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Cosmetics Europe Long Range Science Strategy for Non-Animal Safety Assessments

Bertrand Desprez[1], Martina Klaric[1], Rob Taalman[1], Andreas Schepky[2], Bas Blaauboer[3]
1: Cosmetics Europe, Brussels, Belgium, 2: Beiersdorf AG, Germany, 3: University of Utrecht Institute for Risk Assessment Sciences, Netherlands

Cosmetics Europe
the personal care association

Abstract

The Cosmetics Europe Long Range Science Strategy (LRSS) aims at determining safety of cosmetic ingredients without the use of animals. It will include exposure for relevant use scenarios; local effects; biokinetics; systemic effects where relevant. To provide proof of concept, case studies will be performed using a tiered structure, tier 0 focusing on data collection on structure, exposure, known data for the compound and for similar chemicals, allowing TTC or a read-across approach in a safety assessment. If this is insufficient tier 1 focuses on scientifically based choices of in silico and/or in vitro work, based on hypotheses for understanding of modes of action together with information on biokinetics. In tier 2 experimental work will lead to the determination of a point of departure for a quantitative in vitro-in vivo extrapolation as the basis for a safety assessment. The aim is to show that this will result in safety assessments for use in regulatory frameworks.

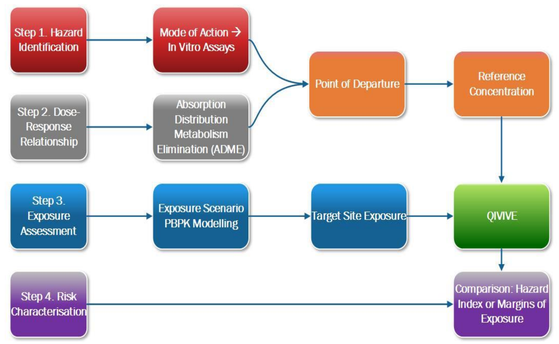
3 Pillars

Cosmetics Europe established the LRSS programme in the form of a consortium. It aims to follow-up om the outcomes of SEURAT-1 and to collaborate with other research initiatives.

The LRSS has three pillars (1) develop non-animal methods, testing strategies and alternative approaches; (2) use them in the risk assessment paradigm on a broad spectrum of effects, addressing the systemic toxicity challenge; and (3) support regulatory use of these approaches and their data

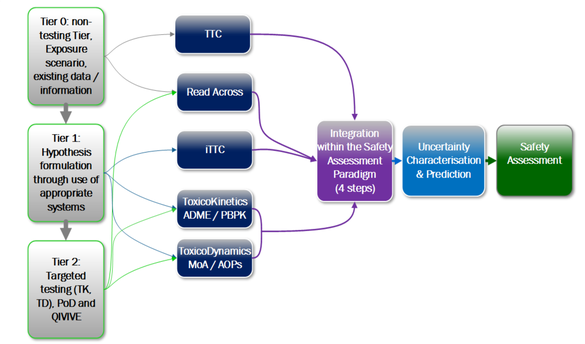
The LRSS intends to employ these pillars throughout the conduct of several case studies

Shifted Safety Assessment Paradigm…



Desprez et al., 2017 (in press)

…and Its Implementation



Scientific workflow driving LRSS case studies, adapted from SEURAT-1 (Berggren et al.) (Adapted by Desprez et al., 2017 (in press))

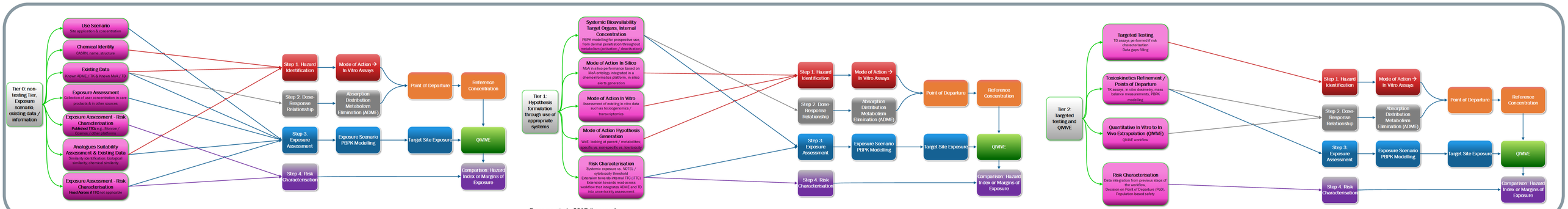
Extensive Inclusion of Kinetics and Mechanistic Considerations

The Safety Evaluation Ultimately Replacing Animal Testing-1 (SEURAT-1) programme showed the need to put efforts on toxico-dynamic (TD) and (toxico-)kinetic (TK) aspects for the next research programmes

It also showed that AOPS, integrated approaches, read-across and thresholds of toxicological concerns (TTCs) are valid approaches. As such, their future role in a toolbox dedicated to systemic toxicity is crucial.

SEURAT-1 ab initio case study set the basis for a scientific workflow in a tiered approach. Tier 0 identifies the use scenario and collects existing information; Tier 1 examines bio-availability and modes of action (MOAs); and Tier 2 applies targeted testing, biokinetic, point of departure (PoD) derivation. This ab initio case study showed that TTCs and read-across can be used and that further work is needed on TD and TK.

Breakdown into Research Projects



Desprez et al., 2017 (in press)

Case studies: the overarching piece of the LRSS

- The LRSS will apply the above described workflow in several case studies. Case studies have a key place in research programmes.
- They use quality-checked data as a control benchmark for comparison purposes.
- SEURAT-1 successfully used this approach for to provide proof of concept for TTC, read across and ab initio workflows and approaches. Similarly the LRSS will perform case studies to provide proof of concept.

Conclusion

- The LRSS scientific workflow addresses the 4 critical steps of the safety assessment paradigm.

This is achieved by strategic integration of non-animal approaches and modern toxicology tools – both mechanistic (e.g., AOPs) and kinetic ones (e.g., PBPB, QIVIVE).

It follows up on the lessons learned from SEURAT-1 and its outcomes & recommendations.

- The LRSS has **5 strengths:**

(1) extensive inclusion of toxico-kinetic methods and approaches (ADME, PBPK, QIVIVE) and their integration to perform safety assessments;

(2) a robust workflow; (3) regulatory orientation in which all the approaches are meant for regulatory acceptance;

(4) complementarity with other research programmes: whilst ToxCast is orientated towards risk assessment & screening, and EuToxRisk has the indispensable mechanistic emphasis, the LRSS put efforts on kinetic aspects and how to match them with MoA

(5) The LRSS moves the shifted assessment paradigm from theory to practice. What the LRSS will accomplish is aimed at cosmetics but is definitely relevant to other types of chemicals. It aims to be beneficial to the scientific community and make the most of non-animal test approaches for robust safety assessments.

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