Unilever

ICCR's Best Practices for Promoting Next-Generation Risk Assessment of Cosmetic Ingredients

Matt Dent

19 February 2026

SERS
Safety, Environmental & Regulatory Science




Talk Outline

- The ICCR and the Principles of NGRA
- Applying the Principles to Case Studies
- Developing Best Practice
- What Next?

SERS
Safety, Environmental & Regulatory Science

SERS
Safety, Environmental & Regulatory Science

The ICCR

The International Cooperation on Cosmetics Regulation is a voluntary international group of cosmetics regulatory authorities from Brazil, Canada, Chinese Taipei, the European Union, Israel, Japan, Republic of Korea, and the United States who meet on an annual basis to discuss cosmetics safety and regulation, as well as enter into a constructive dialogue with relevant cosmetics industry trade associations.

https://www.iccr-cosmetics.org

ICCR Work Products

The experts that participate in the ICCR have produced:

- White papers that provide a background on the current status across jurisdictions on a given matter or approach
- General principles that should be considered in addressing a particular regulatory issue in a manner that is specific to cosmetic products
- Recommendations on specific regulatory/safety issues that can include definitions, acceptable levels, methodologies, endorsement of other international standards as applicable to cosmetic products, etc.

https://www.iccr-cosmetics.org

SERS
Safety, Environmental & Regulatory Science

Unilever

Development of the Principles

2016

The ICCR approached Cosmetics Europe to ask for help in defining a way to integrate non-animal test data for cosmetic ingredient safety assessment

→ "Integrated Strategies" Joint Regulator-Industry Working Group formed

2016-2017

The Joint Working Group agreed that to build on a solid foundation, we would first define the Principles underpinning the use of new methodologies in the risk assessment of cosmetic ingredients

2018

The "ICCR Principles of NGRA" were published in Computational Toxicology

https://doi.org/10.1016/j.comtox.2018.06.001

Computational Toxicology 7 (2018) 20–26

Contents lists available at ScienceDirect

Computational Toxicology

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

ELSEVIER

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

Matthew Dent[a,*], Renata Teixeira Amaral[b], Pedro Amores Da Silva[b], Jay Ansell[c], Fanny Boisleve[d], Masato Hatao[e], Akihiko Hirose[f], Yutaka Kasai[g], Petra Kern[h], Reinhard Kreiling[i], Stanley Milstein[j], Beta Montemayor[k], Julcemara Oliveira[l], Andrea Richarz[m], Rob Taalman[n], Eric Vaillancourt[o], Rajeshwar Verma[l], Nashira Vieira O'Reilly Cabral Posada[l], Craig Weiss[p], Hajime Kojima[f]

[a] Unilever Safety and Environmental Assurance Centre, Colworth Science Park, Sharnbrook, Bedfordshire MK44 1LQ, UK
[b] ABIHPEC – Association of the Cosmetic, Toiletry and Fragrance Industry (ABIPHEC), Av. Paulista, 1313 Cerqueira César, São Paulo, SP 01311-000, Brazil
[c] US Personal Care Products Council (PCPC), 1620 L St. NW, Suite 1200, Washington, D.C. 20036, USA
[d] Johnson & Johnson Santé Beauté France, Domaine de Maigremont, CS 10615, F-27106 VAL DE REUIL Cedex, France
[e] Japan Cosmetic Industry Association (JCIA), Metro City Kamiyacho 6F, 5-1-5, Toranomon, Minato-ku, Tokyo 105-0001 Japan
[f] National Institute of Health Sciences, 1-18-1 Kamiyoga, Setagaya-ku, 158-8501 Tokyo, Japan
[g] Kao Corporation, External Relations & Government Affairs 2-1-3, Bunka, Sumida-Ku, Tokyo 131-8501 Japan
[h] Procter and Gamble Services Company NV, Temselaan 100, B-1853 Strombeek-Bever, Belgium
[i] Clariant Produkte (DE) GmbH, Global Toxicology and Ecotoxicology, Am Unisys-Park 1, 65843 Sulzbach, Germany
[j] US Food and Drug Administration (US FDA), Office of Cosmetics and Colors (OCAC), Center for Food Safety and Applied Nutrition (CFSAN), 5001 Campus Drive, College Park, MD 20740, USA
[k] Cosmetics Alliance Canada, 420 Britannia Road East Suite 102, Mississauga, ON L4Z 3L5, Canada
[l] Brazilian Health Regulatory Agency (ANVISA), Gerência de Produtos de Higiene, Perfumes, Cosméticos e Saneantes, SIA Trecho 5, lote 200, Area Especial 57 – CEP 71205-050, Brazil
[m] European Commission, Joint Research Centre (JRC), Directorate for Health, Consumers and Reference Materials, Chemical Safety and Alternative Methods Unit, Via E. Fermi 2749, 21027 Ispra, VA, Italy
[n] Cosmetics Europe, Avenue Herrmann-Debroux 40, 1160 Auderghem, Belgium
[o] Health Canada (HC), Consumer Product Safety Directorate, Healthy Environments and Consumer Safety Branch, 269 Laurier Ave. W., Ottawa, ON K1A 0K9, Canada
[p] Independent Cosmetic Manufacturing and Distributors (ICMAD), 21925 Field Parkway, Suite 2015, Deer Park, IL 60010, USA

SERS
Safety, Environmental & Regulatory Science

Unilever

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

SERS
Safety, Environmental & Regulatory Science

https://doi.org/10.1016/j.comtox.2018.06.001

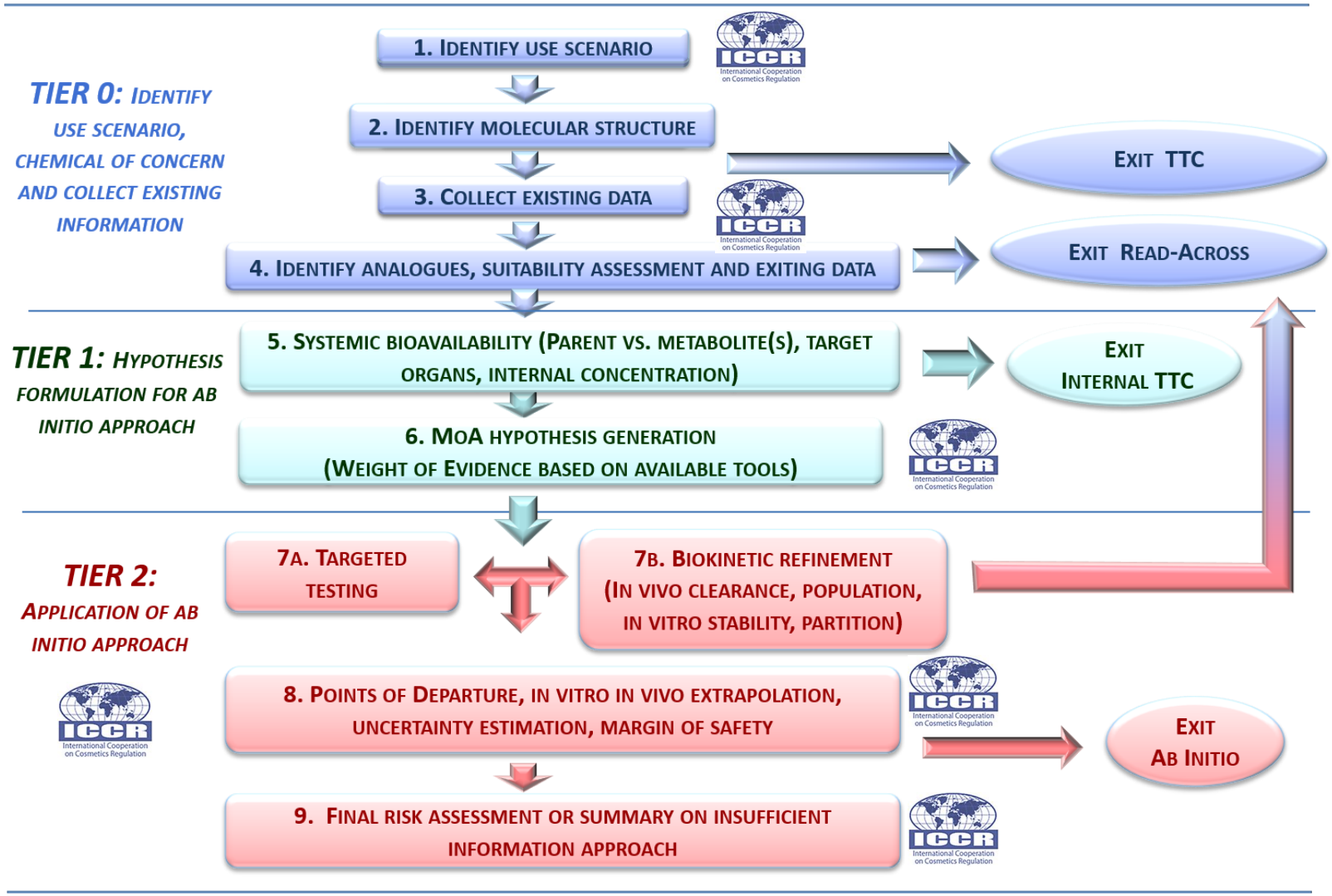
From Principles to Application

The Joint Working Group built on the foundations of the principles to describe the tools that may be useful in the risk assessment of cosmetic ingredients, and how they could be applied.

https://www.iccr-cosmetics.org

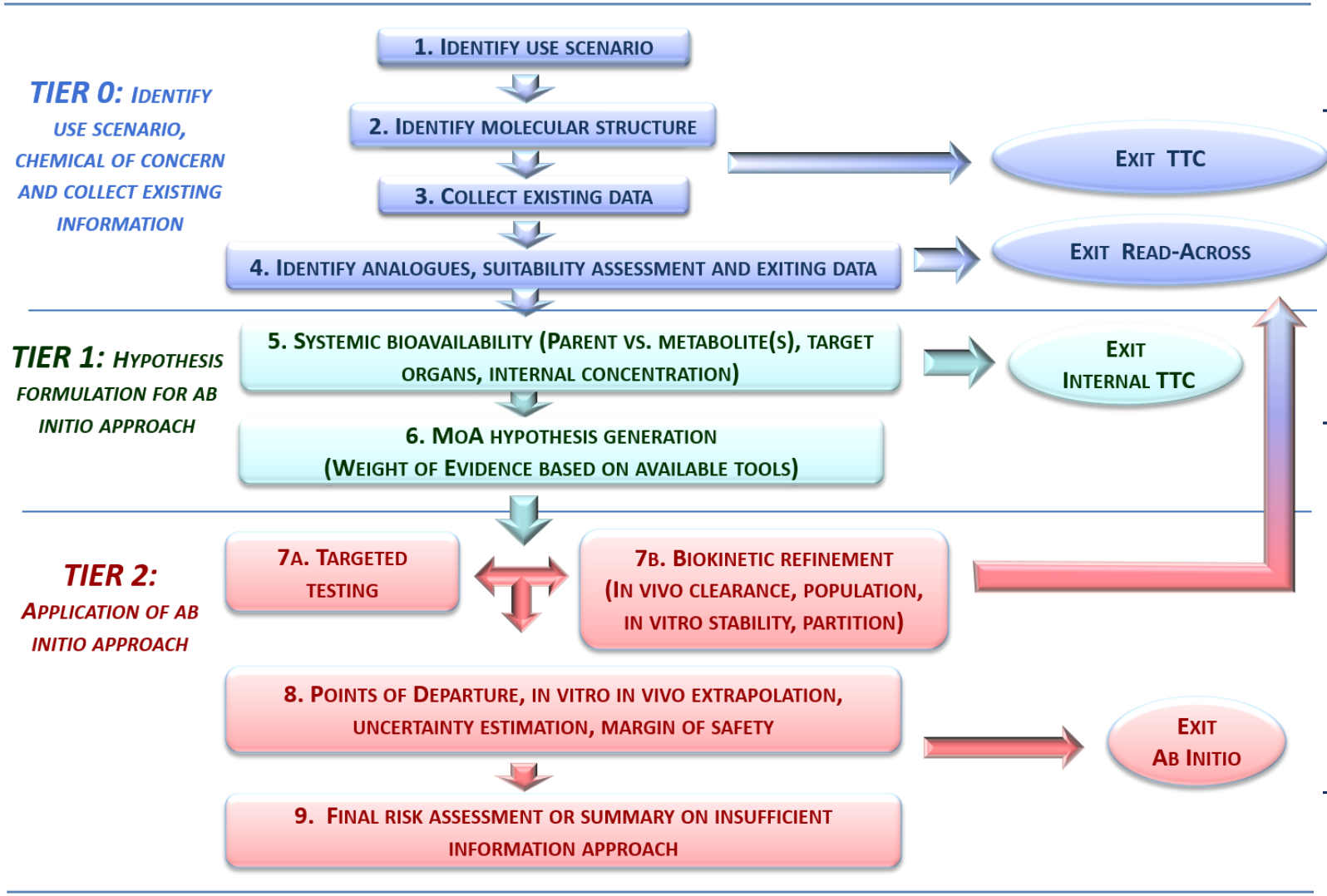
SERS
Safety, Environmental & Regulatory Science

The Seurat-1 workflow



Continue through tiers until there is sufficient information to make a decision: assessment may be complete at any tier Berggren *et al.*, (2017) *Computational Toxicology* 4: 31-44. https://doi.org/10.1016/j.comtox.2017.10.001

Mapping different NAMs to the workflow



- Read across
- Exposure-based waiving
- *In silico* tools

- Metabolism and metabolite identification
- Physiologically-based kinetic modelling
- *In chemico* assays
- 'Omics
- Reporter gene assays
- *In vitro* pharmacological profiling

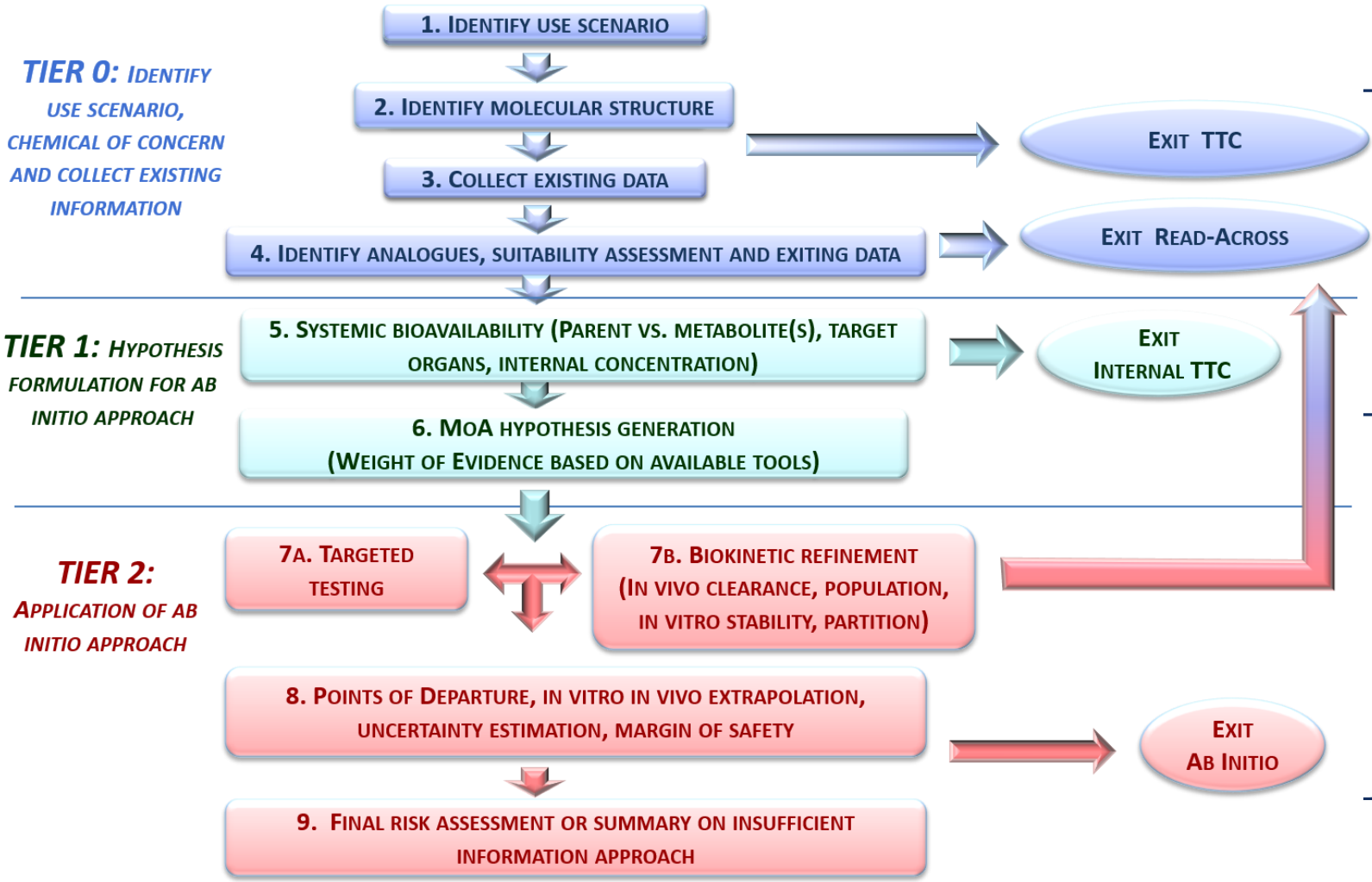
- 3D culture systems
- Organ-on-chip
- Pathways modelling
- Human studies

Key: Readiness judged by ICCR in 2018

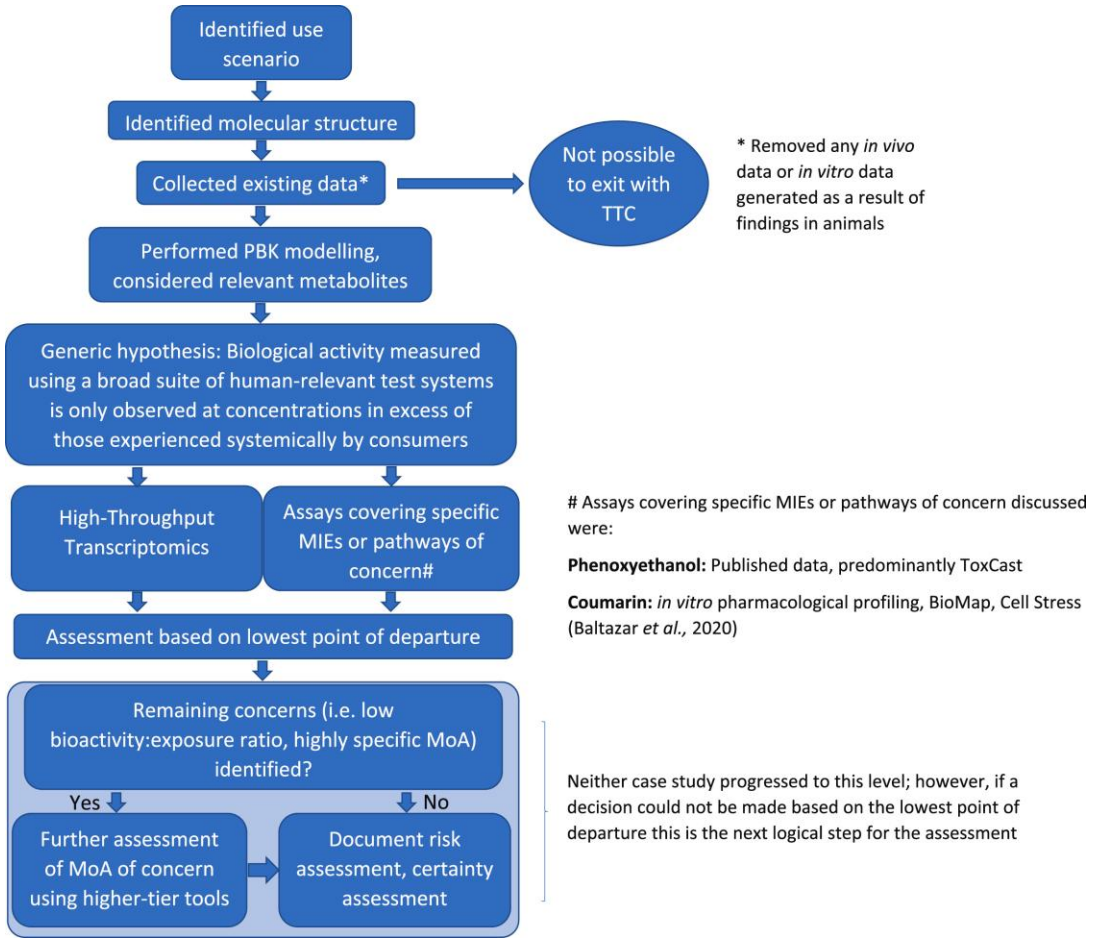
https://www.iccr-cosmetics.org/component/attachments/?task=download&id=85

- Already in common use
- Mature with likely utility
- Insufficiently developed

Unilever



- Read across
- Exposure-based waiving
- *In silico* tools
- Metabolism and metabolite identification
- Physiologically-based kinetic modelling
- *In chemico* assays
- 'Omics
- Reporter gene assays
- *In vitro* pharmacological profiling
- 3D culture systems
- Organ-on-chip
- Pathways modelling
- Human studies



Dent et al, 2021

Workshop in Canada: 2019

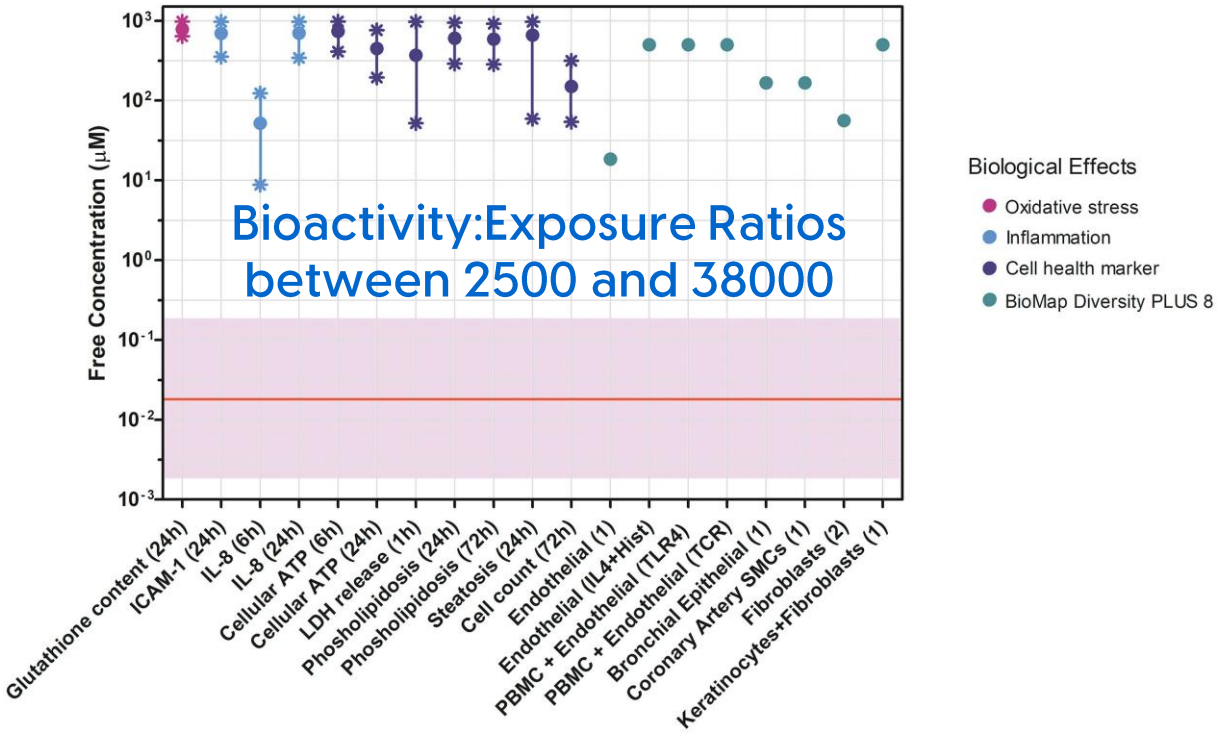
Case studies play a pivotal role in assessing and applying new approaches

ICCR held a workshop to discuss the ability of NGRA to support robust decision making

Two systemic toxicity case studies that were "works in progress" were discussed: Coumarin (Baltazar et al., 2020) and Phenoxyethanol (OECD 2021)

- What were the common tools?
- How were the ICCR Principles being applied?
- What was the decision output?

SERS
Safety, Environmental & Regulatory Science



Dent et al, 2021

Workshop in Canada: 2019

Case studies play a pivotal role in assessing and applying new approaches

ICCR held a workshop to discuss the ability of NGRA to support robust decision making

Two systemic toxicity case studies that were "works in progress" were discussed: Coumarin (Baltazar et al., 2020) and Phenoxyethanol (OECD 2021)

- What were the common tools?
- How were the ICCR Principles being applied?
- What was the decision output?
  - **"Protection not Prediction"**

SERS
Safety, Environmental & Regulatory Science

Workshop Outputs: Jobs to be done

Unilever

1. Increase confidence in exposure predictions (including metabolites)
2. Determine whether tools give us enough biological coverage
3. Be explicit about the level of confidence in the assessment
4. Develop agreed standards for using tools and reporting data
5. Distinguish between adaptation and adversity
6. Develop an updated risk assessment workflow
7. More case studies

Regulatory Toxicology and Pharmacology 125 (2021) 105026

Contents lists available at ScienceDirect

Regulatory Toxicology and Pharmacology

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

Paving the way for application of next generation risk assessment to safety 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 [b], 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]

SERS
Safety, Environmental & Regulatory Science

Workshop Outputs: Jobs to be done

Unilever

1. Increase **confidence** in exposure predictions (including metabolites)
2. Determine whether tools give us enough biological coverage
3. Be explicit about the level of **confidence** in the assessment
4. Develop **agreed standards** for using tools and reporting data
5. Distinguish between adaptation and adversity
6. Develop an updated risk assessment workflow
7. **More case studies**

Regulatory Toxicology and Pharmacology 125 (2021) 105026

Contents lists available at ScienceDirect

Regulatory Toxicology and Pharmacology

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

Paving the way for application of next generation risk assessment to safety 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 [b], 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]

SERS
Safety, Environmental & Regulatory Science

Unilever

Identifying Best Practice from Case Studies

The Joint Working Group identified examples of NGRA in the literature, and used these to identify best practice of the application of the ICCR principles

"Highlighting best practices to advance NGRA of cosmetic ingredients"

Vaillancourt et. al., 2025

SERS
Safety, Environmental & Regulatory Science

Unilever

1

"Human Relevance"

Document the relevance of the hypothesis/hypotheses

Identify relevant exposures

Identify human-relevant test systems.

Identify assays/ biomarkers relevant to the hypothesis

2

"Exposure-led"

External vs internal exposure

Exposure refinement

3

"Hypothesis Driven"

Hypothesis may be highly specific or generic

Clearly articulate the hypothesis and sub-hypotheses so that the reader can transparently follow

SERS
Safety, Environmental & Regulatory Science

Unilever

Overarching safety assessment hypothesis:

The use of x % of propylparaben in leave-on or rinse-off cosmetics does not induce skin sensitization.

Sub-hypothesis

Based on their highly similar chemical structure, the target chemical propylparaben has similar bioavailability and bioactivity as the source chemicals methylparaben, ethylparaben and butylparaben.

In this assessment, the read-across hypothesis was followed by a step-by-step breakdown of the considerations that underpin the hypothesis (or further sub-hypotheses), including chemical structure, available *in vivo* data, quantitative and qualitative metabolism, and potency trend

SERS
Safety, Environmental & Regulatory Science

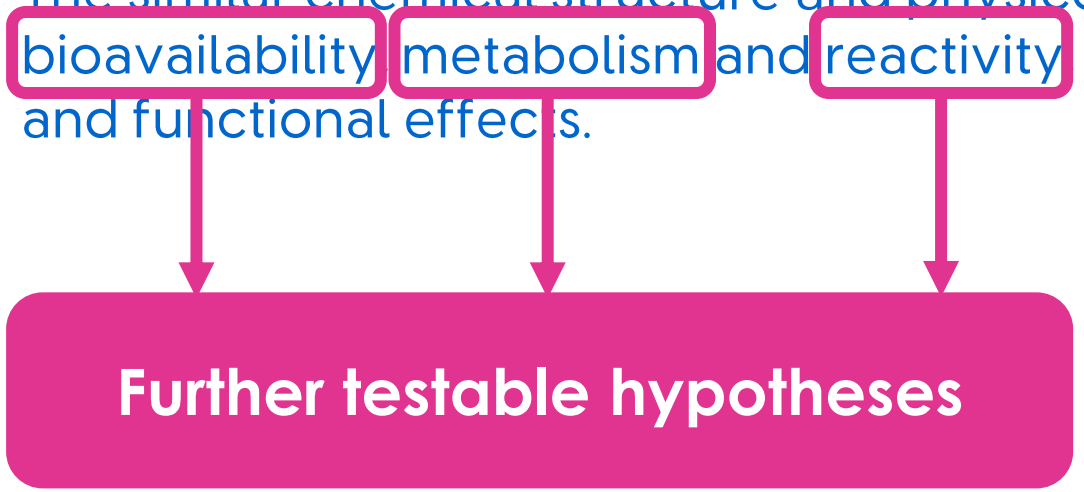
Unilever

Overarching safety assessment hypothesis:

The use of x % of propylparaben in leave-on or rinse-off cosmetics does not induce skin sensitization.

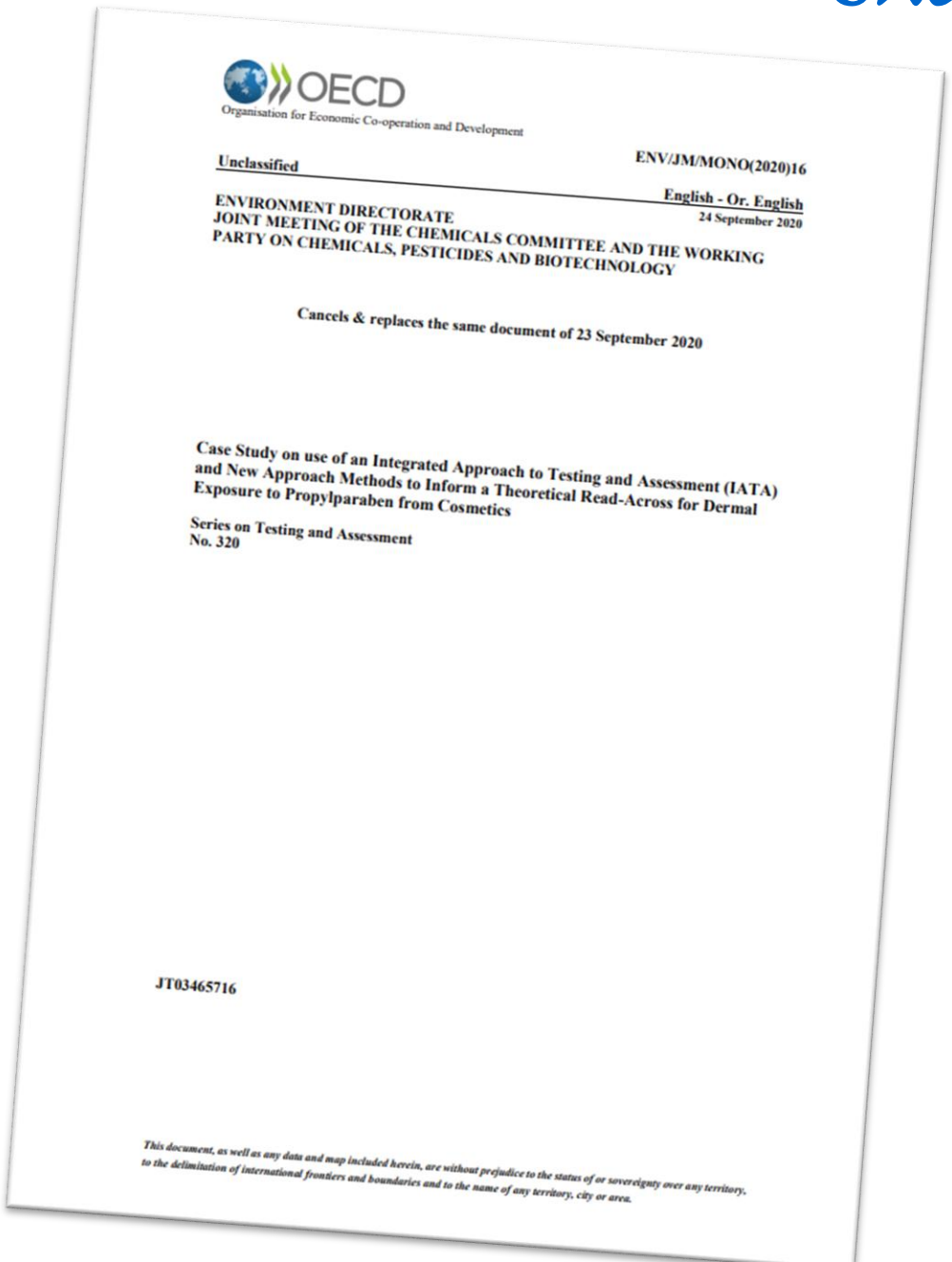
Sub-hypothesis

The similar chemical structure and physicochemical characteristics result in similar bioavailability, metabolism and reactivity which then result in similar biological and functional effects.



SERS
Safety, Environmental & Regulatory Science

Proper articulation of the hypotheses provides clarity of the structure of the assessment and the lines of evidence needed to make a conclusion, demonstrating the suitability of the NAMs selected to test the hypotheses



OECD
Organisation for Economic Co-operation and Development

Unclassified

ENV/JM/MONO(2020)16

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 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

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

SERS
Safety, Environmental & Regulatory Science

Digging Deeper

- Best practices reflecting application of the ICCR Principles had been identified and highlighted
- The next level of best practice still needed by risk assessors to help practical application of NAMs and safety assessment workflows
- →International Collaboration on Cosmetics Safety

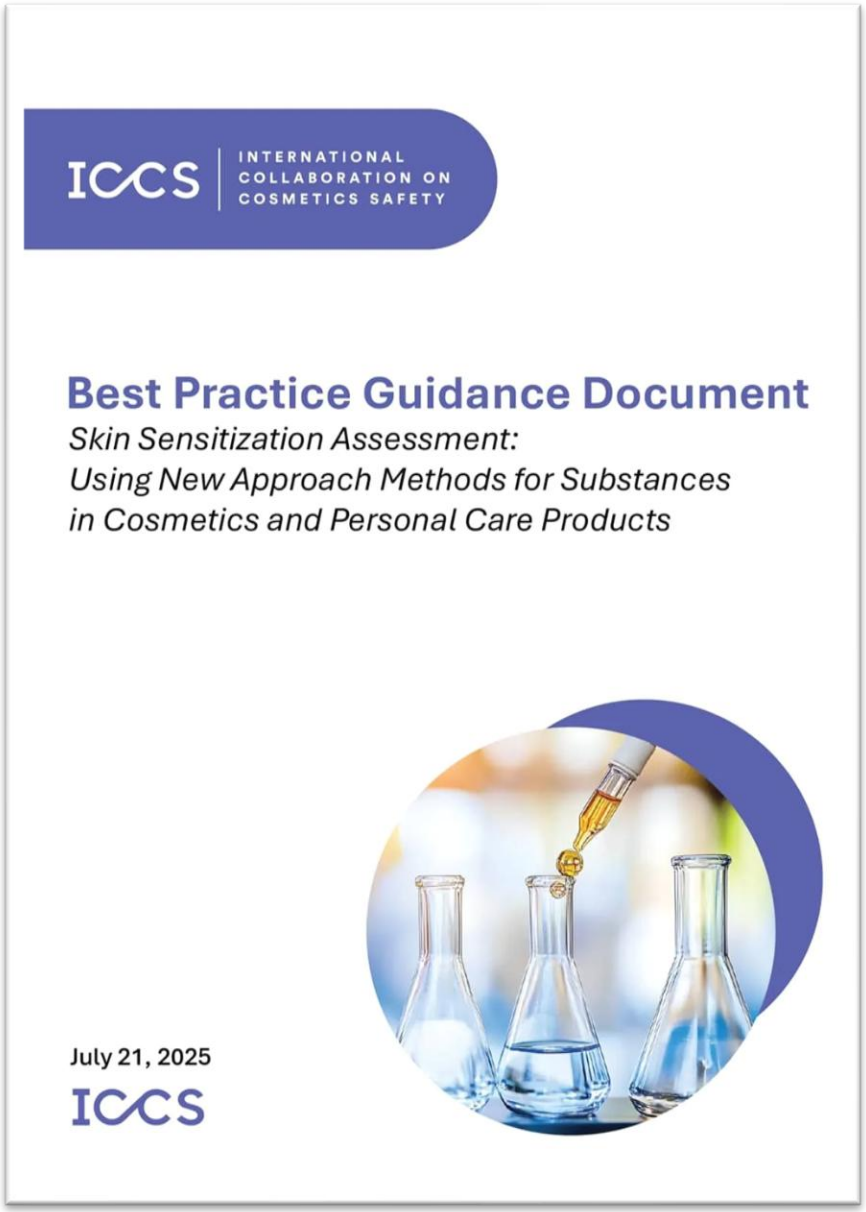
SERS
Safety, Environmental & Regulatory Science

Unilever

ICCS Best Practice

Not to be confused with ICCR, ICCS is a global, not-for-profit organization with members from cosmetic manufacturers, ingredient manufacturers, NGOs, and trade associations.

ICCS draws on world-leading expertise of its members to develop best practice guidance documents that support the use of NAMs



SERS
Safety, Environmental & Regulatory Science

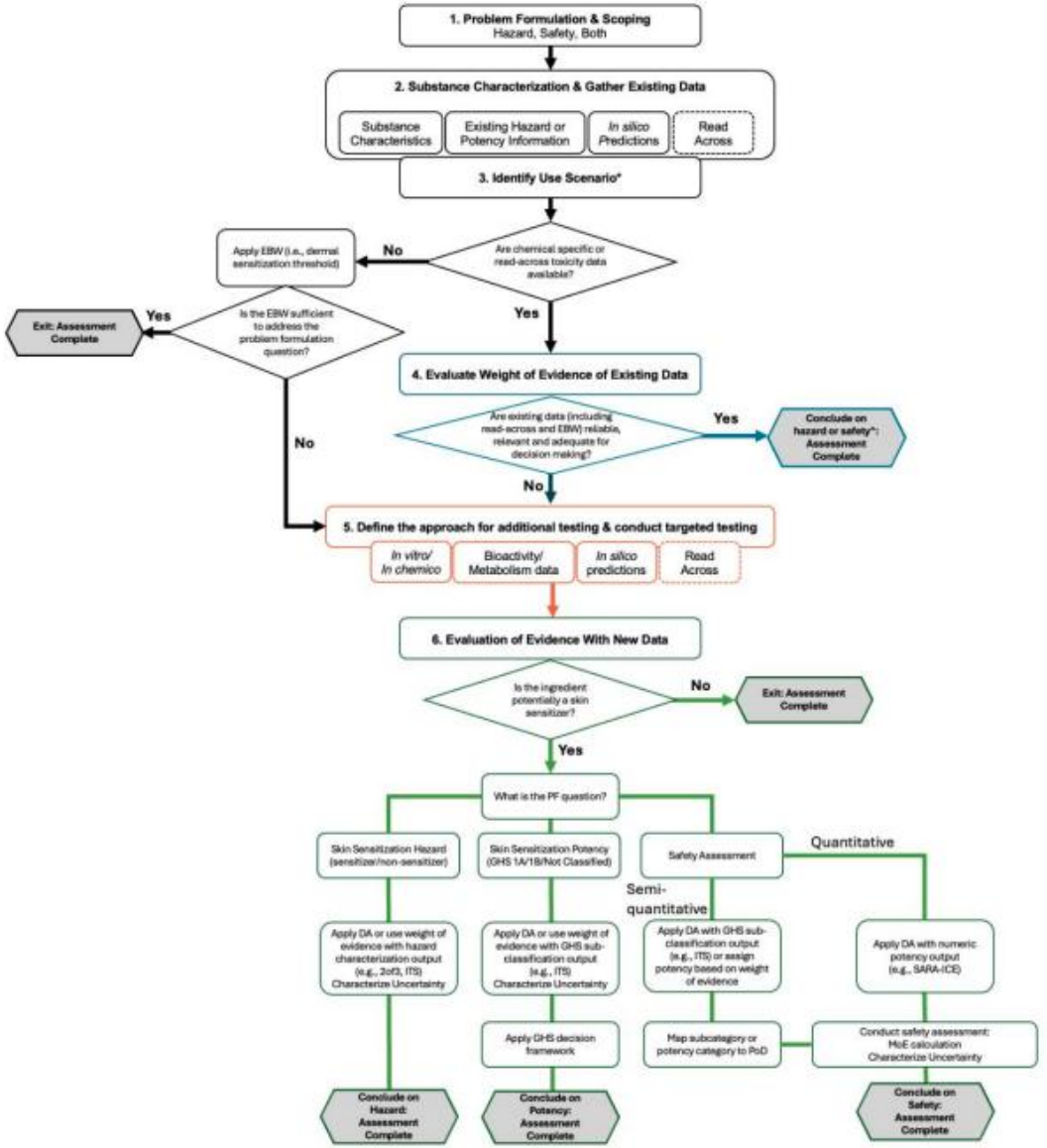
Unilever

ICCS Best Practice

A unique resource, providing exposure-led, tiered workflows in accordance with the ICCR Principles

Best Practices being developed for:

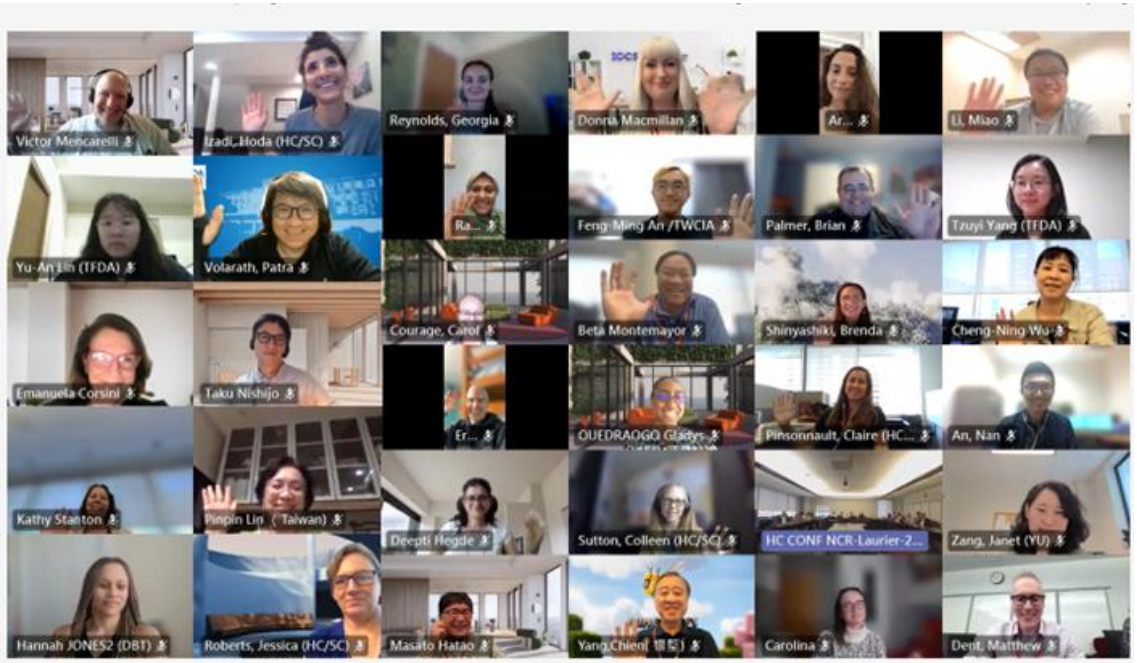
- Skin and eye irritation
- Exposure-based waiving
- Read across
- Others…



SERS
Safety, Environmental & Regulatory Science

Unilever

Back to the ICCR: Ottawa 2025



SERS
Safety, Environmental & Regulatory Science

Continuing to move from Principles into Application by conducting case studies based on ICCS Best Practice Guidance.

Unilever

1 Case studies have shown the value of the ICCR Principles of NGRA

2 Case studies can be used to highlight best practice

3 It's time to move beyond case studies to applying NGRA for real world safety decisions

SERS
Safety, Environmental & Regulatory Science