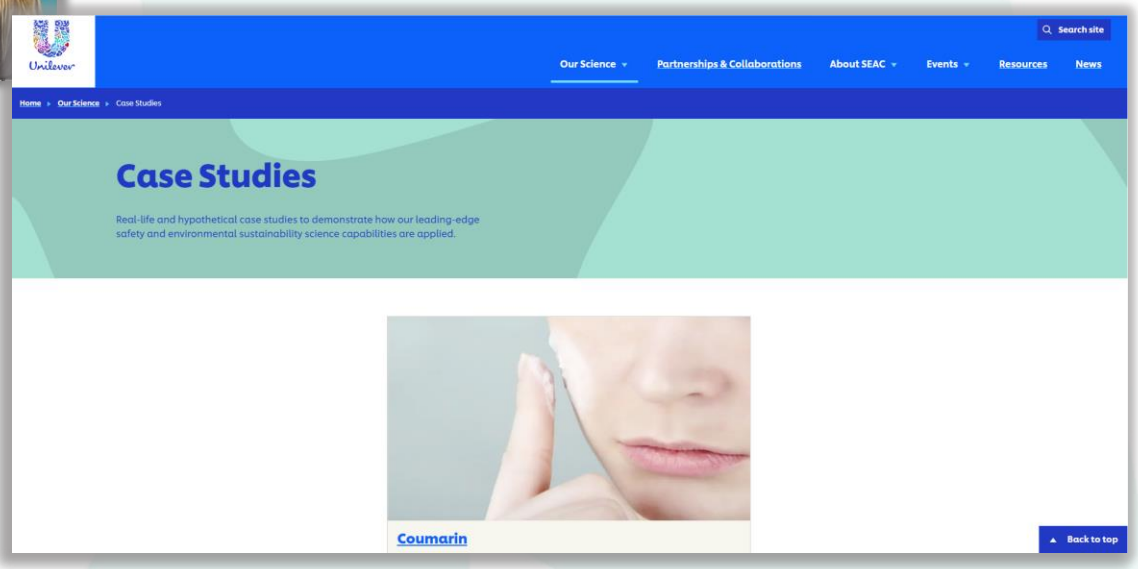
Unilever

Safety & Environmental Sciences website: https://seac.unilever.com/



- **Summary of SEAC science capabilities for expert audiences**:
  industry, regulator & academic scientists

- **Microsite covering**:
  - Our Science → **case studies**
  - Partnerships & Collaborations
  - About SEAC
  - Events
  - Resources
  - News



https://seac.unilever.com/our-science/case-studies/coumarin/

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Série de Webinars em Ciência *In Vitro*

https://seac.unilever.com/news/2022/seac-scientists-collaborate-to-launch-latam-in-vitro-science-webinars/

Em português e/ou espanhol!

Tópicos já abordados:

- Sensibilização dérmica
- Irritação ocular e dérmica
- Segurança ambiental
- Processo de validação de métodos alternativos
- Status regulatório no Brasil e América Latina
- Química analítica na avaliação de segurança humana e ambiental

Gravação dos Eventos passados podem ser acessados:

YouTube TOXIN LABORATÓRIO DE ENSINO E PESQUISA EM TOXICOLOGIA IN VITRO

https://www.youtube.com/@laboratoriotoxin5356/playlists

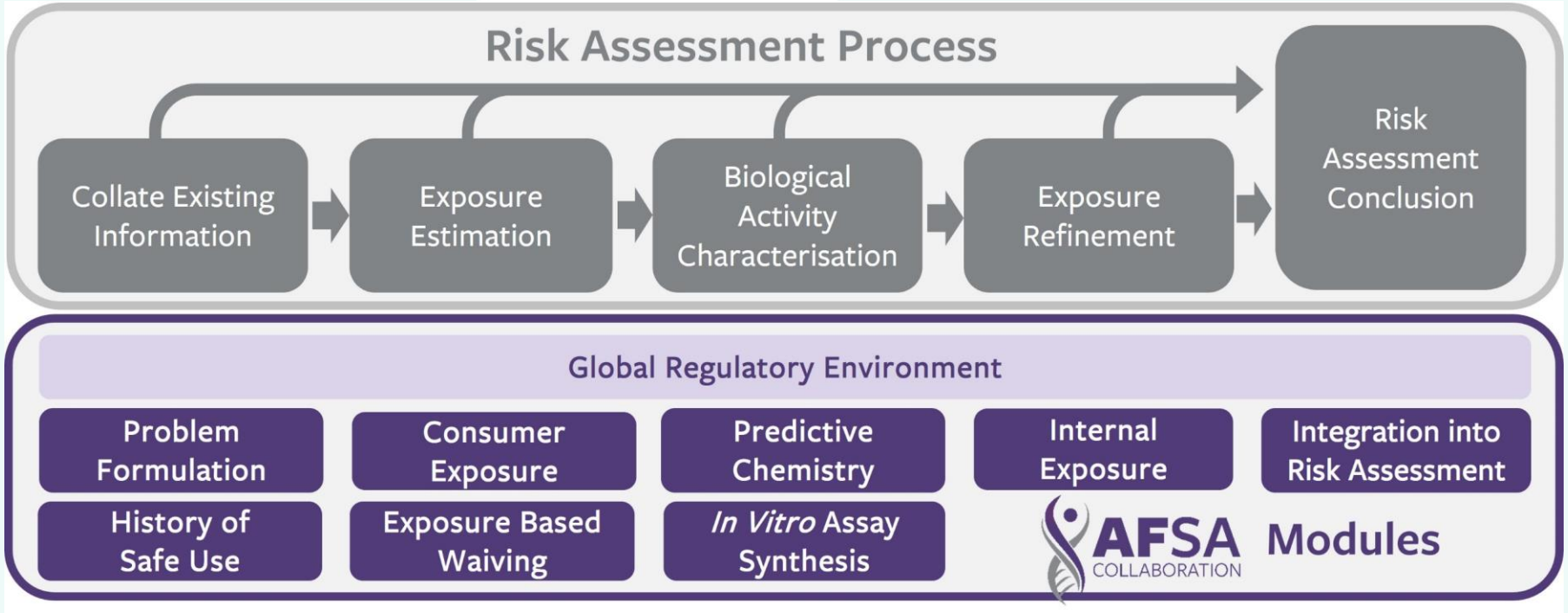
Master Class in Animal-Free Safety Assessment for Cosmetics

- **Covering Risk Assessment from start to finish**

Audience:

- Product and chemical safety assessors and regulators
- Regulatory affairs and compliance specialists
- CRO/GLP laboratories
- Small and medium enterprises
- Graduate students
- Non-governmental organizations

https://www.afsacollaboration.org/masterclass/



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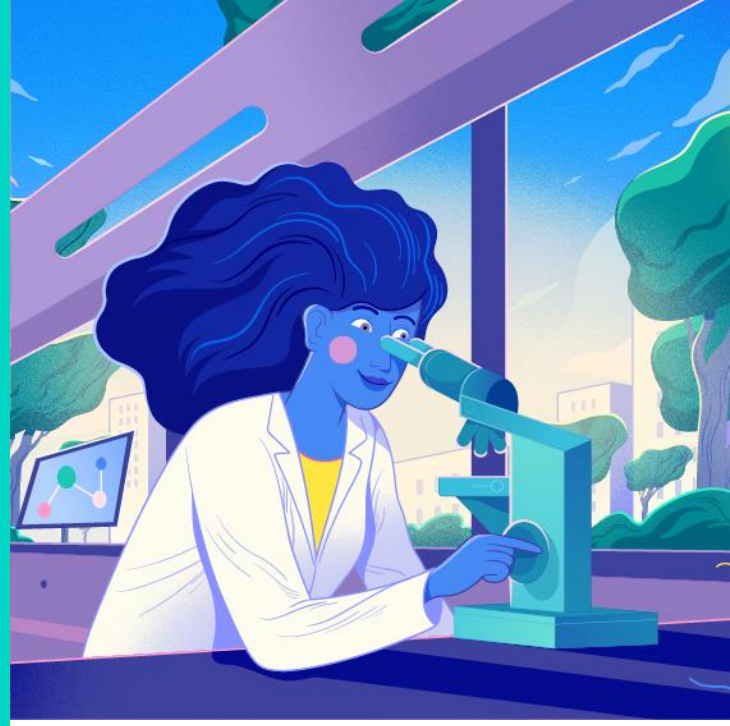
Matt Dent

Carl Westmoreland

Julia Fentem

ABIHPEC
Associação Brasileira da Indústria de Higiene Pessoal, Perfumaria e Cosméticos



Unilever