IDEA: International Dialogue for the Evaluation of Allergens

WORKSHOP

PROJECT: Skin sensitisation potency measurements and risk assessment without a requirement for animals

JULY 1, 2025

(Brussels and online)

A SUMMARY

(Final September 4, 2025)

Participants:

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IDEA: summary of overarching objectives

- Foster engagement with all relevant scientific, industry and regulatory stakeholders
- Provide high quality fragrance aggregate and use data
- Generate surveillance data – providing early insights into fragrance allergy [Extended Fragrance Ingredients Surveillance Study (EFISS)]
- Integrate New Approach Methodologies (NAMs) into Quantitative Risk Assessment (QRA) – deriving reliable No Expected Sensitisation Induction Levels (NESILs) without recourse to animal data

Brief summary of recent previous IDEA workshops

October 7 2022: Introduction to the Reference Chemical Potency List (RCPL): development, roll-out, features and purpose.

September 22 2023: (a) Initial evaluation of NAMs for measurement of sensitising potency using the RCPL; (b) Consideration of requirements for assessment of weak/very weak skin sensitisers; (c) Initial consideration of additional uncertainty factors when using NAMs.

October 19 2024: (a) Plans for extension of the RCPL; (b) Initial evaluation of 2 NAMs (GARDskin Dose-Response and Linear Regression model); (c) Considerations of uncertainty.

WORKSHOP July 1st 2025: (MAIN THEMES)

- RCPL: original development, recent extension and benefits
- Brief introduction to NAMs (a) regression model, (b) GARDskin -DR, (c) SARA-ICE
- Overview of NAMs and potency assessment: progress, achievements and limitations
- Assessing a NAM-based QRA: maintaining a QRA approach based upon generation of a NESIL; retaining Safety Assessment Factors (SAFs) – possibly with additions
- Variability and uncertainty: defining a way forward

The Workshop Programme

Welcome, domestic arrangements and introductions (M Vey; J Bridges)

Background, brief summary of outcomes of previous workshops and purpose of the 2025 workshop (I Kimber)

The RCPL: original development, recent extension and benefits (A Irizar)

RCPL: general discussion and key conclusions (H Bender)

Introduction to skin sensitisation potency approaches using NAMs: (a) Regression model (A Natsch), (b) GARDskin-DR (A Forreryd), (c) SARA-ICE (E Reinke and N Gilmour)

Overview of NAMs, potency assessment and QRA: (a) Evaluation of NAMs versus RCPL potency values (PV) (A Natsch), (b) Addressing a NAM-based QRA (P Kern), Variability and NAM-based NESILs – initial proposals (P Griem)

Discussion on addressing variability and uncertainty and the way forward (All)

Key conclusions (H Bender et al)

The RCPL: original development, recent extension and benefits

KEY CONCLUSIONS

Following a presentation describing the purpose and recent extension of the RCPL the following key conclusions were agreed:

- The original RCPL (Irizar et al., 2022) provided an innovative resource for evaluating the ability of NAMs to predict accurately the potency of skin sensitising chemicals/fragrance materials. (It is acknowledged of course that there are other models available).
- The RCPL has recently been extended and now comprises 110 chemicals, primarily fragrance materials. A manuscript describing the extended RCPL has been submitted for publication.

- For each chemical in the extended RCPL a potency value (PV) has been derived based upon the best available human and animal data, but excluding consideration of non-animal (*in vitro* or *in silico*) data.
- The extended RCPL embraces a broad range of chemistry, a wide spectrum of potency, and includes both direct and indirect (pre- and pro-) haptens.
- An advantage of the RCPL is that it does not rely on the categorisation of chemicals into discrete potency classes.
- It is concluded that the RCPL provides a robust approach for determining the ability of individual NAMs, or combinations of NAMs, to provide reliable measurements of skin sensitising potency that can be employed with confidence for development of effective risk assessments without recourse to animal data.

[*Following the meeting some suggestions were received from one attendee proposing slightly less firm language for certain bullet points. However, a golden rule of IDEA Workshops is that the exact wording of key conclusions agreed during the course meeting will not be changed subsequently. The suggestions made will be considered in any future broader communication, and the need for additional evidence will be reflected in the workflow resulting from the Workshop]*

Introduction to the skin sensitisation potency approaches using NAMs

A brief general introduction was provided for 3 NAMs [Regression model (Natsch and Gerberick, 2022a; b; Natsch, 2023), GARDskin-DR (Gradin et al., 2024: Donthamsetty et al., 2024; Lee et al., 2025) and SARA-ICE (Reinke et al., 2025)]. The performance of each of these 3 NAMs had been evaluated for their ability to derive acceptable measures of skin sensitising potency using the RCPL.

Overview of NAMs, potency and QRA

Issues addressed included: (a) an evaluation of the performance/predictive accuracy of the selected NAMs versus PVs of the extended RCPL, (b) issues associated with developing

NAM-based QRA and (c) variability of NAM-based NESILs and the potential assignment of adjustment factors.

There followed a general discussion on addressing variability and areas of uncertainty in adopting NAM-based risk assessments for skin sensitisation of fragrance materials.

KEY WORKSHOP CONCLUSIONS

- There is confidence that NAM data can reliably predict skin sensitiser potency (for fragrance materials)
- Based upon the above there is trust that this can be used to develop risk assessments without recourse to animal data
- Future work should focus on how best to translate the use of NAM-derived potency measurements into effective risk assessments (there may be more than one approach)
- The above will likely include further consideration of uncertainty and related adjustment factors
- In order to build confidence in NAMs-based QRA, case studies on maximum acceptable concentrations of fragrance ingredients in consumer products will need to be developed and reviewed.

References

Donthamsetty S, Forreryd A, Sterchele P, Huang X, Gradin R, Johansson H, Mattson U, Lee I, Api AM, Ladics G (2024) GARDskin dose-response assay and its application in conducting quantitative risk assessment (QRA) for fragrance materials using a next generation risk assessment (NGRA) framework. Regul. Toxicol. Pharmacol. 149 doi: 10.1016/j.yrtph.2024. 105597.

Gradin, R., Tourneix F, Mattson U, Andersson J, Amaral F, Forreryd A, Alepee N, Johansson H (2024) In vitro prediction of skin-sensitizing potency using the GARDskin dose-response assay: a simple regression approach. Toxics 12, 626 doi: 10.3390/toxics 12090626.

Irizar A, Bender H, Griem P, Natsch A, Vey M, Kimber I (2022) Reference Chemical Potency List (RCPL): a new tool for evaluating the accuracy of skin sensitisation potency measurements by new approach methodologies (NAMs). Regul. Toxicol. Pharmacol. 134, 105244 doi: 10.1016/j.yrtph.

Lee I, Forreryd A, Ma, N, Schember I, Lavelle M, Gradin R, Mattson U, Johansson H, Donthamsetty S, Ladics G, Api AM (2025) Determining a point of departure for skin sensitization potency and quantitative risk assessment of fragrance ingredients using the GARDskin dose-response assay. ALTEX 42, 263-277.

Natsch A (2023) Integrated skin sensitization assessment based on OECD methods (III): adding human data to the assessment. ALTEX 40, 571-583.

Natsch A, Gerberick GF (2022a) Integrated skin sensitization assessment based on OECD methods (I): Deriving a point of departure for risk assessment. ALTEX 39, 636-646.

Natsch A, Gerberick GF (2022b) Integrated skin sensitization assessment based on OECD methods (II): Hazard and potency by combining kinetic peptide reactivity and the ‘’2 out of 3’’ approach. ALTEX 39, 647-655.

Reinke EN, Reynolds J, Gilmour N, Reynolds G, Strickland J, Germolec D, Allen, DG, Maxwell G, Kleinstreuer NC (2024) The skin allergy risk assessment – integrated chemical environment (SRA-ICE) defined approach to derive points of departure for skin sensitization. Curr. Res. Toxicol. 8:100205 doi: 10.1016/j.crtox.2024.100205