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IFRA Report on the IDEA (International Dialogue for the Evaluation of Allergens) 6th Annual Review

Reporting on the IDEA collaborative and science-based approach to develop a common understanding of risk assessment methodologies for fragrance allergens

Tuesday 29 November 2022 – hybrid event
Albert Borschette Conference Centre, Rue Froissart 36, 1040 Brussels, Belgium

Moderator: Hans Bender

Report prepared by the IFRA team.

In attendance:

In-person: Api Anne-Marie (RIFM), Arregui Cristina (IFRA), Bassoni Caroline (COSMED), Bender Hans (moderator), Bianchini Martina (IFRA), Bridges Jim (IDEA Supervisory Group), Coenraads Pieter-Jan (SCCS), Corsini Emanuela (University of Milano), de Lusignan Charles (IFRA), Dorts Jennifer (IFRA), Dvořáková Dana (IFRA), Elyahmadi Chaima (IFRA), Giusti Anna (BfR), Giusti Arianna (Cosmetics Europe), Gliewe Hans Holger (IFRA), Griem Peter (Symrise), Kern Petra (P&G), Kimber Ian (IDEA Supervisory Group), Koppitz Tobias (DVRH), Ingels Hans (DG GROW), Irizar Amaia (IFRA), Rizos-Georgios Manikas (DG GROW), Mateo Montalcini Solange (L'Oréal), Perrichet Aurelie (IFRA), Robinson Jan (A.I.S.E.), Rogiers Vera (SCCS), Rustemeyer Thomas (IDEA Supervisory Group), Schellauf Florian, (Cosmetics Europe), Schutte Katrin (DG ENV), Smith Mark (NATRUE), Suzuki Pamina (Cosmetics Europe), Theewis Joris (IFF), Thierse Hermann-Josef (BFR), Varik Hettel (DG GROW), Vey Matthias (IFRA), Zängerle Leo (Weleda), Rösch Hans-Jörg (Wala).

Virtual: Andreeva Gergana (BNAEOPC), Bagdassarian Valentina (NCPHA), Basketter David (consultant), Bernauer Ulrike (SCCS), Castillo Germán (AEFAA), Catone Tiziana (ISS), Chaudry Qasim (SCCS), Chhuon Cindy (A.I.S.E.), Chira Paula (Ministerul Mediului), Corrado Galli (SCCS), Cresti Raffaella (ISS), Dellera Claudia (AISPEC), Fajfar Simona (Ministrstvo za Zdravje), Gaffet Eric (SCCS), Goursot Jean-Francois (PRODAROM), Greim Helmut (IDEA Supervisory Group), Grenier Natacha (DG SANTE – SCCS Secretariat), Hareng Lars (BASF), Hemingway Dave (A.I.S.E.), Huggard Joseph (Consultant), Jöckel Karl-Heinz (University of Essen, IDEA EFISS Steering Committee), Klenow Stefanie (BfR), Klug Felix (BASF), Koutsodimou Aglia (Greek Authorities), Massé Philippe (PRODAROM), Millet Sybille (COSMED), Miteva Anna (BNAEOPC), Nakopoulou Chrysanthi (AADE), Natsch Andreas (Givaudan), Nicolai Suna (BfR), Ruśkowska Patrycja (Ministerstwo Rozwoju I Technologii), Varela Marta (IFRA), White Ian (IDEA Supervisory Group), Wijnhoven Susan (SCCS), Woutersen Marjolijn (RIVM), Żandarska Katarzyna (PSPKD).

Summary of discussions

Welcome by the European Commission: *Hans Ingels*

- DG GROW is glad to host the event as a recognition by the European Commission of the value and collaborative efforts of this multipartite project.
- Project started almost 10 years ago with the goal to provide a solid and transparent framework for assessing fragrance allergens and ultimately, enhance consumer protection. Expectations are high in this regard.
- The Commission is satisfied with the progress accomplished by the platform over the years – whose work has been based on the principles of scientific integrity, transparency, trust and collaboration.
- DG GROW hopes that IDEA Regular Reviews will continue and wishes a successful event and outcomes.

Opening remarks by the Chair of the IFRA Board: *Hans-Holger Gliewe*

- Multi-stakeholder platforms are very valuable to continuously improve risk assessment methodologies for fragrance allergens, to support the safe use of fragrances.
- IFRA has been a key driver for the development of this platform and would like to renew its commitment to this work. Appreciation for the support of the European Commission and the participation of all in these debates was highlighted.

The IDEA Journey – Background and summary of key achievements during 10 years of dialogue: *Jim Bridges*

- Risk assessment comprises two components: 1) intrinsic hazard and 2) total exposure.
- History and role of IDEA were shared. The IDEA project started in 2013, after the publication of the SCCS opinion on fragrance allergens in 2012.
- The aim was to rebuild trust through the independent re-evaluation of the 2008 risk assessment methodology and how it was employed to determine the contact dermal allergy potential of individual fragrance materials.
- The revision of the exposure assessment methodology was one of the first priorities of the IDEA project (through QRA method), followed by the assessment of new approaches methodologies.
- Many projects are now ongoing, and it is essential to maintain the dialogue for the successful continuation of the IDEA project, especially given current discussion in Europe on the future of risk assessment.

QRA2 – a critical tool to ensure safe use of fragrance materials including the context of aggregate exposure – Background of and experience with the QRA2: *Anne Marie Api / Peter Griem*

- Sensitizing fragrance ingredients have different potencies, and therefore, adequate skin sensitization risk management measures need to be chemical specific.
- The safe use of fragrance ingredients depends on the product type and takes into account maximum concentration levels per product group taking based on a good understanding of human exposure
- RIFM evaluates the safety of hundreds of potentially skin sensitizing fragrance raw materials, through the Quantitative Risk Assessment for dermal sensitization (QRA2). This tool incorporates aggregate exposure and revised sensitization assessment factors.
- The Creme RIFM Aggregate Exposure Model is a probabilistic tool based on real world data (from Europe and the US) to estimate aggregate exposure from consumer product ingredients.
- While realistic, there are still many conservative assumptions in the model.
- Dermal sensitization QRA is used to determine the maximum acceptable concentration for fragrance ingredients.

The SCCS requested access to the Creme RIFM Model on a case-by-case basis linked to dossier evaluation. RIFM responded that this can be arranged.

Development of the Reference Chemical Potency List: RCPL – IDEA's approach to NAMs: *Ian Kimber*

- Skin sensitization potency is the ease with which a chemical (contact allergen) is able to induce skin sensitization.
- There is a need for New Approach Methodologies (NAMs) that can accurately measure skin sensitisation if effective risk assessments are to be made without the use of data from studies using experimental animals.
- The purpose of the Reference Chemical Potency List (RCPL) is to provide a system for evaluation of the ability of single NAMs (or groups of NAMs) to reliably measure the skin sensitization potency of chemicals.
- The RCPL is the integration of the best available human data and animal data (primarily LLNA data).
- RCPL constitutes of 33 readily available chemicals comprising a wide range of chemistry, and skin sensitizing potency. It includes both direct- and indirect (both pre- and pro-) haptens.
- The potency is expressed as a Potency Value (PV) derived from the best available human and animal (LLNA) data.
- Chemicals are ranked according to PV without the use of potency categories.
- The RCPL is one of the tools to assess the potency of fragrance allergens, but there are also other tools including human and animal data.
- The objective is to promote the use of the RCPL amongst stakeholders and the relevant community for the evaluation of candidate NAMs for skin sensitization.
- In due course, a review of the value of the RCPL in practice may lead to its update on the basis of input received.

Update on the status of the IDEA Surveillance Study - The industry's stewardship program to learn from the market: *Thomas Rustemeyer / Matthias Vey*

- The IDEA Surveillance study is the first of its kind by industry. It puts industry in the best position to promptly react to observations made in consumers.
- From previous meetings, it was concluded that for the design of the study, a surveillance system alone may not verify whether the QRA is preventing skin sensitization.
- Diagnostic patch testing of dermatology clinic patients (surveillance) was seen as a critical pillar in the long-term evaluation of the QRA.
- The project (Extended Fragrance Ingredients Surveillance Study) is a partnership with clinics in different European regions, sponsored by the industry. The industry is not involved in the patch design nor in the follow-up analysis.
- The objective was to respond to expectations from the European Commission and its risk assessors, that QRA2 used by the industry – supported by the IFRA Product Stewardship Program – and combined with clinical surveillance – would deliver.
- Data entered on a total of 379 patients. The clinical work was completed mid-November 2022. Currently, the work is in the data analysis phase.
- As a result of the pilot status, no unexpected reactions have been observed by the clinics to any of the 7 additional materials at any of the concentrations utilized in the range-finding.
- The work is now moving to the main part of the study – it will be a long-term commitment of over approximately 5 years (3 cycles). Each cycle will last around 15-18 months.

Perspective of the European Parliament on the IDEA project: *Tilly Metz*

- A higher level of protection for humans and the environment should not and does not need an increase in animal testing. The Chemical Strategy aims at reducing the dependency on animal testing and understands the importance of animal-free innovation to deliver its objectives.
- Non-animal methods have considerably developed over the past decades. There is still much potential, which needs to be recognized and reflected in the upcoming legislation (e.g., REACH and all initiatives and programs which have the potential to replace animal testing).

- In September 2021, the European Parliament adopted a resolution asking the European Commission to develop a concrete action plan to accelerate the transition to non-animal testing. Unfortunately, we are still waiting for this action plan to be implemented.
- In August 2022, the European Citizens Initiative (ECI) (Safe Cruelty Free Cosmetics) collected over 1,4 million signatures. This shows that the EU citizens continue to care about animals and animal testing and want EU action.
- To achieve the ambitious goals of the CSS, a more dynamic and science-based approach is required in order to increase acceptability and accelerate the use of innovative non-animal testing models.
- We need to work together to speed up the development and specifically the validation of new methods. Awareness raising, training and education is still necessary. Adequate funding remains a key success factor.

Roundtable on risk assessment of fragrance allergens - Q&A session: *BfR (Hermann-Josef Thierse); EC DG ENV (Katrin Schutte); EC DG GROW (Rizos-Georgios Manikas); IDEA (Jim Bridges), IFRA (Matthias Vey); SCCS (Vera Rogiers)*

Three questions served as a basis for feeding the debate:

1) What is the future for risk assessment to ensure safe use of fragrance allergens?
2) How reliable is risk assessment based on NAMs only?
3) Where should IDEA focus its future efforts?

The outcome of the roundtable discussion is reported in the below key conclusions jointly agreed by all participants of the meeting. It was further highlighted that the focus should be on individual chemical risk assessment rather than generic approaches. Further looking into potential respiratory effects remains a topic of high interest.

Key conclusions: Final statement

The 6th Annual Review of IDEA provided a valuable opportunity for transparent and multi-stakeholder dialogue on risk assessment as basis for meaningful subsequent risk management for fragrance allergens. The continuation of the IDEA project and these reviews is encouraged, especially in the context of increased demand for high standard risk assessment.

State of the art (quantitative) risk assessment continues to be seen as the only scientifically defensible approach to ensuring safe use of fragrance materials. The successful development and application of QRA2 by industry marks a significant milestone in this context. There is a definite need for continuous refinement (e.g., mixtures, pre-haptens, better understanding exposure), complementary in market and epidemiological surveillance. A procedure is required to provide risk assessment agency experts advising regulators (especially SCCS) with specific access to tools and models, e.g., the Creme RIFM Aggregate Exposure Model.

The development and validation of NAMs are critical elements of future risk assessment as part of a weight of evidence approach. The current use of NAMs to assess potency – especially by using the RCPL – is a first step in a longer journey to make NAMs quantitative as basis for a NESIL (No expected Sensitization Level), the starting point in the QRA.

Looking ahead, IDEA is encouraged to continue on its path of multi-stakeholder dialogue, based on concrete projects like NAMs validation, broadened surveillance and continuous refinement of QRA.

Closing remarks by the President of IFRA: *Martina Bianchini*

- Thanking the Commission for hosting the event.
- Good to have come to a shared understanding and work plan.