IDEA

Risk assessment of fragrance materials (FMs)

The role of the IDEA Project

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Background on risk assessment

Definition

Risk assessment is the evaluation of the probability of particular adverse health effects occurring to man or other species from a chemical under defined exposure conditions.

It comprises two components:

i) *Hazard* the adverse effect on health identified as being caused by the chemical and its potency

ii) *Total exposure* estimate to the chemical of interest

Regulation

Is predicated on the characterisation of an exposure level (so called threshold level or NOAEL/NESIL) below which the adverse effect of concern will not occur.

Background to IDEA formation

Risk assessment of chemicals in the EU: A brief history

- Prior to 1996 the EU scientific advice on chemicals (including cosmetics) was provided by Scientific Committees (SC's) comprising Representatives of Member States. BSE, and other concerns resulted in a complete restructure of the roles of the SC's (8 in all) and membership being confined to independent, internationally recognised, scientific experts
- Two such committees were the SCCP (Consumer Products) and the CSTEE (chemicals)
- A Coordinating Committee (SSC),with all the Chairs focussed on BSE but also addressed issues such as harmonisation of Risk Assessment Methodology.

EU Risk assessment of cosmetic ingredients

The EU Scientific Committee on Consumer Products (and its successor committee the Scientific Committee on Consumer Safety, SCSS) had a broad brief. However, most of its work, was on the risk assessment of cosmetic ingredients, specifically for dermal sensitization and irritancy.

It therefore took particular interest in the publication by fragrance industry scientists of 'Dermal sensitisation quantitative risk assessment (QRA) for fragrance ingredients' Api et al 2008) and how it was applied in practice.

In 2012 the SCCS published its concerns (340 pages)

These may be summarised as:

* ‘Safe levels’ determined by the industry for a number of FM’s were not sufficiently supported by the available data.

* The industries response to the concerns of the SCCS were often very slow and /or inadequate. This resulted in an increasing lack of trust of the industries submissions.

* Often the data submitted to it had serious gaps, in particular, on pre and pro haptens, estimates of potential total (aggregate) exposure, effects of multiple exposure.

Response of IFRA to the 2012 SCCS report

In 2013 IFRA set up the IDEA project with the aim of rebuilding 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 FM's.

To oversee the scientific aspects of IDEA a small Supervisory Group (SG) was established with input from the EC.

The members selected were the former chairs of the SCCS (Dr. Ian White), the SCHEER (Prof. Helmut Greim who had also been involved as an advisor to RIFM) and the SCENHIR (Myself, who was appointed to chair the SG). The group has since expanded to include Prof. Ian Kimber and Prof. Thomas Rustemeyer.

IDEA TASK’s

Criteria for a trusted, health risk assessment

- **T** = Threshold for the adverse effect(s) well identified
- **R** = Reference points and read across (chemicals/situations) clearly defined and justified
- **U** = Utilisation of **all** the relevant information, including previous risk assessments
- **S** = Science based, taking fully into account current scientific understanding and avoidance of bias; hazard assessed by NAM unless-unreliable
- **T** = Transparent weighting of all the data for both relevance and quality (including reasons for any data discounted-an objective weight of evidence)
- **E** = Exposure estimate, including relevant co-exposures with any extrapolations justified
- **D** = Deficiencies/uncertainties in the assessment clearly stated along with how they are addressed and the rational for this specified.

Initial IDEA Actions

- Identify research and other priorities.
- Introduce Workshops to involve leading scientists and dermatologists and those with expertise relevant to dermal contact dermatitis.
- Arrange for general Annual Meetings to take place at EU Institution facilities to allow wider stakeholder input.
- Initiate a sustainable dialogue with the Commission with full transparency of IDEA activities.

The first challenge: Exposure Assessment (QRA2)

* A revision of the exposure assessment methodology was agreed to be the priority along which involved a reconsideration of the uncertainties in estimates. (known as the SAF values).

* An aggregate exposure was developed and integrated (the RIFM-Creme model) utilizing the revised SAF values. The new method was evaluated prior to publication by both the SCCS and the EU Joint Research Centre. After helpful dialogue they both gave it their broad support and it was published. (Updating skin sensitisation quantitative risk assessment (QRA2) for fragrance materials, Api et al, 2020)

The second challenge: Hazard assessment

- Starting in 1999 the EU issued a series of Directives on the banning of animal tests for hazard assessment of cosmetic ingredients, resulting in an outright ban in 2013 (regardless of whether or not there is an appropriate replacement (EU Cosmetic Directive 1223/2009)
- As a consequence, instead of using LLNA test results as the primary means of identifying FM allergenicity; hazard assessment was required to depend on a non-animal based methodology.

New Approaches Methodology which have been examined

- In vitro tests e.g. DPRA, other OECD approved NAM tests
- In Silico Tests e.g. ToxTree, Derek NEXUS, extensive use of existing data bases on many FM's and related chemicals.

These methods provide a sound basis to identify FM's that initiate the sensitisation process.

As a first step towards reliable potency information from NAMs as basis for a refined risk assessment IDEA has established a thoroughly reviewed potency list of chemicals to be used as reference (positive controls) for in vitro testing (known as the Reference Chemicals Potency List - RCPL)

Ongoing IDEA activities

IDEA Ongoing

The surveillance project - A multi-centre, clinic project is underway which will facilitate dermal allergy assessment.

NAM methodology - Application of the RCPL achievement

Integrated clinical and laboratory studies e.g. hydroperoxide formation.

Methodology for the identification of pre and pro haptens

The need for dialogue with all stakeholders

IDEA was introduced to both improve the scientific basis for the risk assessment of fragrance materials and its practical application. Effective, formal and informal dialogue with the SCCS, JRC and scientists from many other organisations has been vital.

Such dialogue is crucial to the successful continuation of the IDEA project