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Introduction: Hypothesis led safety assessment of cosmetics

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Animal Free Safety Assessment

- Increasing desire globally to perform chemical safety assessments without new animal testing
- Reflected in legislation restricting the use of animal testing for cosmetics
- Requires increasing reliance on improved exposure estimates coupled with hypothesis-led molecular characterization of a chemical's potential for bioactivity
- New approach to chemical safety assessment not yet reflected in formal regulatory guidance

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Next Generation risk assessment (NGRA)

International Cooperation on Cosmetics Regulation (ICCR)

Overarching

1. The overall goal is a human safety risk assessment
2. The assessment is exposure led
3. The assessment is hypothesis driven
4. The assessment is designed to prevent harm

Risk assessment process

5. Using a tiered and iterative approach
6. Appropriate appraisal of existing information
7. Using robust and relevant methods and strategies

Documenting risk assessments

8. The logic of the approach should be transparently and explicitly documented
9. Sources of uncertainty should be characterized and documented

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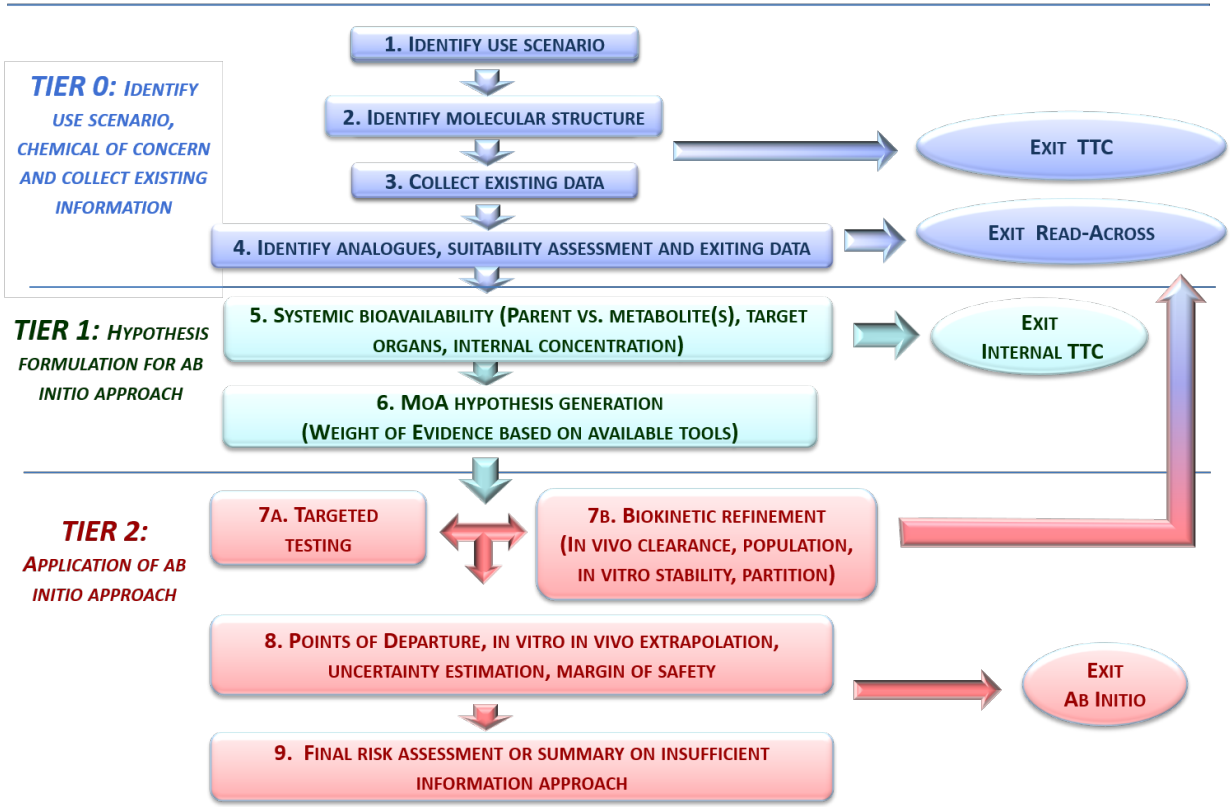
Dent et al. 2018. Principles underpinning the use of new methodologies in the risk assessment of cosmetic ingredients. Comput. Toxicol. 7: 20–26

SEURAT Workflow

- to assess chemical safety without relying on any animal testing
- hypothesis formulation based on existing data, *in silico* modelling, biokinetic considerations
- followed by targeted non-animal testing



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

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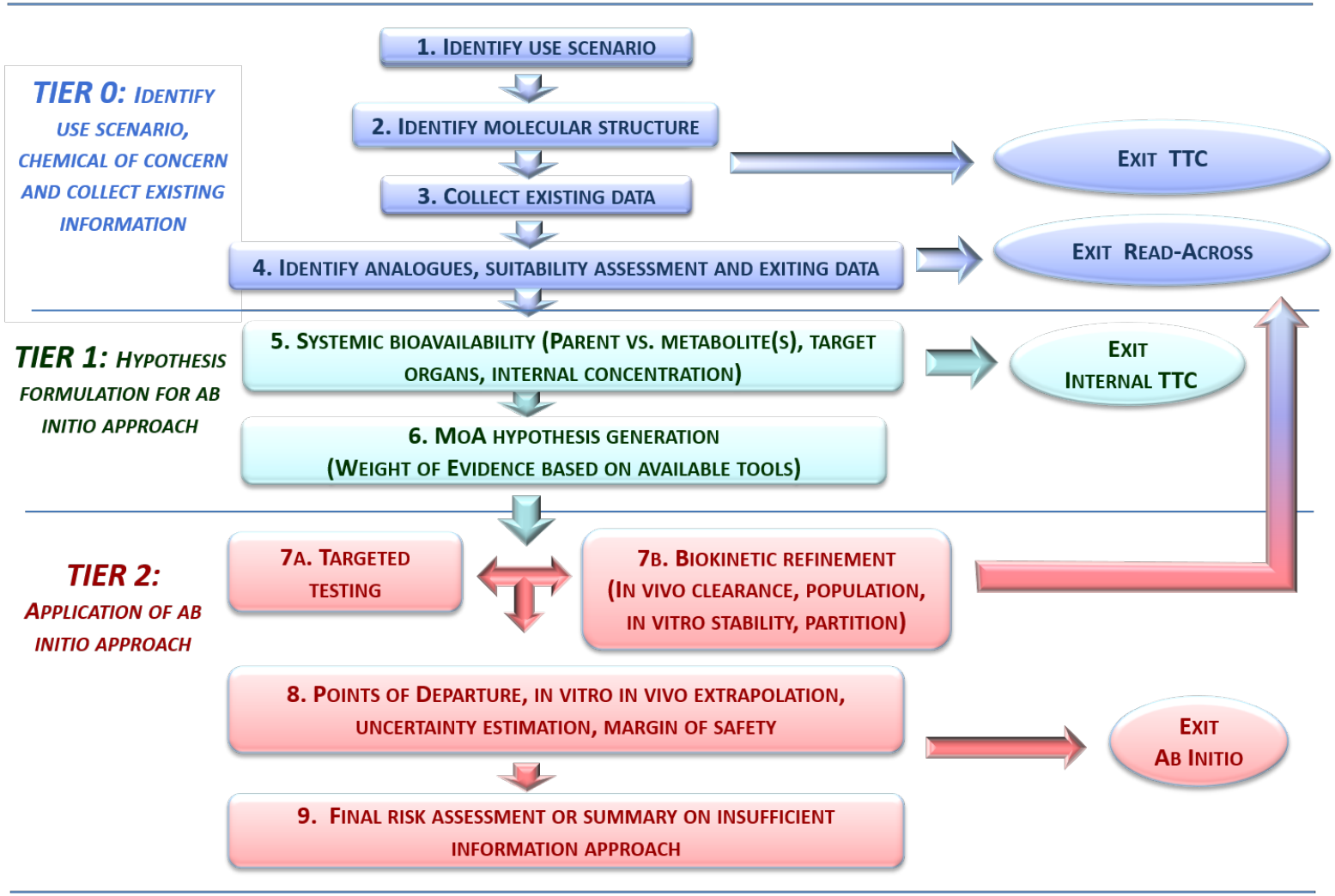
SEURAT Workflow



In silico tools

Exposure-based waiving

Read across

Metabolism, 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

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Amaral et al. 2018. Report for International Cooperation on Cosmetics Regulation Regulators & Industry Joint Working Group (JWG): Integrated Strategies for Safety Assessment of Cosmetic Ingredients: Part 2.

Animal Free Safety Assessment: Cosmetics

- HSI-coordinated collaboration of industry and non-profit partners
- Support chemical safety decisions without new animal testing
- Build capacity in the application of animal-free ‘next generation risk assessment’ (NGRA) approaches for decision-making

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Modules in development

0. **Overarching Process Considerations**
1. **Problem formulation** (hypothesis generation)
2. **Consumer exposure** (use habits, exposure routes, etc.)
3. **Predictive chemistry** (read-across, Q/SAR, etc.)
4. **Exposure-based waiving** (TTC)
5. **Internal exposure** (PBPK, IVIVE)
6. ***In vitro* assay synthesis** (IATA, defined approaches)
7. **Integration into risk assessment** (WoE, MoS determination, etc.)
8. **History of safe use**

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Dissemination channels

- Lectures & small group trainings
- Webinars
- Videos
- 1-pagers
- Continuing education sessions
- Symposia
- AFSAcollaboration.org

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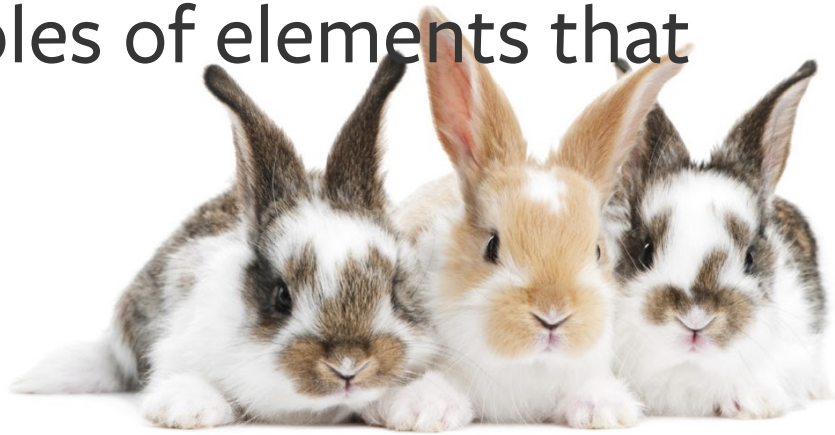
Wrap up

- Increasing desire globally to perform chemical safety assessments without new animal testing
- NGRA approach to cosmetic safety assessment involves hypothesis-driven, exposure-led bespoke evaluation using in silico and in vitro methods and approaches
- Based on principles outlined by ICCR, SEURAT workflow
- Following speakers will present examples of elements that inform an NGRA



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Thank You !

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