

A close-up photograph of several purple flowers, possibly from the Asteraceae family, covered in small water droplets. The flowers are set against a dark, blurred background, creating a soft, ethereal atmosphere. The lighting highlights the texture of the petals and the glistening droplets.

How the fragrance industry engages in alternatives to animal testing

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CAAT 2nd Pan-American Conference for Alternative Methods

Rio de Janeiro, 23-24 August 2018

- **Short introduction to IFRA**
 - Structure
 - Vision and mission
- **IFRA/RIFM and application of AAT in the safety assessment and self-regulatory (IFRA Standards) process**
- **Additional engagement in AAT 'promotion' (other than via CAAT)**
 - EPAA
 - IDEA



1

Short introduction to IFRA



THE INTERNATIONAL
FRAGRANCE ASSOCIATION

Representing the
interests of the
fragrance industry
worldwide since
1973

ifraorg.org



IFRA membership: *three types of members*



8

Regular Members
(global companies)

21

National Associations
(organized in four
Regional Committees)

7

Supporting Members
(in countries with no
National Association)

IFRA membership: *Regular Members*


We create chemistry


FRAGRANCES










GROUPE





IFRA membership: *National Associations in four regions*



North America

United States
(+ Canada)

Latin America

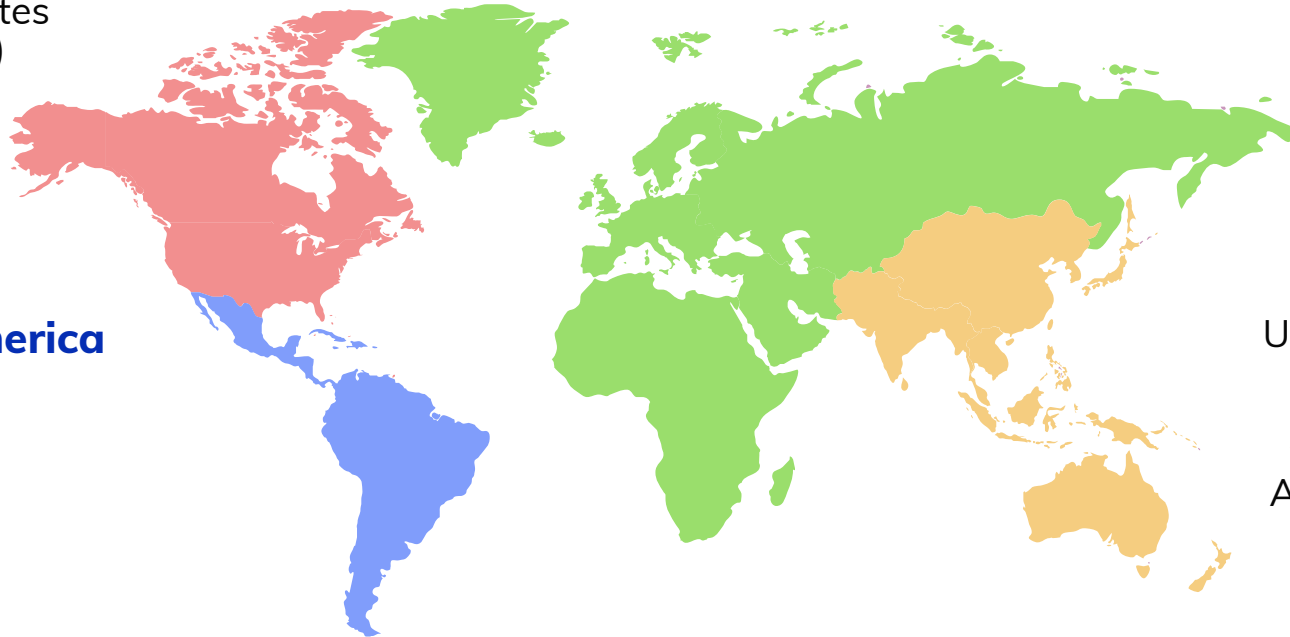
Argentina
Brazil
Chile
Colombia
Mexico

Europe (+ Africa and Middle East)

France
Germany
Italy
Netherlands
South Africa
Spain
Switzerland
Turkey
United Kingdom

Asia-Pacific

Australia (+ NZ)
China
Indonesia
Japan
Korea Republic
Singapore





Our vision

A world where people enjoy the socio-economic, environmental and cultural value of fragrances



Our mission

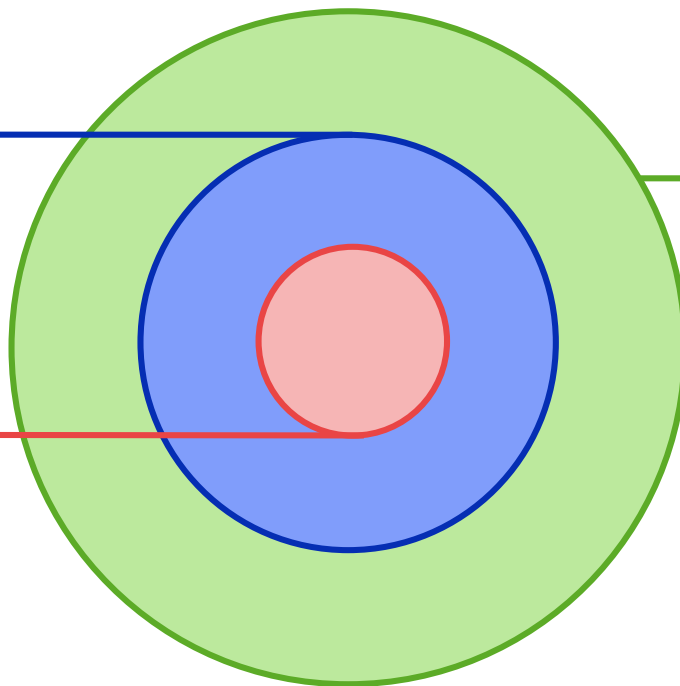
To represent the interests of the fragrance industry worldwide, in a way that maximizes societal benefit and respects the environment

Serve our members

Provide global coordination and deliver tools and services to members

Safety and policy

Help ensure safety, co-develop policy and deliver advocacy



Stakeholder engagement

Partner with governments, academia, civil society, value chain partners and others to educate, inform, listen and build strategic alliances

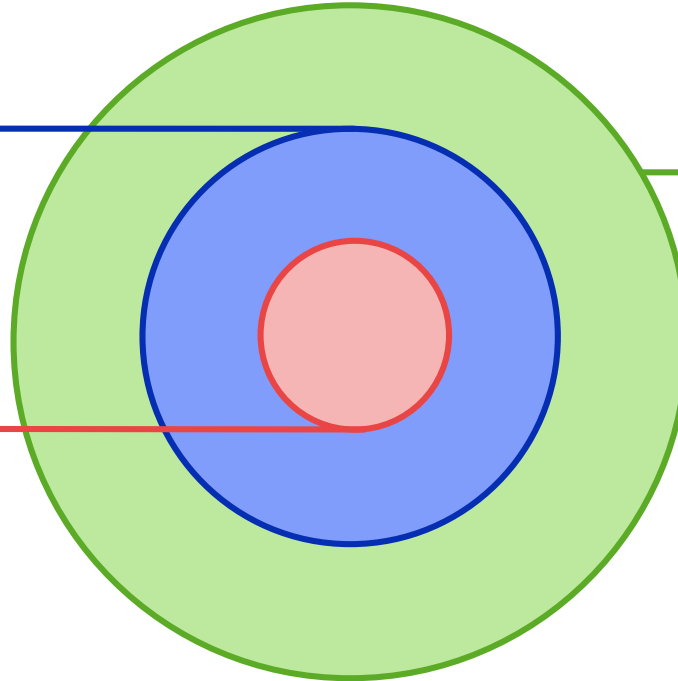
Serve our members

IFRA engagement provides means to members to behave ethically and in a legally compliant way

Safety and policy

Gain broad acceptance for relevant risk assessment tools (TTC / Aggregate exposure / probabilistic exposure modelling)

Advance AAT under IDEA



Stakeholder engagement

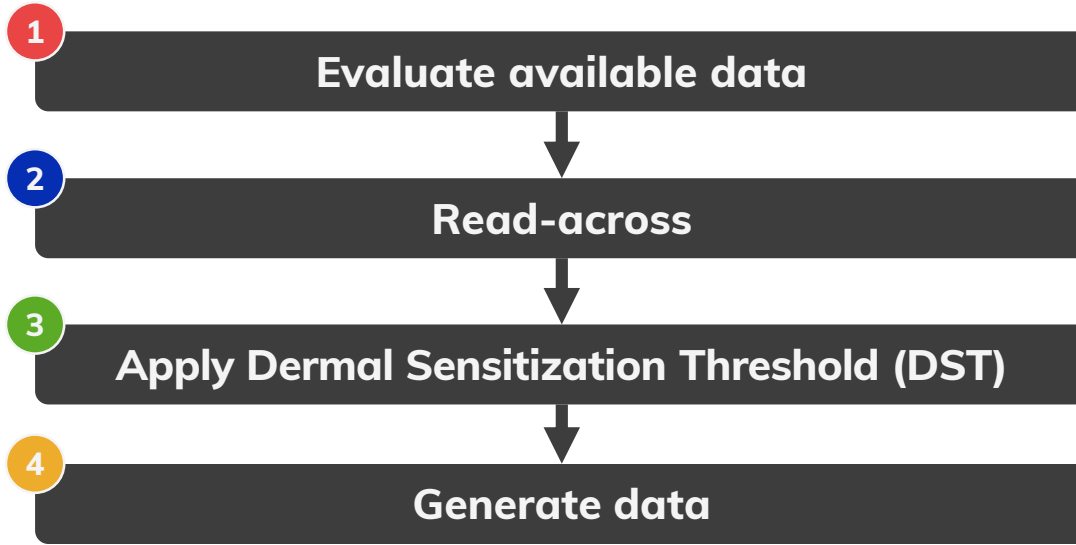
Promote AAT (such as via CAAT and EPAA)



2

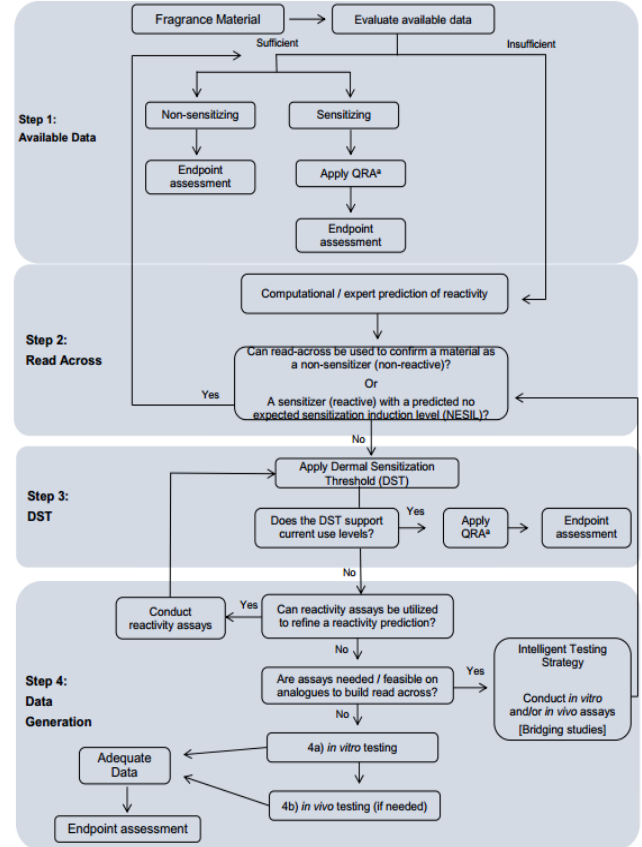
IFRA/RIFM and application of AAT
in the safety assessment and self-
regulatory (IFRA Standard) process

Acceptance by application: RIFM safety assessments

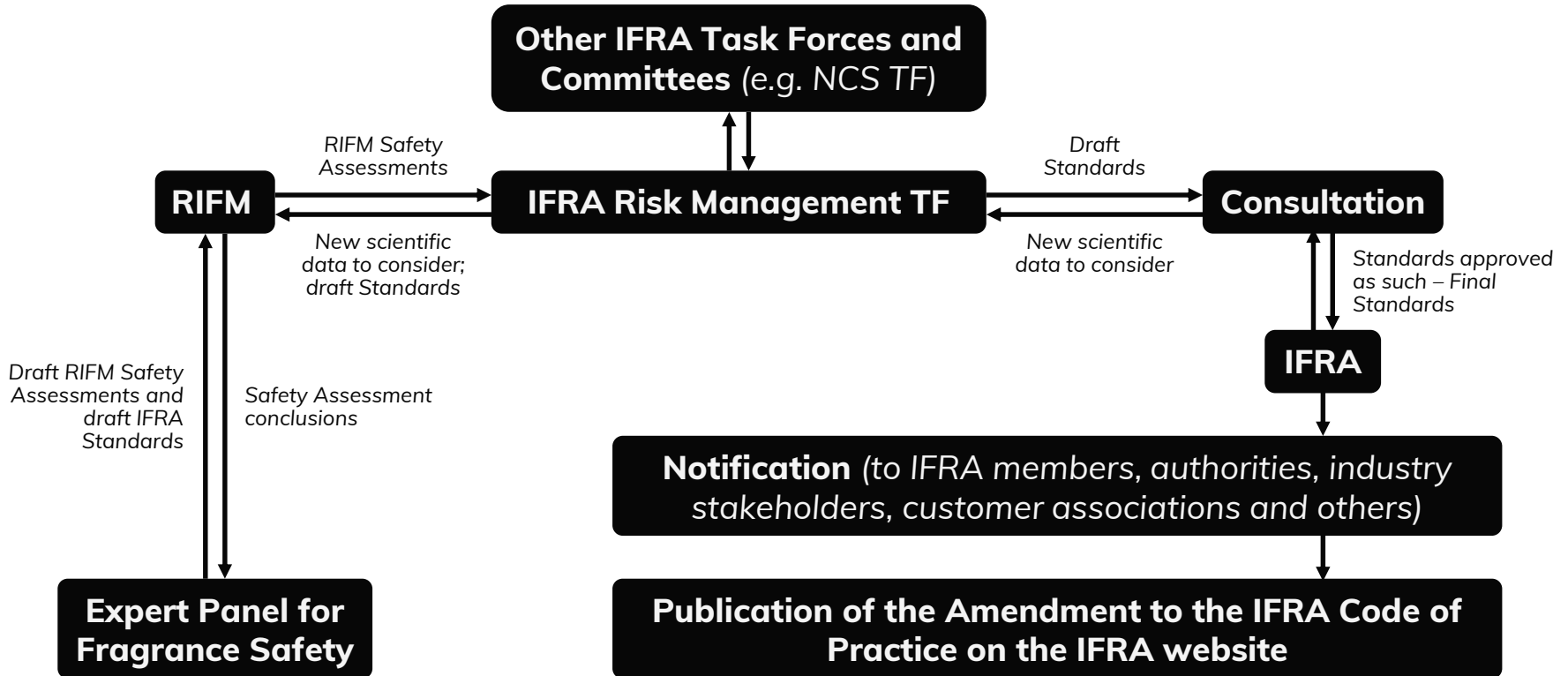


Part of 'Criteria Document'

Api et al, Food & Chemical Toxicology 82 (2015), S1 – S19



Acceptance by application: IFRA Standards-setting procedure



○ Enhancement of RIFM-Creme Aggregate Exposure model

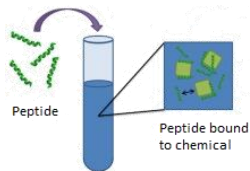
- Broaden scope by considering new applications, regions, keeping ingoing data up to date, etc.

○ Dermal Sensitization threshold (DST)

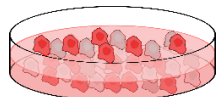
- Identifies an exposure below which there is a low concern for the induction of sensitization
- RIFM collaborated with R. Safford and D. Roberts to extend DST for reactive chemicals and identify high potency chemicals

Safford, R.J., Api, A.M., Roberts, D.W., Lalko, J.F., 2015b. Extension of the Dermal Sensitisation Threshold (DST) approach to incorporate chemicals classified as reactive. *Regulatory Toxicology and Pharmacology*, 72, 694-701.

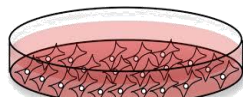
Roberts, D.W., Api, A.M., Safford, R.J., Lalko, J.F., 2015. Principles for identification of High Potency Category Chemicals for which the Dermal Sensitisation Threshold (DST) approach should not be applied. *Regulatory Toxicology and Pharmacology*, 72, 683-693



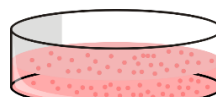
DPRA



KeratinoSens™



h-CLAT



U-Sens™



PPRA



Sens-IS

2013/14

2014

2015/16

~50 RIFM fragrance ingredients in collaboration with Cosmetics Europe

~50 RIFM fragrance ingredients

68157

Cutaneous and Ocular Toxicology <http://informahealthcare.com/cot>
ISSN: 1556-9527 (print), 1556-9535 (electronic)
Cutan Ocul Toxicol, Early Online: 1-5
© 2014 Informa Healthcare USA, Inc. DOI: 10.3109/15569527.2014.979425

informa
healthcare

RESEARCH ARTICLE

Correlation between experimental human and murine skin sensitization induction thresholds

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Part 2 in progress



3

Additional engagement in AAT 'promotion'



- **Member of the European Partnership for Alternative Approaches to Animal Testing (EPAA) since March 2012 (via IFRA Europe)**
- **Engagement of IFRA and IFRA Europe staff:**
 - Industrial co-chairmanship of Steering Committee (*Charles Laroche*)
 - Members of the Projects Platform team (*Amaia Irizar*)
 - Members of the Skin Sensitisation team (*Amaia Irizar*)



○ Current/recent activities in which IFRA staff are engaged:

- Assessing the skin sensitisation potential of difficult to test substances in 3D skin models (to be presented in EUROTOX2018)
- Workshop on Toxicokinetics and Read-Across (Q4 2017, manuscript submitted for publication)
- Workshop on Repeat-Dose toxicity (in Q4 2018)
- Organization of skin sensitization AAT knowledge sharing workshop (planned for Q1 2019)

- **IFRA staff are members of the following OECD groups on Test Guideline Development:**
 - Expert Group on Skin Sensitisation (*Matthias Vey*)
 - Expert Group on Define Approaches for Skin Sensitization (*Amaia Irizar*)
- **IFRA is a member of ECVAM Stakeholder Forum (ESTAF)**

- IDEA is a multi-stakeholder initiative supported by the European Commission developed to provide a broadly agreed & transparent framework for assessing fragrance sensitizers in a global multi-stakeholder dialogue (www.ideaproject.info).
- IDEA is committed to the integration of non-animal data to replace the LLNA as key starting point in skin sensitization RA.
- This is a goal shared by various stakeholders such as the EU Joint Research Centre (JRC), which expressed interest in liaising with the IDEA project.
- Following a first landscape meeting on 26 April 2016, a workshop was organized on 16-17 May 2018 in Brussels.

- Lead to definition of a **quantitative non-animal testing framework** for using potency information for skin sensitisation quantitative risk assessment (QRA) for fragrance materials.
- Bring together different parties who have shown potentially **promising methodologies** for **quantitative assessment of potency**.
- **Share case studies** explaining the application and current status of the approaches using only non-animal derived data for the determination of a no-expected sensitization induction level (NESIL) to serve as point of departure in QRA.
- **Facilitate open discussion** on the shared approaches with the interest of further progression in this area.

Speakers

Andreas Natsch (Givaudan)

Petra Kern (P&G)

Morihiko Hirota (Shiseido)

Masaaki Miyazawa (Kao)

Carsten Goebel (Coty)

Nicola Gilmour (Unilever)

Hervé Groux (Inmunosearch)

Other speakers

Devin O'Brien
(RIFM)

Silvia Casati
(JRC)

Observers

Bertrand Desprez
(Cosmetics Europe)

George Manika
(DG Grow)

Katrin Schütte
(DG ENV)

- **The workshop revealed that there is a wide range of non-animal approaches that can predict sensitization potency of fragrance substances for use in risk assessment**

- **A justifiable point of departure (e.g. NESIL) can be obtained if:**
 - Non-animal tests based on the Adverse Outcome Pathway are used,
 - A quantitative data integration procedure is applied, and
 - Uncertainty in the model can be assessed

- **Uncertainty can be reduced by additional data within an IATA (Integrated approach to assessment and testing). This is easier for substances from data rich vs. data poor domain**

- **Models should be made fully transparent to allow critical review of combined approaches – this requires:**
 - Details of input data and training sets
 - Underlying mechanistic assumptions
 - Algorithms
 - Basis for expert judgement



4

Conclusions

How the fragrance industry engages in alternatives to animal testing

Conclusions

We give **practical effect** to this commitment: we **publish our safety assessments and Standards** to show how we apply alternatives, especially in the sense of performing read across and using refined exposure approaches

IFRA is **committed to replacing animal testing** and continues to **strengthen its engagement** on alternatives through EPAA, CAAT and other platforms

Through **IDEA**, we will move **towards QRA3**, which will allow to derive limits for sensitizers based solely on non-animal test systems



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