The International Collaboration for Cosmetics Safety (ICCS): *Accelerating Global Adoption of Animal-Free Safety Science for Cosmetic Product and Ingredient Safety Assessment*

Dr Gavin Maxwell, Unilever & ICCS Core Acceptance Team (CAT) vice chair

Session: On the Edge of the NAMs Frontier: Pioneering Efforts Toward Intra- and Internationally Harmonized Regulatory Applications of New Approach Methodologies

SOT 2024

ICCS

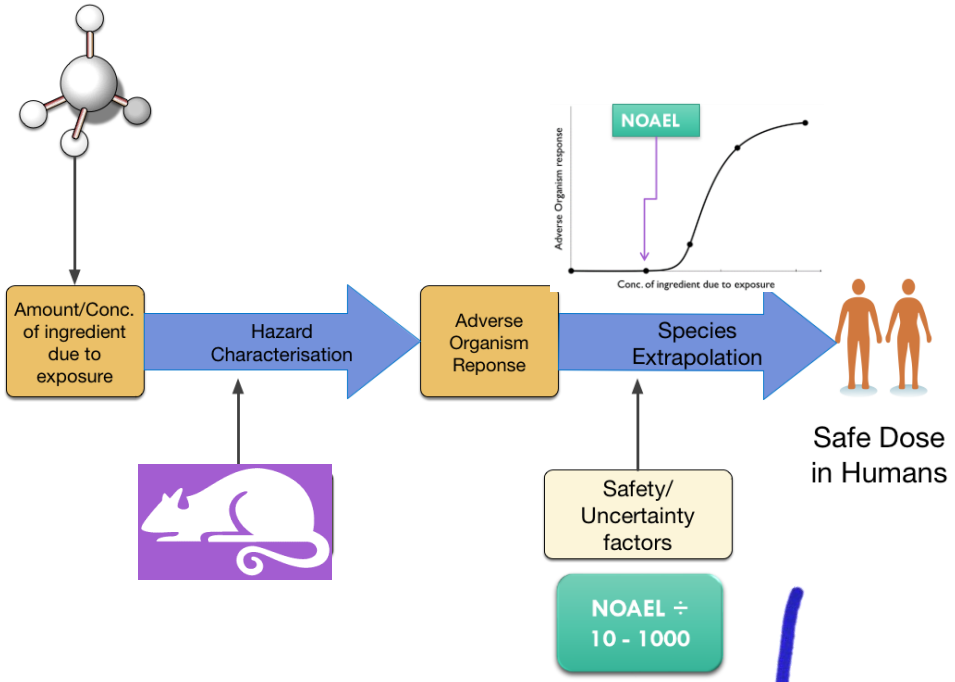
INTERNATIONAL COLLABORATION ON COSMETICS SAFETY

Conflict of Interest Statement

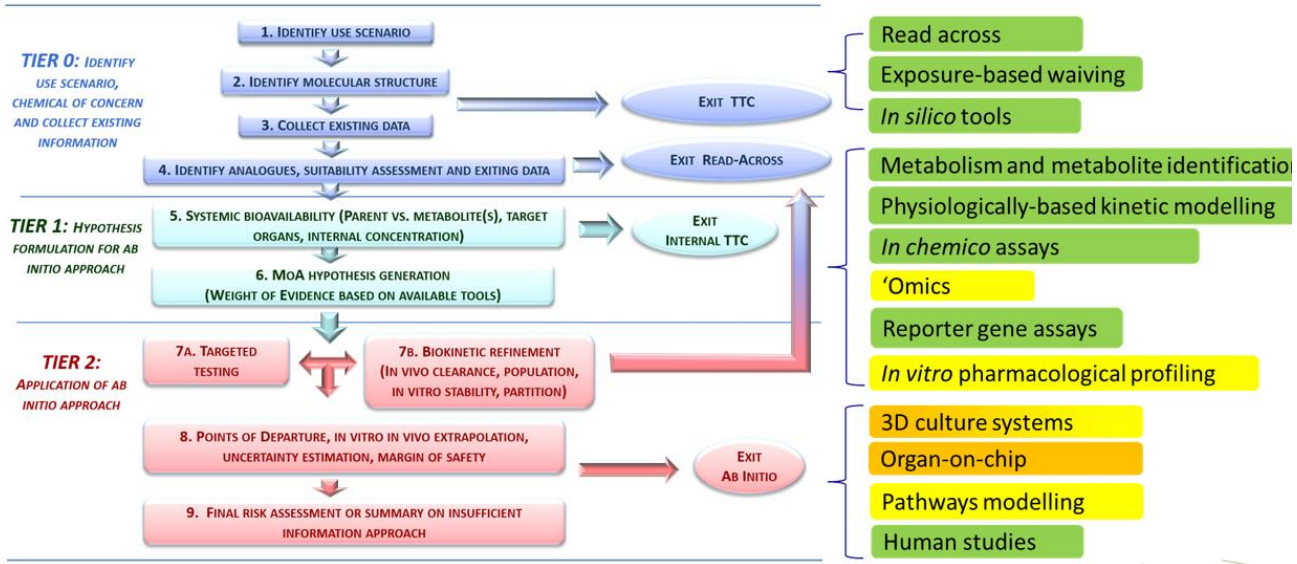
- Gavin Maxwell is an employee of Unilever (www.unilever.com)
- Unilever are members of the International Collaboration of Cosmetics Safety (ICCS)

NGRA paradigm shift is underway

‘Traditional’ Risk Assessment

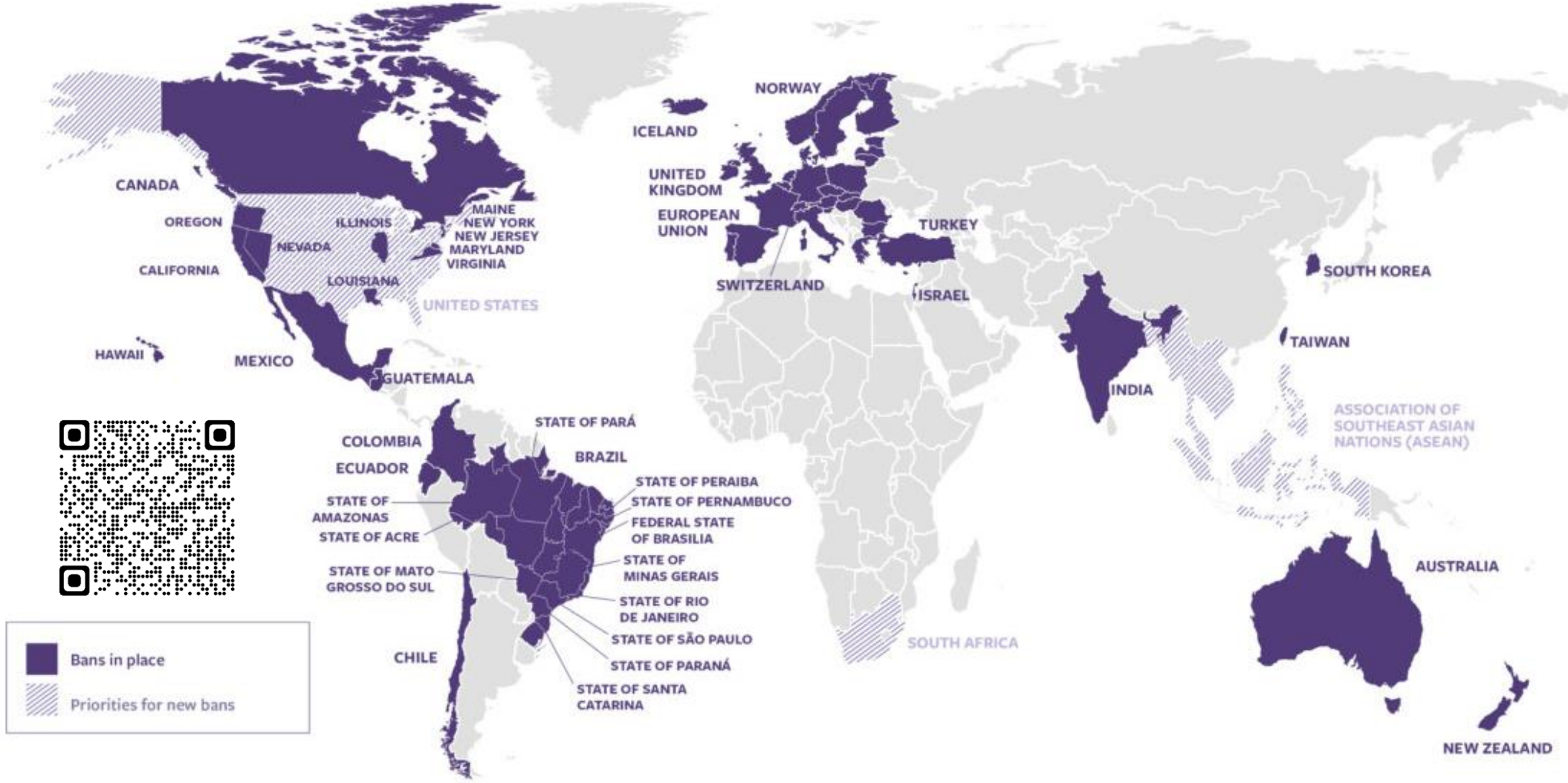


‘Next Generation’ Risk Assessment



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

For Cosmetics, transition to Animal-Free Safety Assessment has been accelerated by animal testing bans but there's plenty left to do to end animal testing globally



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

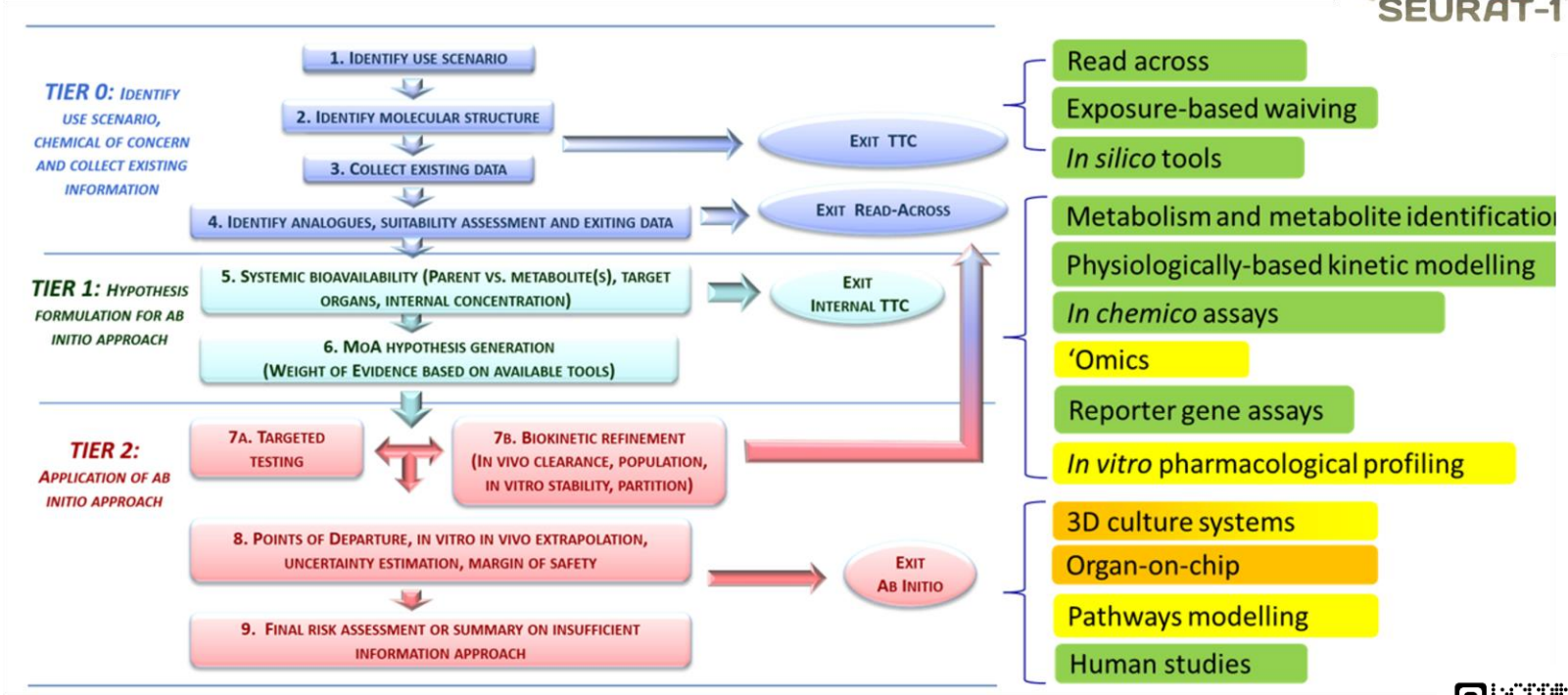
Transition to Animal-free Safety Assessment for Cosmetics
= non-animal NAMs and NGRA approaches accepted for Cosmetic Safety Assessment & Cosmetic Ingredient registration

Acceptance and/or Education & Training challenges:

- Skin & Eye Irritation
- Genetic Toxicity
- Skin Sensitization

Scientific, Acceptance and Education & Training challenges:

- Systemic Exposure & Effects (including DART)
- Carcinogenicity
- Occupational Safety
- Environmental Exposure & Fate, Effects



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

https://www.iccr-cosmetics.org//downloads/topics/iccr_integrated_strategies_for_safety_assessment_of_cosmetic_ingredients_part_2.pdf

NGRA principles & NGRA frameworks for Systemic Safety & Skin Sensitization have created a common language for scientific dialogue on regulatory use

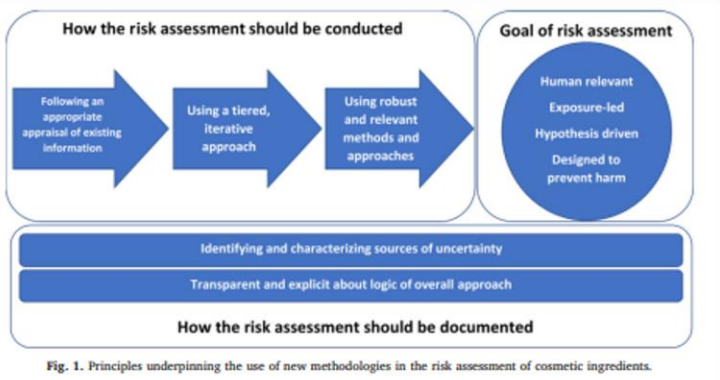
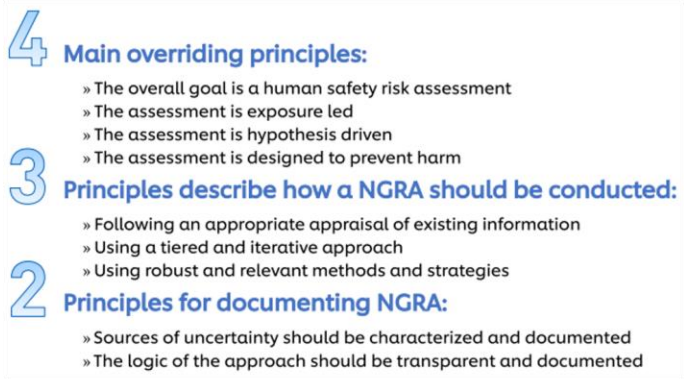
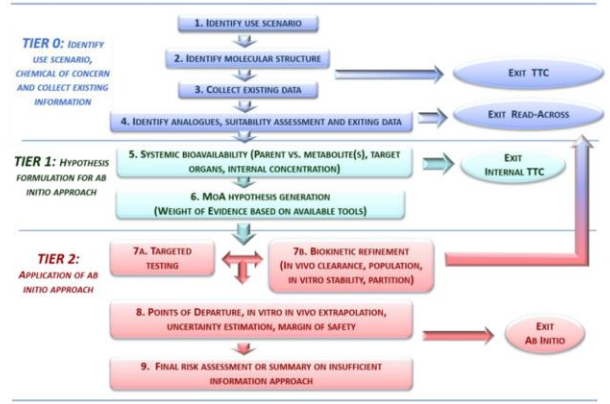


Fig. 1. Principles underpinning the use of new methodologies in the risk assessment of cosmetic ingredients.





Computational Toxicology 7 (2018) 20–26

Contents lists available at ScienceDirect

Computational Toxicology

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

Principles underpinning the use of new methodologies in the
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[i], Nashira Vieira O'Reilly Cabral Posada[i], Craig Weiss[p], Hajime Kojima[f]

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-

Regulatory Toxicology and Pharmacology 125 (2021) 10

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Regulatory Toxicology and Pharm

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

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

M.P. Dent[a,*], E. Vaillancourt[b], R.S. Thomas[c], P.L. Carmichael[a], G. Ouedraogo[d], H. Kojima[e], J. Barroso[f], J. Ansell[g], T.S. Barton-Maclaren[b], S.H. Bennekou[h], K. Boekelheide[i], J. Ezendam[j], J. Field[k], S. Fitzpatrick[k], M. Hatao[l], R. Kreiling[m], M. Lorencini[n,1], C. Mahony[o], B. Montemayor[p], R. Mazaro-Costa[q], J. Oliveira[r], V. Rogiers[s], D. Smegal[k], R. Taalman[t], Y. Tokura[u], R. Verma[k], C. Willett[v], C. Yang[w]

ARTICLE INFO

ABSTRACT

European Commission

Scientific Committee on Consumer Safety

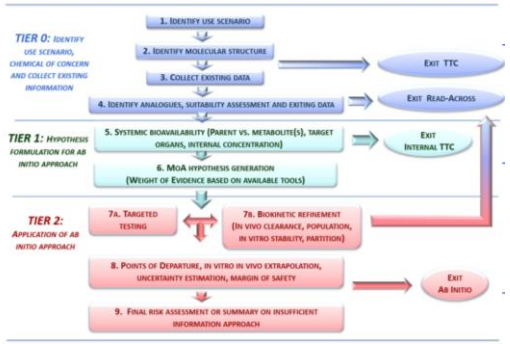
SCCS

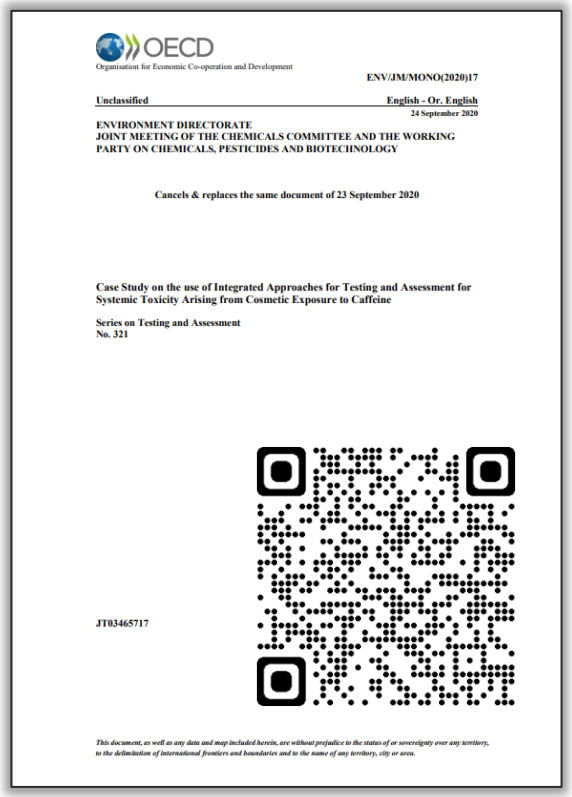
THE SCCS NOTES OF GUIDANCE FOR THE TESTING OF COSMETIC INGREDIENTS AND THEIR SAFETY EVALUATION

12TH REVISION

ICCS

Cosmetic NGRA/Integrated Approach for Testing & Assessment (IATA) case studies are an important tool for facilitating scientific dialogue with regulators




OECD
Organisation for Economic Co-operation and Development
ENV/JM/MONO(2020)17
Unclassified
English - Or. English
24 September 2020
ENVIRONMENT DIRECTORATE
JOINT MEETING OF THE CHEMICALS COMMITTEE AND THE WORKING PARTY ON CHEMICALS, PESTICIDES AND BIOTECHNOLOGY
Cancels & replaces the same document of 23 September 2020
Case Study on the use of Integrated Approaches for Testing and Assessment for Systemic Toxicity Arising from Cosmetic Exposure to Caffeine
Series on Testing and Assessment
No. 321
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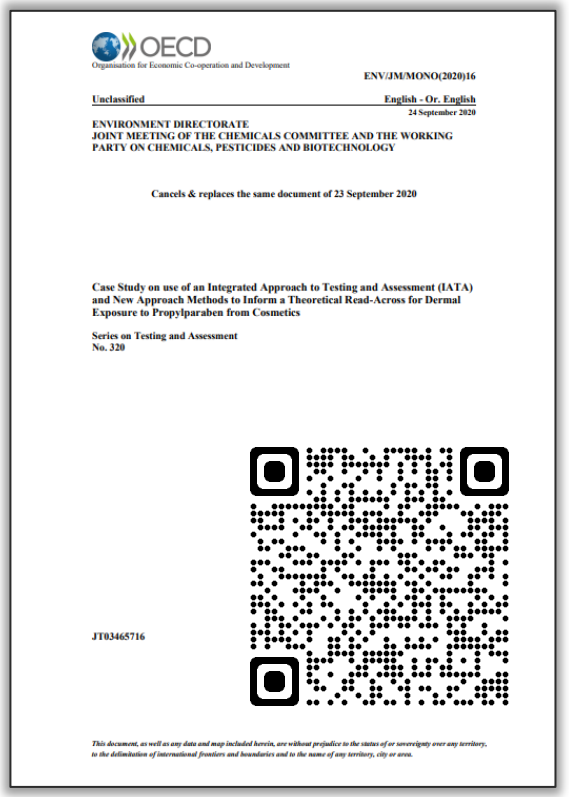
Caffeine NGRA OECD IATA case study – Sept 2020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24 September 2020
ENVIRONMENT DIRECTORATE
JOINT MEETING OF THE CHEMICALS COMMITTEE AND THE WORKING PARTY ON CHEMICALS, PESTICIDES AND BIOTECHNOLOGY
Cancels & replaces the same document of 23 September 2020
Case Study on use of an Integrated Approach to Testing and Assessment (IATA) and New Approach Methods to Inform a Theoretical Read-Across for Dermal Exposure to Propylparaben from Cosmetics
Series on Testing and Assessment
No. 320
JT03465716
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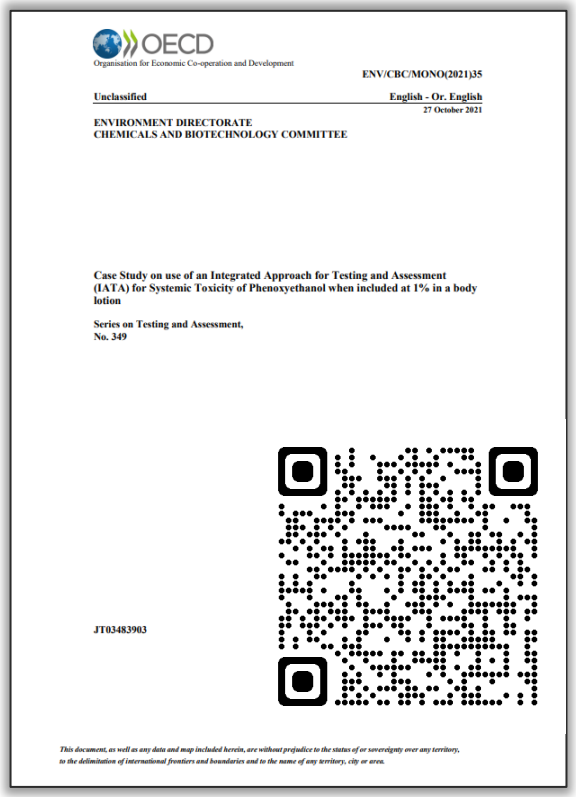
Propylparabens NGRA OECD IATA case study – Sept 2020


OECD
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ENV/CBC/MONO(2021)35
Unclassified
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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
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Phenoxyethanol NGRA OECD IATA case study – Oct 2021

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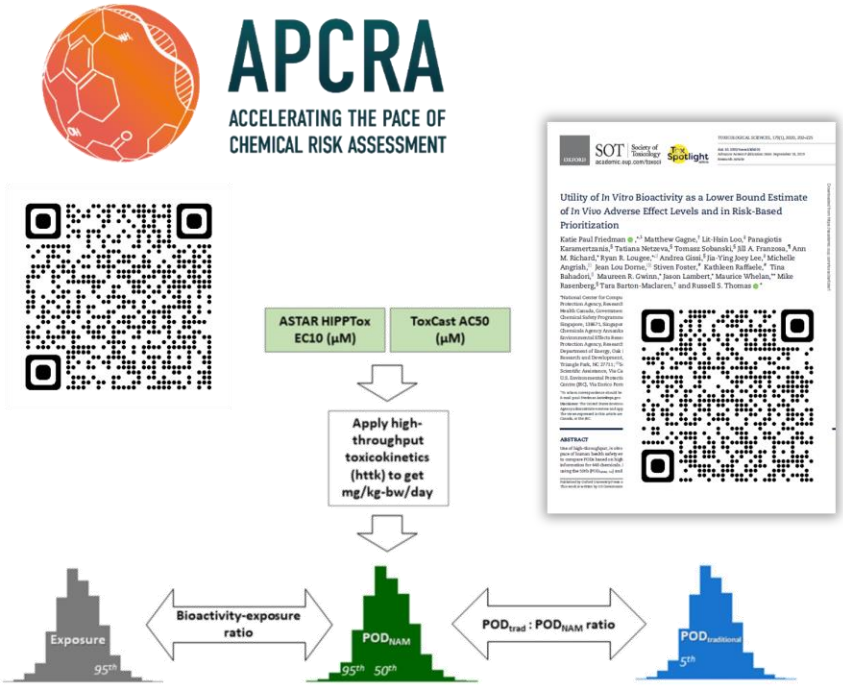
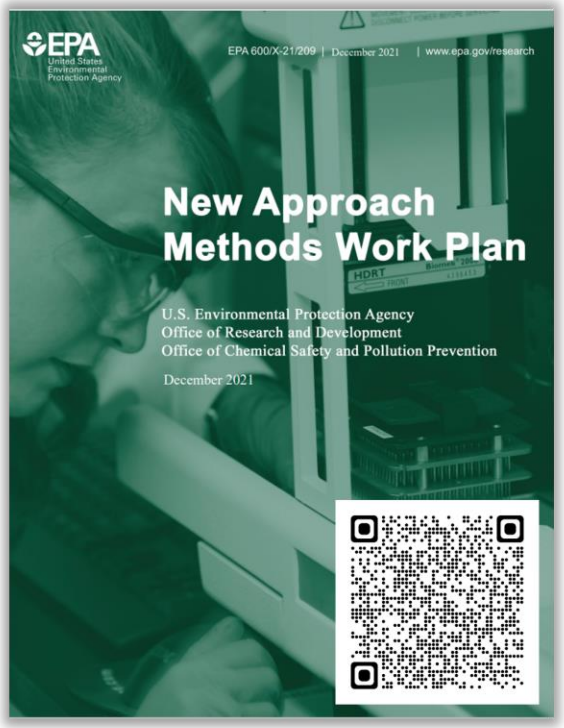
In parallel, increasing global consensus within chemical regulators on value of similar NAM toolboxes for screening, hazard characterisation & risk assessment

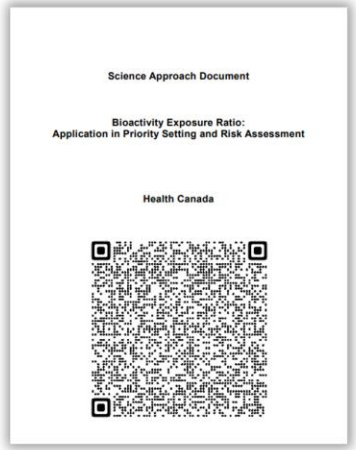


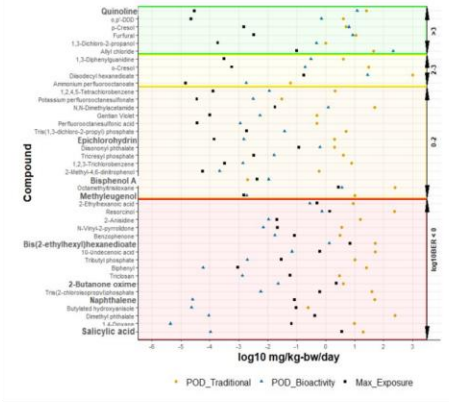
Paul Friedman et al. 2020

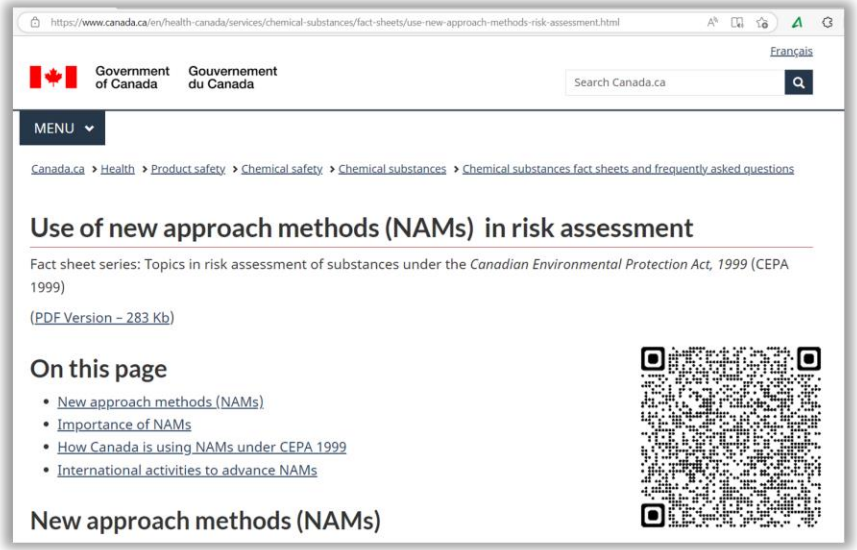
APCRA 'proof-of-concept' case study demonstrated the feasibility of applying a high throughput NAM-based approach for screening-level assessments - $POD_{NAM\ 95}$ value less than or equal to the $POD_{traditional}$ value for 89% chemicals. **Bioactivity-exposure ratio** useful metric for chemical prioritization



New Approach Methods Work Plan (epa.gov)







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Opportunity to accelerate chemical transition to non-animal safety assessment through learning from cosmetic experience (The Good, the Bad & the Ugly)

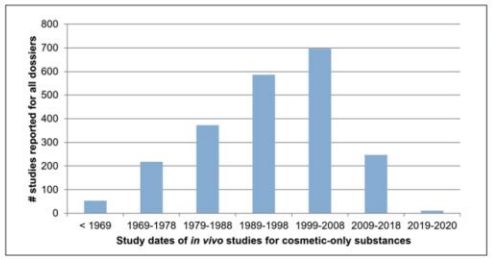


Fig. 1: All *in vivo* studies reported in cosmetic-only dossiers by study or report date as indicated in the ECHA database
Includes studies reported in publications; most of these pre-date 2009. The interval was selected to be consistent with the period when REACH was implemented in the EU. REACH was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

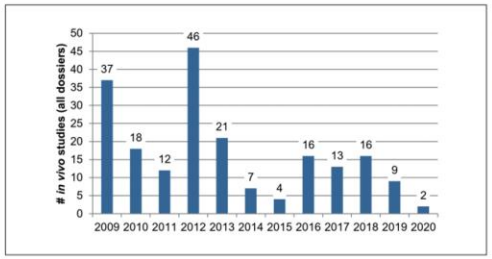
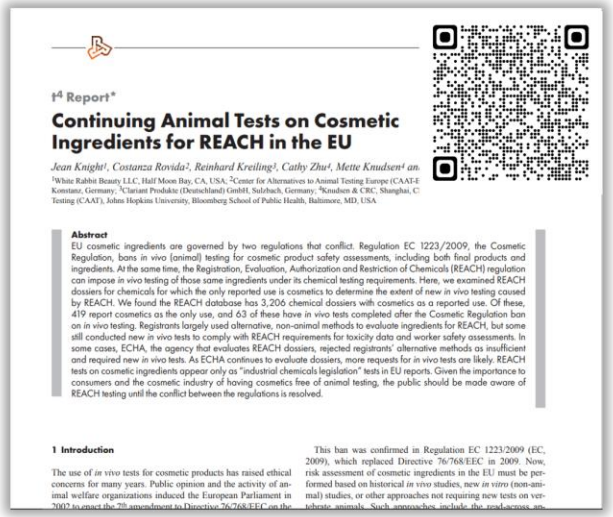


Fig. 2: Number of unique *in vivo* tests for cosmetic-only substances in 2009-2020 extracted from the ECHA database
The total number shown, 201, excludes 16 studies reported in dossiers or by registrants as being for a non-REACH purpose, indicating either a dual use or compliance with a non-EU country.



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

[1]White Rabbit Beauty LLC, Half Moon Bay, CA, USA; [2]Center for Alternatives to Animal Testing Europe (CAAT-E Konstanz, Germany; [3]Clariant Produkte (Deutschland) GmbH, Sulzbach, Germany; [4]Knudsen & CRC, Shanghai, C Testing (CAAT), Johns Hopkins University, Bloomberg School of Public Health, Baltimore, MD, USA

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 an

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**

Workshop on the Roadmap towards phasing out animal testing for chemical safety assessments
11 - 12 December 2023, Brussels

Session 1 – Introduction and setting the scene
Session 2: How to replace animal testing for the concern of systemic human health effects?
Session 3: How to replace animal testing for the concern of long-term aquatic toxicity?
Session 4: Partnership for the Assessment of Risks from Chemicals (PARC) - Next-Generation Risk Assessment
Session 5: Enhancing the translation of non-animal methods into regulation
Session 6: Next steps and closing remarks

PARC workshop

"Guiding principles towards "Next-Generation Risk Assessment" (NGRA)-ready chemicals legislation in the EU"

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

ICCS

ICCS | INTERNATIONAL COLLABORATION ON COSMETICS SAFETY

A Global Not-for-Profit
Research & Education Organization

Mission:
Accelerate the global acceptance of animal-free science for human and environmental safety assessment of cosmetics and their ingredients through Science, Education & Training, and Regulatory Engagement

New global, **multi-stakeholder** organization launched in February 2023

Dedicated to advancing animal-free safety assessments for cosmetic products and their **ingredients**

Covering both human health and environmental safety

ICCS Members and Growing…

27 Cosmetic Product and Ingredient Manufacturers

Amorepacific
BASF
Beiersdorf
Chanel
Colgate
Coty
Croda
Estée Lauder
Edgewell
Evonik
Haleon
Henkel
IFF
Innospec
Inolex
Kao
Kenvue (J&J)
L'Oréal
LVMH
Oriflame
P&G
Reckitt
Shiseido
Takasago
Syensqo
Unilever
Wella

10 Cosmetic & Chemical Trade and Research Associations

CAC, Cosmetics Alliance Canada

CE, Cosmetics Europe

CTPA, Cosmetic, Toiletry, Perfumery Assoc. (UK)

EFfCI, European Federation for Cosmetic Ingredients

FCA, Fragrance Creators Association

IFRA, International Fragrance Association

JCIA, Japan Cosmetic Industry Association

CASIC, Latin American Cosmetic, Personal Care and Home Care Industries Association

PCPC, Personal Care Products Council (PCPC)

RIFM, Research Institute for Fragrance Materials

5 NGOS

CFI, Cruelty Free International

HSI, Humane Society International

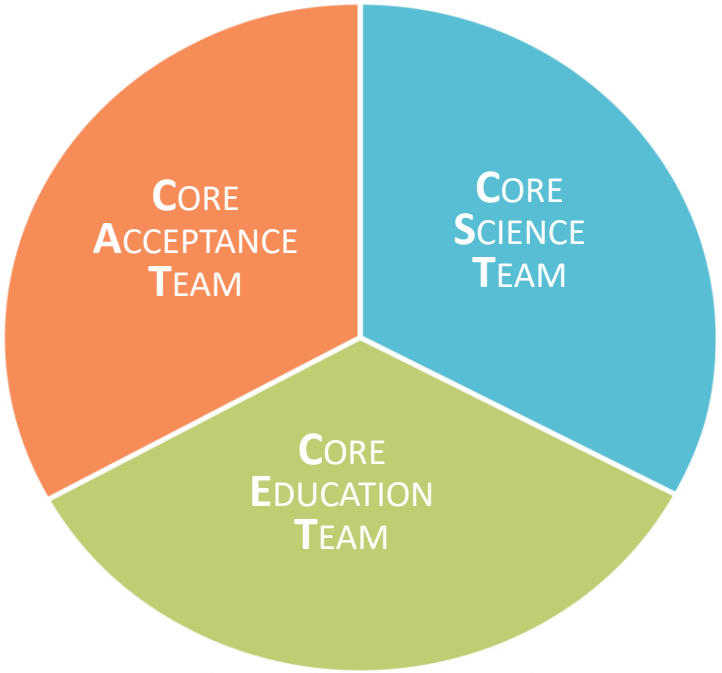
IIVS, Institute for In Vitro Sciences

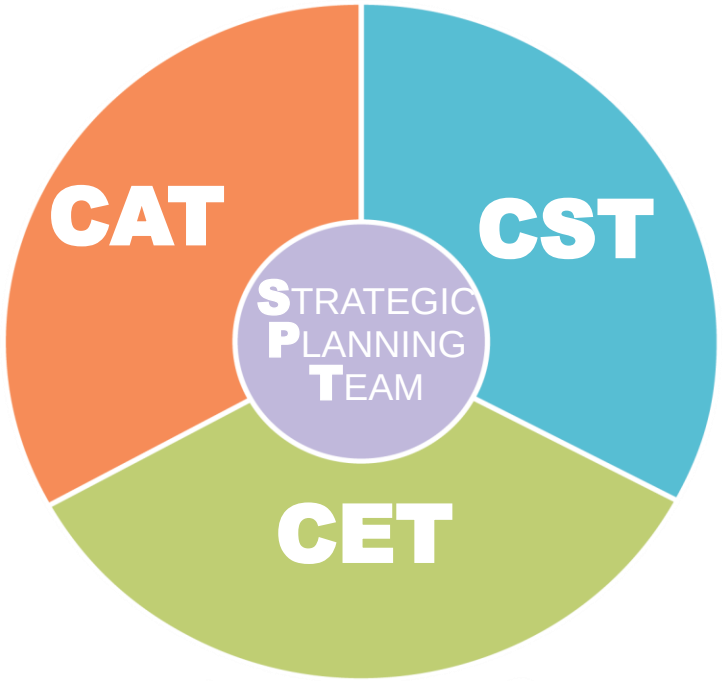
PCRM, Physicians Committee for Responsible Medicine

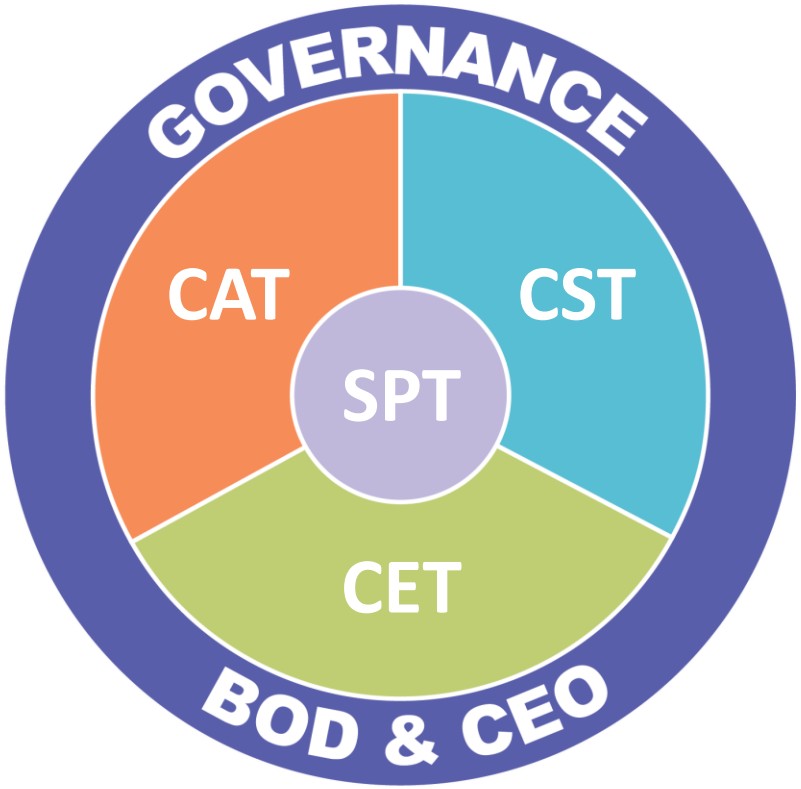
PSCI, Peta Science Consortium International

ICCS

ICCS Pillars to Accomplish our Mission:
Regulatory Engagement, Science, Education & Training







Representative		Organization
Government/Regulatory Agencies		
Tomasz	Sobanski	European Chemicals Agency (ECHA)
Tara	Barton-MacLaren	Health Canada
Marize	Campos Valadares	Universidade Federal de Goiás/ ANVISA (Brazilian Regulatory)
Alison	Harrill	US Environmental Protection Agency (US EPA)
Katie	Paul-Friedman	US Environmental Protection Agency (US EPA)
Validation Bodies of Governments		
Maurice	Whelan	European Commission Joint Research Center/ ECVAM
Takao	Ashikaga	Japanese Ceneter for Validation of Alternative Methods (JaCVAM)
Nicole	Kleinstreuer	US National Center for the Evaluation of Alternative Toxicological Methods (NICEATM/ICCVAM)
Octavio	Presgrave	Brazilian Center for Validation of Alternative Methods (BraCVAM)
Research Institutes and Experts		
Carole	Yauk	University of Ottawa
Kristin	Schirmer	Swiss Federal Institute of Aquatic Science and Technology (EAWAG)
Nathalie	Burden	UK National Center for the 3Rs (NC3RS)
Scott	Belanger	Independent environmental expert
Charlie	Menzie	Independent environmental expert

Science Advisory Committee

Core Science Team: Aim & Objectives

Build a Robust Scientific Toolbox

1 **Identify** regional stakeholder & regulatory needs

2 **Prioritize** activities where ICCS can have best impact

3 **Develop** ICCS as a Center of Competence in NGRA

Delivery Teams

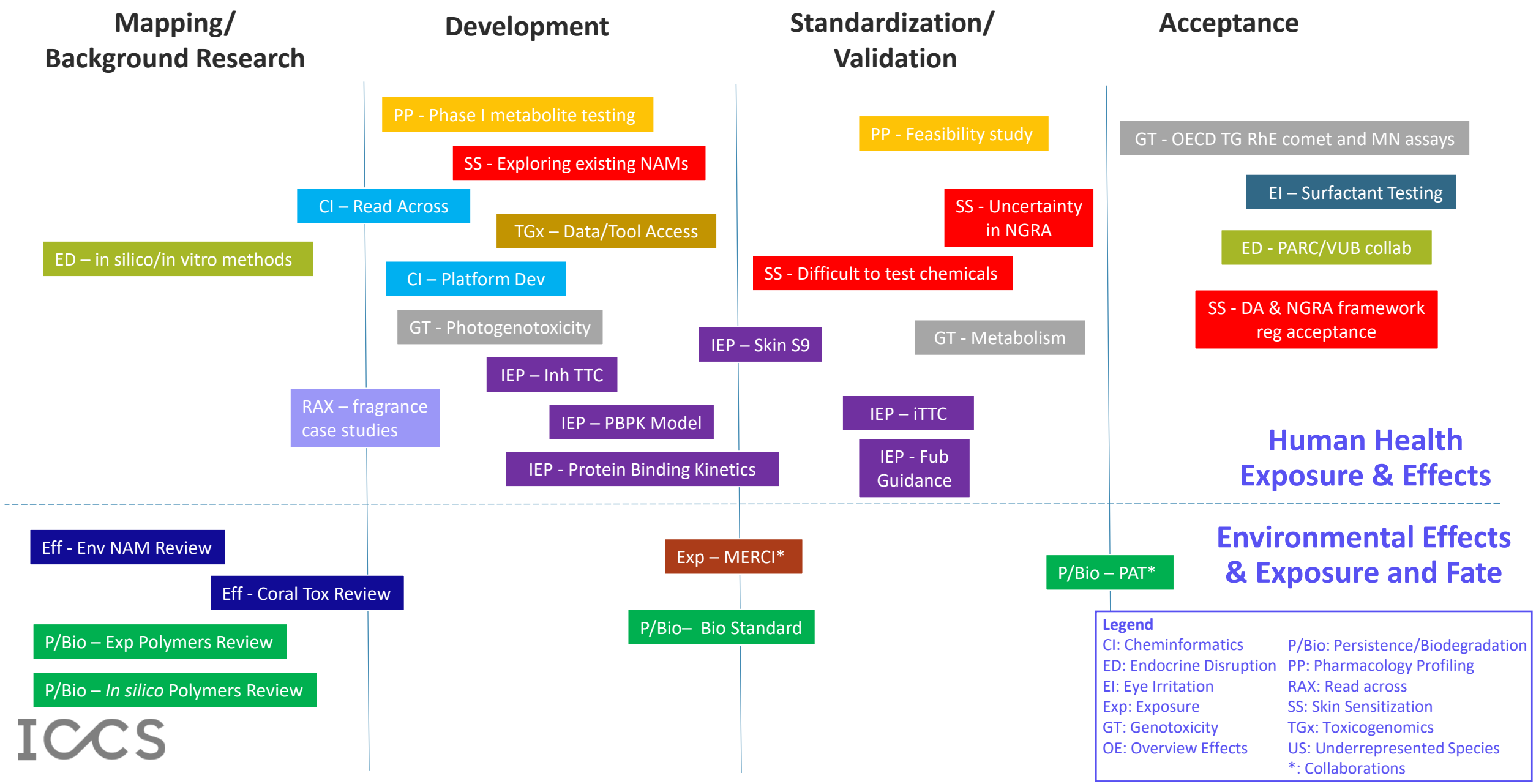
Human Health Effects	Environmental Effects
Human Health Exposure	Environmental Exposure and Fate
Safety Decision (Case Studies)	

ICCS Core Science Team (CST):

- Develops and oversees science projects
- Focuses on NAMs and Next Generation Risk Assessment (NGRA) frameworks for cosmetic products and ingredients to protect human and environment health
- Engages with external Science Advisory Committee to shape ICCS science strategy and projects

ICCS

On-going ICCS Core Science Team (CST) projects (Key: Delivery Team – Project)



Legend

CI: Cheminformatics	P/Bio: Persistence/Biodegradation
ED: Endocrine Disruption	PP: Pharmacology Profiling
EI: Eye Irritation	RAX: Read across
Exp: Exposure	SS: Skin Sensitization
GT: Genotoxicity	TGx: Toxicogenomics
OE: Overview Effects	US: Underrepresented Species
	*: Collaborations

Core Acceptance Team: Aim & Objectives

Accelerate Uptake of Animal-Free Safety Assessments for Cosmetics

1 **Standardization & Validation** of animal-free safety assessment approaches for regulatory use

2 **Regulatory Acceptance** of NAMs and Next Generation Risk Assessment (NGRA) frameworks for Cosmetics

3 **Global Alignment** of Cosmetic and Chemical regulatory information requirements

Multi-stakeholder collaborations (e.g. ICCS) are needed to efficiently address these strategic challenges

ICCS Core Acceptance Team (CAT):

- Drives standardization & supports global validation
- Coordinates regulator & stakeholder engagement to support scientific dialogue and peer review
- Develops and provides expert input to regulatory guidance
- Ensures ICCS Science & Education strategies address regulatory needs

ICCS

Core Acceptance Team: Standardization & Validation

Accelerate acceptance of animal-free safety assessment approaches through driving standardization & supporting global validation

Work with ICCS science team to define:

- standardization & validation priorities
- existing / planned case studies

Strategic Mapping

- Collaborate to drive standardization & support global validation of animal-free safety assessment approaches

Collaboration

Outreach

- Outreach to OECD, Validation bodies & ICCR to identify overlapping priorities
- Engage Scientific Advisory Committee

Regulatory Guidance

- Provide expert input to draft technical guidance for regulatory use of animal-free safety assessment approaches

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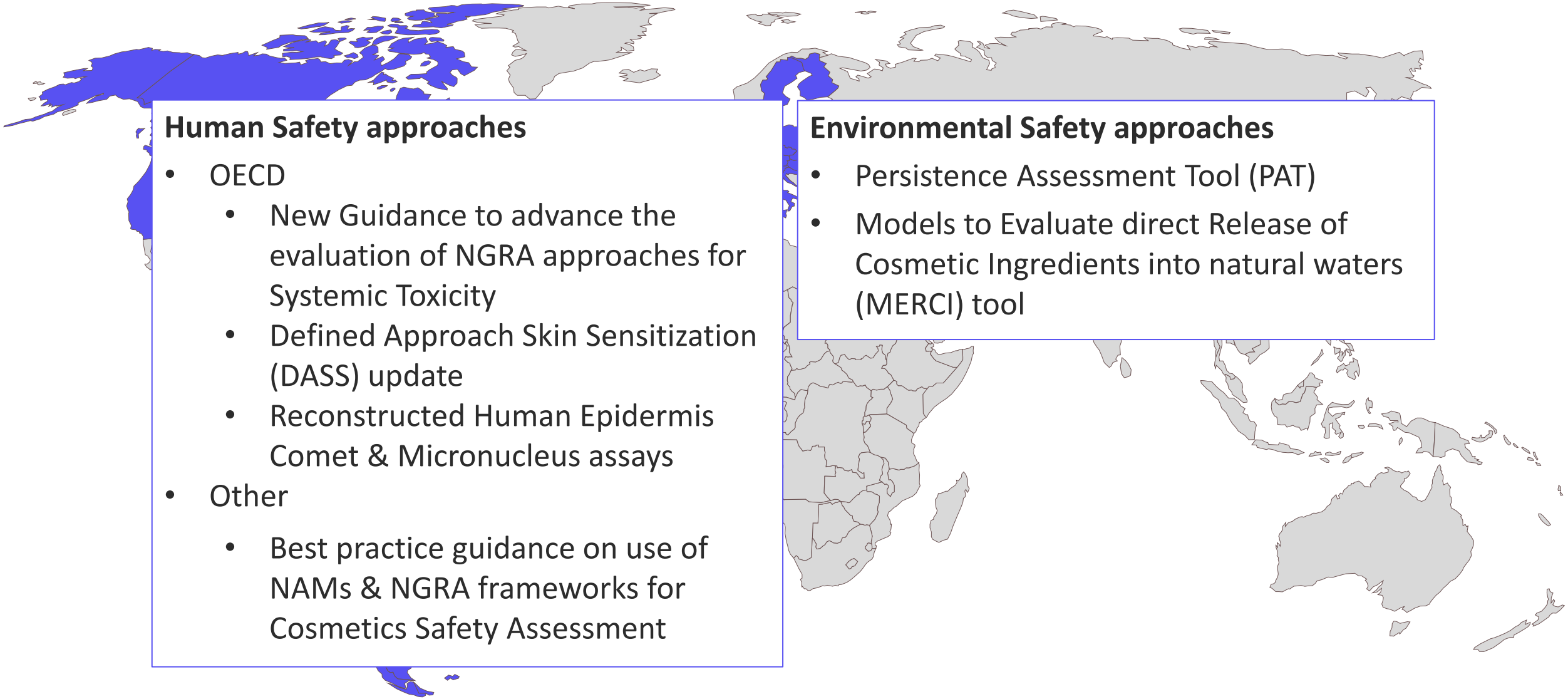
Core Acceptance Team (CAT) Standardisation & Validation 2024 priorities



Human Safety approaches

- OECD
  - New Guidance to advance the evaluation of NGRA approaches for Systemic Toxicity
  - Defined Approach Skin Sensitization (DASS) update
  - Reconstructed Human Epidermis Comet & Micronucleus assays
- Other
  - Best practice guidance on use of NAMs & NGRA frameworks for Cosmetics Safety Assessment

Environmental Safety approaches

- Persistence Assessment Tool (PAT)
- Models to Evaluate direct Release of Cosmetic Ingredients into natural waters (MERCI) tool

Core Acceptance Team: Regulatory Application

Accelerate acceptance of animal-free safety assessment approaches through scientific dialogue with regulators & stakeholders

Work with local trade associations to map:

- Country/region regulatory frameworks
- Key regulatory/stakeholder organizations

Strategic Mapping

- Organize joint scientific workshops to facilitate peer review of case studies
- Address Cosmetic & Chemical regulatory requirements

Collaboration

Outreach

- Outreach to key organizations to identify opportunities for scientific dialogue
- Develop roadmap for ICCS collaboration

Regulatory Guidance

- Provide expert input to draft technical guidance for regulatory use of animal-free safety assessment approaches

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Core Acceptance Team (CAT) Regulatory Application 2024 priorities

Canada:

- Support ongoing Cosmetics Alliance Canada: Health Canada & Environment Climate Change Canada dialogue on NGRA

US:

- Support ongoing PCPC: FDA dialogue on use of NAMs & NGRA for safety assessment

LATAM:

- Support CASIC efforts to build awareness of NGRA frameworks for Cosmetics

EU:

- Support ongoing Cosmetics Europe: SCCS dialogue on NGRA
- Support development of EU roadmap to phase-out use of animals for Regulatory Testing of Chemicals

UK:

- Support ongoing CTPA: UK Govt dialogue on NGRA
- Support ongoing CTPA efforts to facilitate UK: China networks for regulator knowledge exchange

China:

- Support ongoing CafFCI & CACHA dialogue with NMPA/NIFDC on Special Use Cosmetics

Japan:

- Support JCIA efforts to build awareness of NGRA frameworks for Cosmetics

S. Korea:

- Build awareness of NGRA frameworks for Cosmetics

Core Education Team: Aim & Objectives

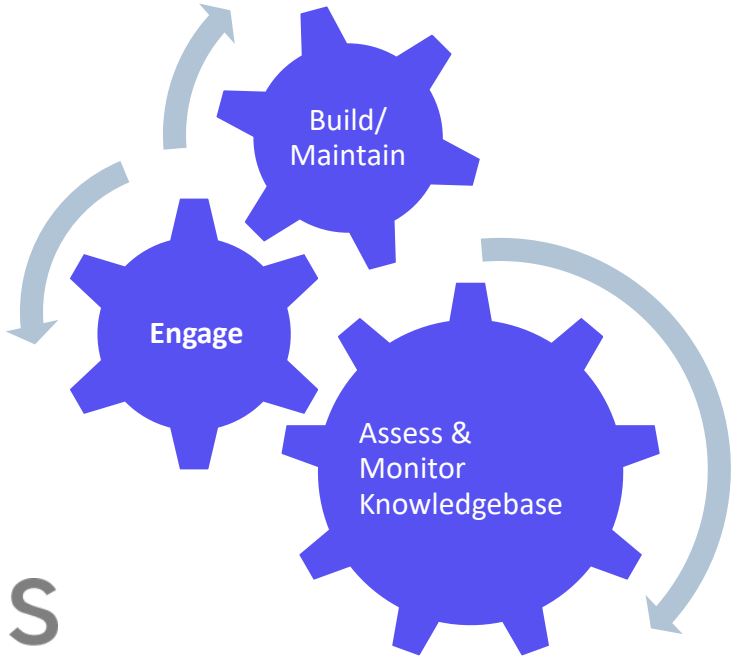
Support and Design Continuous Educational Programs

1 **Understand** education needs from various stakeholders

2 **Facilitate** awareness & engagement with existing activities

3 **Fill gaps** through coordination with Acceptance & Science Teams

An Iterative Approach



ICCS Core Education Team (CET):

- Coordinates stakeholder engagement to connect science and acceptance activities to further uptake and use
- Identifies outreach and education gaps for prioritization. Seeks to complement, not duplicate
- Differentiates education needs for different audiences (users of tools and users of data) and regions
- Ensures science results in educational tools which address regulatory acceptance needs

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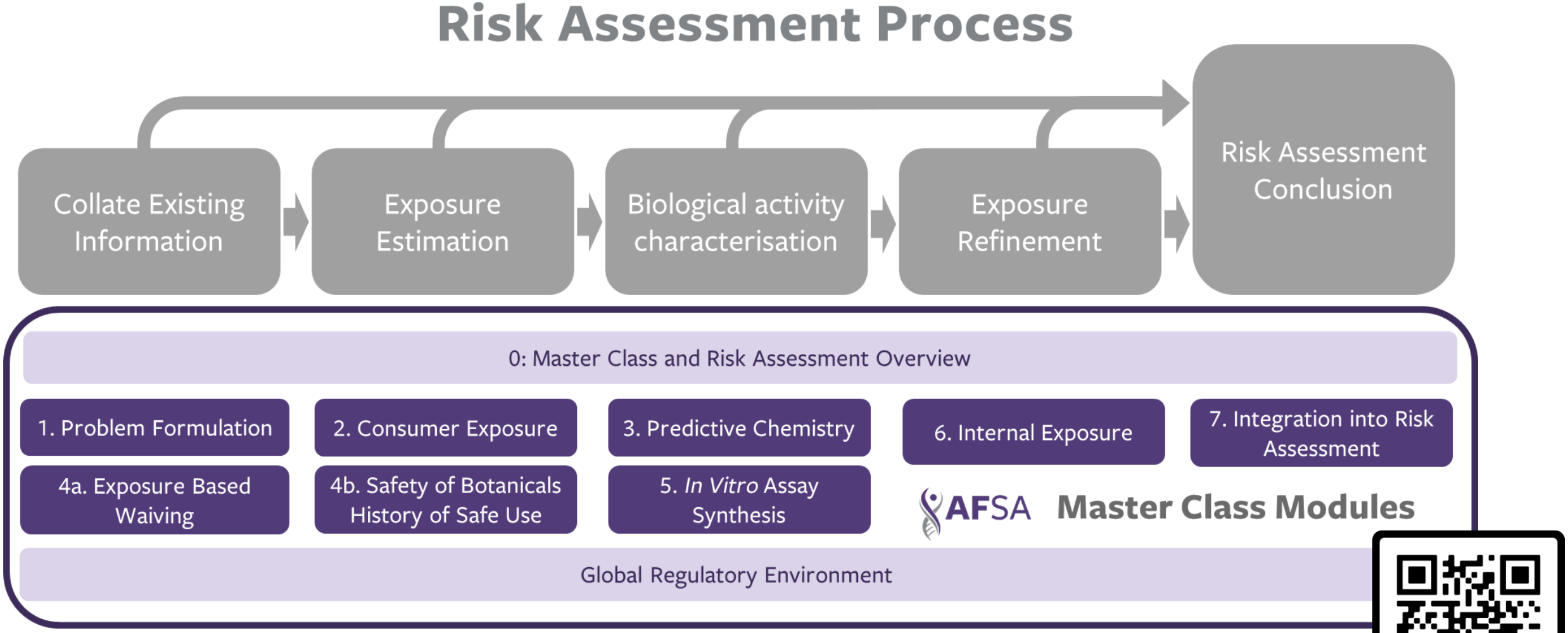
CET: Facilitate awareness & engagement with existing activities – AFSA Masterclass

AFSA Masterclass - Covering Risk Assessment from start to finish



https://www.afsacollaboration.org/masterclass

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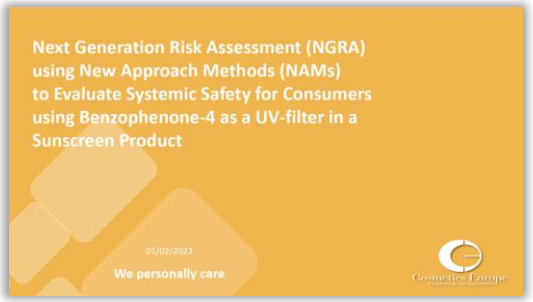
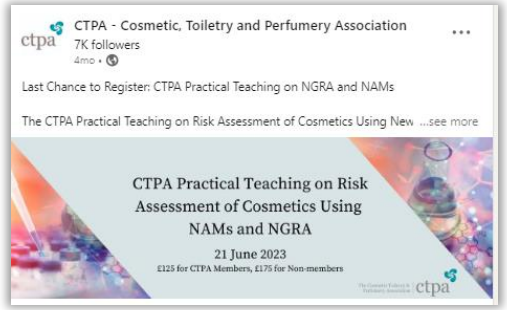
CET: Accelerating global capacity-building through NGRA/IATA case studies

- **NGRA/IATA Case studies** continue to be an important tool for facilitating scientific dialogue.
- Once created the same resources can also be re-used for education and training activities.
  - ICCS case study review and planning by the Safety Decision team is ongoing.
  - Re-use of BP4 NGRA case study as education & training content captured to illustrate

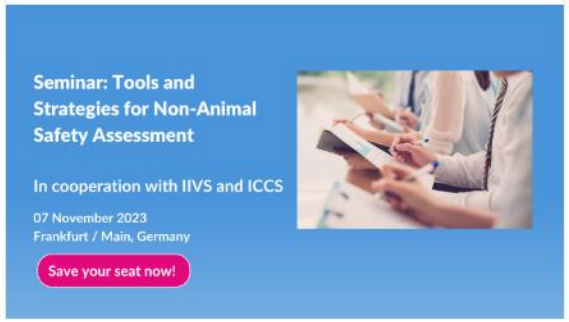


BP4 NGRA dossier presented to SCCS – Feb 2023



CTPA training workshop – June 2023

ASCCT workshop – Oct 2023



DGK/IKW seminar – Nov 2023

EPAA NAM User Forum – Dec 2023

Conclusions

- **A paradigm shift is well underway** as use of NAMs and NGRA for Cosmetic Safety Assessment and ingredient registration becomes increasingly widespread, accelerated by animal testing bans

- **ICCS aims to support the transition to animal-free safety assessment for cosmetics** through targeted research, regulatory engagement and education & training activities

- **Increased industry: regulator scientific dialogue** is needed to build confidence in existing NAMs & NGRA approaches for regulatory use and focus research on addressing key regulatory needs

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Thank you!

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