IDEA

International Dialogue for the Evaluation of Allergens

IDEA: The first six years

Prof Jim Bridges

Chair, IDEA Supervisory Group

Annual Review 2019 ● European Parliament ● 25 February 2019

IDEA: The background

- In 2008 RIFM published their ‘Quantitative Risk Assessment’ methodology (QRA1) for dermal exposure to individual fragrance ingredients.
- It has been subsequently applied by the industry to more than 100 fragrance ingredients.
- The EU Scientific Committee on Consumer Products (SCCP) had a number of concerns and could not endorse the industry proposed QRA1.

- In 2012 the SCCS restated serious concerns about the suitability of QRA1.
- They also expressed their dissatisfaction with the reaction of the industry to these and other issues related to the risk assessment of fragrances.

Fragrance industry response: Establishment of IDEA - primary aims

Develop and adopt a transparent and robust risk assessment framework, based on the best available science, to identify consumer exposure conditions both to single and mixtures of fragrance ingredients (in different formulations) that will not result in induction of skin sensitization and potentially subsequently lead to allergic contact dermatitis

IDEA: Operational framework

Establish an independent expert Supervisory Group *(NB. The SG includes three former chairs of EU Scientific Advisory Committees SCCS, SCHER, SCENHIR)* to:

- Set up a multi-stakeholder network of experts
- Oversee the scientific aspects of the aims (in particular through workshops and task forces)
- Ensure transparency of all activities
- Co-ordinate with a Management Team to facilitate these objectives

IDEA: Operational framework

The Annual Review is designed to:

- monitor and validate the progress made
- update the programme and priorities as necessary
- provide the opportunity to ensure that all stakeholders can express their views and ask questions

Its organization is overseen by the European institutions

The industry's Quantitative Risk Assessment (QRA 1)

Exposure assessment

↓

↓

Use estimate and SAF values

↓

CEL

(Consumer Exposure level)

↓

Hazard assessment

↓

LLNA and HRIPT

↓

NESIL (No Expected Sensitisation Induction Level)

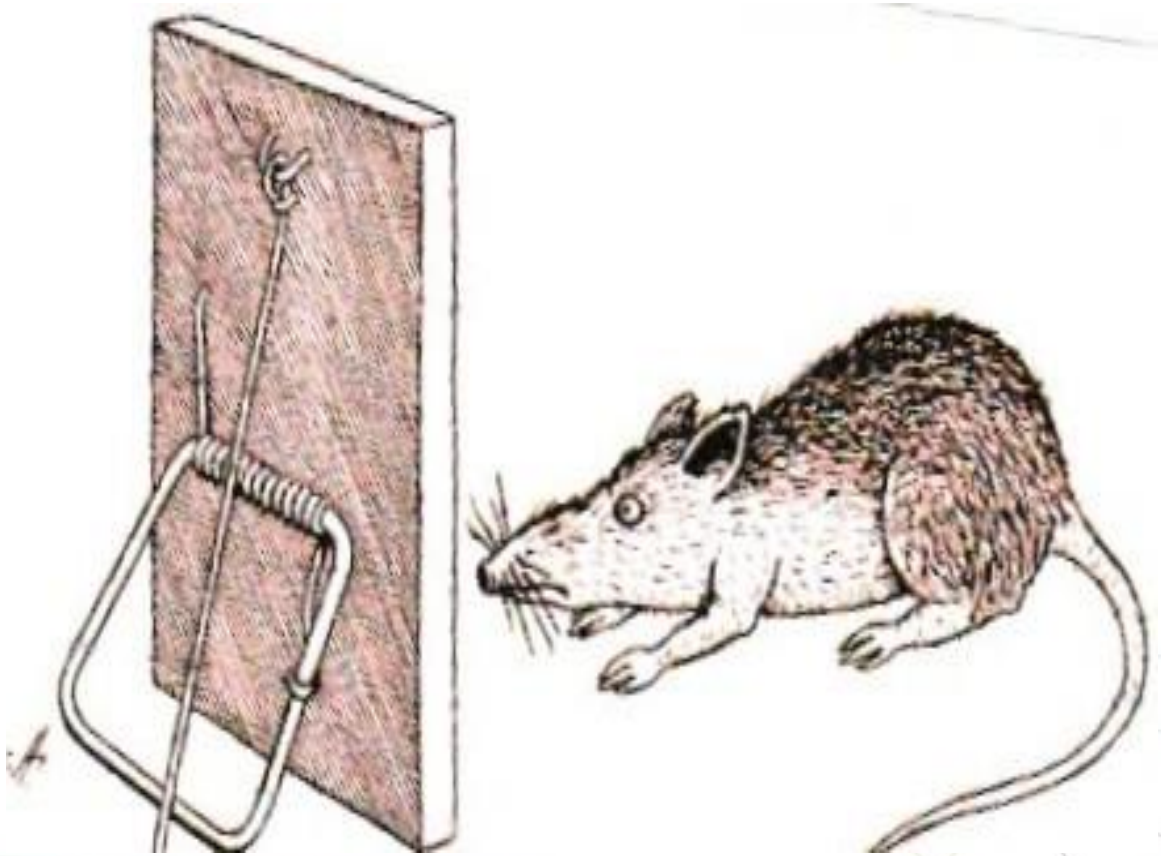
↓

AEL (Acceptable Exposure Level)

↓

Risk conclusions

Have all the key issues been addressed?



Initial priority: methodology of QRA1

- Ensure the scientific rationale for each of the uncertainty factors (SAFs) used in QRA1

- Revise the exposure assessment methodology of QRA1: Replace the original individual fragrance exposure assessment by an aggregate exposure methodology

Review of uncertainty factors (SAFs)

Principle: weighing of the evidence, and clarification of uncertainties arising and their implications, is important in any risk assessment

Action: review the following SAF values

- Occlusion
- Inter-individual variability
- Effects of vehicle/matrix
- Frequency/duration of product use
- Skin condition

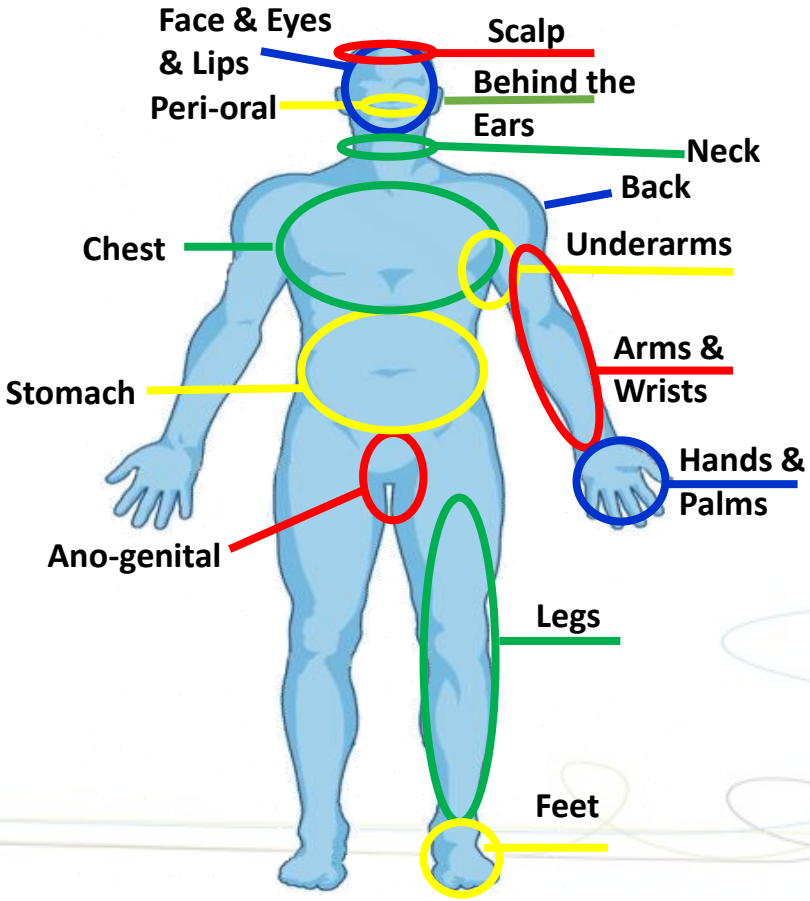
Assessment of aggregate exposure

Principle: To determine the potential for contact allergy to be induced, there should be a reliable estimate of the total exposure to the fragrance substance and the skin surface area to which the subject may be exposed.

Rationale: This is based on the understanding that a certain number of Langerhans cells are required to be activated to initiate the cascade of events leading to the exceedance of the hazard threshold.

Revised exposure methodology

Application sites



QRA2

Following a transparent dialogue, for which IDEA is grateful:

- the revised QRA methodology (QRA2) was submitted to the JRC and then subsequently to the SCCS
- the SCCS published their Opinion on October 2018, acknowledging the progress made under IDEA, requesting some adjustments on the methodology and pointing out its potential applicability for skin sensitization risk assessment in general

Issues not addressed specifically in QRA1: pre- and pro-haptens

Principle: chemical and or biological conversion of a fragrance could result in a hapten. How does the methodology incorporate this?

Action: several workshops have been held to discuss this issue and a framework is being prepared. In addition a task force is examining levels of the putative haptens (hydroperoxides) in various products

Development of a clinical surveillance programme

Principle: Collecting information on development of contact allergy rates in the clinics is vital to provide learnings on exposure conditions of the patients to:

- gain greater insight as to whether the risk assessment and management measures in place are adequate and broad enough in scope
- allow corrective measures to be identified and taken if needed

Action: a pilot study is being set up to determine the concentrations for patch testing of seven well known and evaluated test materials. The protocol has been developed and agreed. Currently confirming with a number of clinics their willingness to participate in the initial dose range finding and pilot study.

Integrating non-animal data

Rationale: The first phase of IDEA focused on assessment factors and exposure (the weakest parts of QRA1 as identified by the SCCS). The hazard assessment aspects, based largely on findings in the mouse LLNA test and HRIPT, were not considered.

Important new issues: The ban of animal testing (in the EU and beyond) means that the mouse LLNA test can only be used as historic data. In most EU countries testing of chemicals on humans (even for confirmatory purpose) seems unacceptable on ethical grounds, preventing HRIPT data generation.

What is needed: An entirely new framework for the assessment of hazard and potency must be identified, which is acceptable to the EU Commission.

Conclusions

Achievements to date:

Cooperation and transparency: IDEA has established a network of leading experts willing to aiding the projects objectives. This involves multi-stakeholder (including industry scientists, clinicians, RIFM, academia). The project has also had very valuable inputs from the SCCS and JRC.

QRA2 revised methodology: A publication is almost completed

The ongoing challenges:

Methodology is needed for:

- identifying and characterising pre- and pro-haptens
- non -animal, non HRIPT, hazard assessment

Learning from clinical experience in developing the risk assessment strategy

If we want things to stay the same, things will have to change

Tomasi di Lampedusa in *The Leopard* (1958)