

# Givaudan<sup>®</sup>

ENGAGING  
THE  
SENSES



The QRA methodology such as used today by IFRA to set  
Standards based on induction levels

Graham Ellis, Head of Global Toxicology, Givaudan Fragrances

IDEA Workshop, March 19th 2013

# The QRA methodology such as used today by IFRA to set Standards based on induction levels

- Where have we come from?
- Where are we now?
  - What are the IFRA QRA Categories?
  - How are they defined?
  - Practical considerations
  - The organisational process leading to IFRA Standards
- Evaluating and integrating future change

Where have we come from?

## Qualitative

- GPMT, Buehler/OET, human data

## Quantitative

- LLNA, human data

## IFRA Standards: Where have we come from?

### Skin contact products

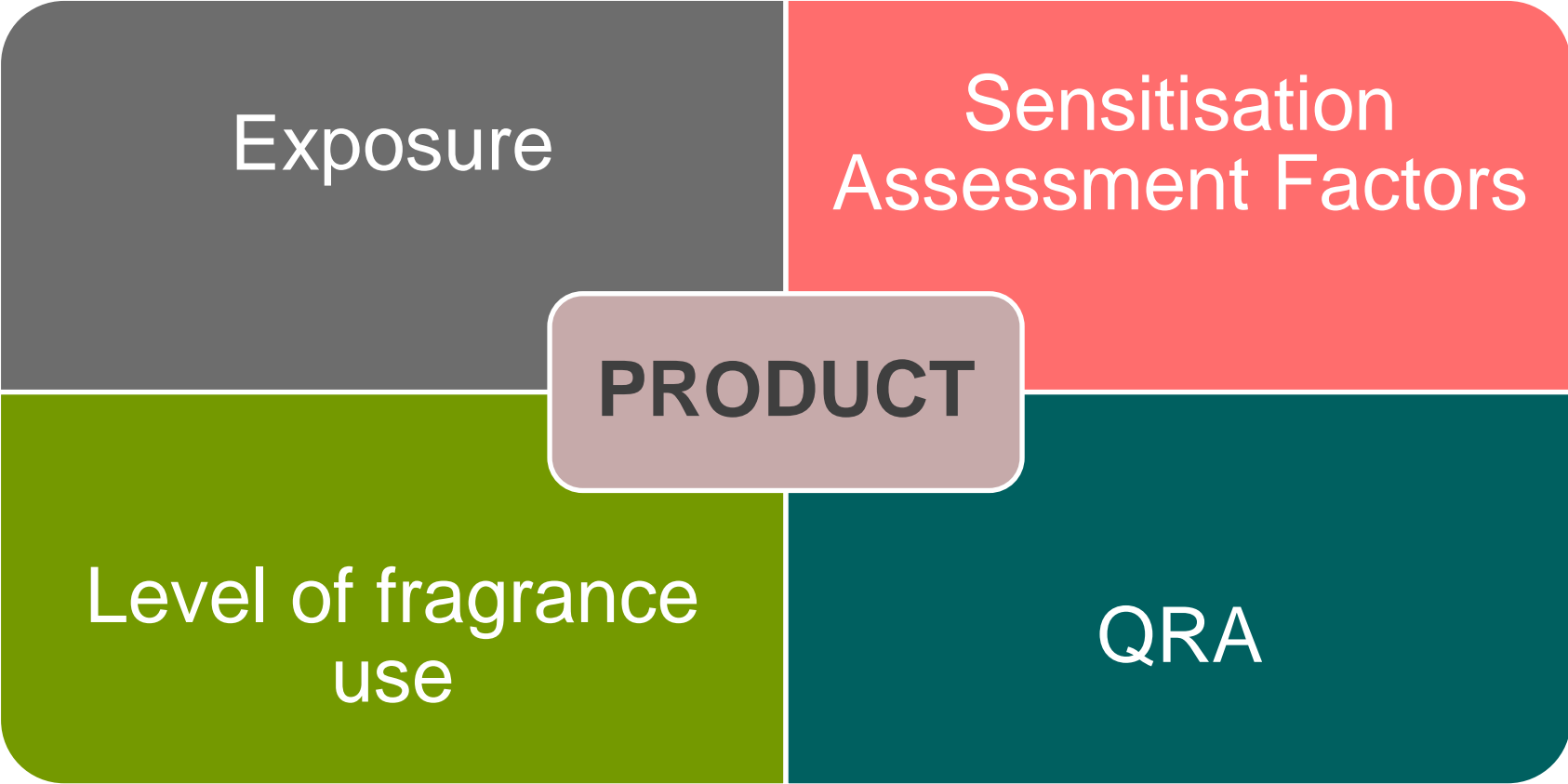
NOEL/10

- Fine fragrances, Creams, Leave-ons, Shampoos, Rinse-offs, Detergents, ...

### Non-skin contact products

NOEL

- Some air fresheners, Toilet blocks, ...



## IFRA Standards - All Change in 2006

- 40th Amendment (2006), IFRA Standards for sensitizing fragrance ingredients are based on the Quantitative Risk Assessment concept
- Over 50 product types considered
- Product types grouped according to:
  - Similar SAFs and Exposure
  - Which lead to similar acceptable use levels of a fragrance ingredient,
- Resulted in 11 product categories in IFRA Standards based on the QRA

An example of constructing IFRA categories

Product types in IFRA product category	Inter-individual SAF	Matrix SAF	Use SAF	Overall SAF	Exposure <sup>a</sup> mg/cm <sup>2</sup> /day	Citral (NESIL = 1400)
Category 3				300	2.2	0.2%
Hydroalcoholic products applied to recently shaved skin	10	3	10	300	(C& R) <sup>b</sup> 2.21	0.2%
Eye products of all types (eye shadow, mascara, eyeliner, eye make-up, etc.)	10	3	10	300	(CTFA, 2005a) 2.17	0.2%
Men's facial creams and balms	10	3	10	300	(EC, 1996) 2.06	0.2%
Tampons	10	1	20	200	(RIFM, 2006) 2.9	0.2%
Category 4				100	2.2	0.6%
Hydroalcoholic products applied to unshaved skin	10	3	3	100	(C& R) <sup>b</sup> 2.21	0.6%
Hair styling aids, hair sprays of all types (pumps, aerosol sprays, etc.)	10	3	3	100	(Loretz et al., 2006) 2.20	0.6%
Body creams	10	3	10	300	(Colipa, 2005) 0.6	0.8%
Category 5				100	4.2	0.3%
Women's facial creams/facial make-up	10	3	3	100	(CTFA, 2002) 3.17	0.5%
Hand cream	10	3	3	100	(Colipa, 2005) 4.2	0.3%

<sup>a</sup> (Source of exposure data).

<sup>b</sup> Cano and Rich (2001), Tozer et al. (2004), Cano (2006).

# Current Scope

- IFRA Standards based on QRA specifically aimed at preventing acquisition (induction) of dermal sensitisation to fragrance ingredients
- Not to be used for other toxicological effects
- Product described (to date) are all retail consumer products
- Products are placed in IFRA Categories according to similar acceptable use levels



<b>IFRA Category</b>	<b>Examples of Products</b>
<b>Category 1</b>	<b>Lip Products, Toys</b>
<b>Category 2</b>	<b>Deodorants/Antiperspirants</b>
<b>Category 3</b>	<b>Hydroalcoholic Products for Shaved Skin, Eye Products, Men's Facial Cream &amp; Balms, Tampons</b>
<b>Category 4</b>	<b>Hydroalcoholic Products for Unshaved Skin, Hair Styling Aids &amp; Sprays, Body Creams</b>
<b>Category 5</b>	<b>Women's Facial Cream/Facial Make-up/ Wipes or Refreshing Tissue, Hand Cream, Facial Masks</b>
<b>Category 6</b>	<b>Mouthwash, Toothpaste</b>
<b>Category 7</b>	<b>Intimate Wipes, Baby Wipes</b>
<b>Category 8</b>	<b>Make-up Remover, Hair Styling Aids Non-Spray, Nail Care</b>
<b>Category 9</b>	<b>Shampoo, Rinse-Off Conditioners, Bar Soap, Feminine Hygiene Pads &amp; Liners, Other Aerosols (including air fresheners sprays but not including deodorant/antiperspirants, hair styling aids spray)</b>
<b>Category 10</b>	<b>Detergents, Hard Surface Cleaners, Diapers</b>
<b>Category 11</b>	<b>All Non-Skin or incidental skin contact products</b>

**All non-skin contact or incidental skin contact.  
Including:**

**Pragmatic  
Level**

**Air Fresheners and Fragrancing of all types (plug-ins, solid substrate, membrane delivery, electrical, pot pourri, powders, fragrancing sachets, incense, liquid refills)**  
**Animal Sprays; Candles; Cat litter**  
**Deodorizers/Maskers Not Intended For Skin Contact (e.g. fabric drying machine deodorizers, carpet powders)**  
**Floor wax; Fragranced lamp ring; Fuels**  
**Insecticides (e.g. mosquito coil, paper, electrical, for clothing)**  
**Joss Sticks or Incense Sticks**  
**Machine Dishwash Detergent and Deodorizers**  
**Machine Only Laundry Detergent (e.g. liquitabs)**  
**Odored Distilled Water (that can be added to steam irons)**  
**Paints; Plastic articles (excluding toys); Shoe Polishes; Toilet Blocks**  
**Treated Textiles (e.g. starch sprays, fabric treated with fragrances after wash, deodorizers for textiles or fabrics, tights with moisturizers)**

**These products result in negligible skin contact.  
Risk of induction of dermal sensitization through normal use is negligible.  
The concentration of fragrance ingredient is not restricted in the finished product.**

IFRA Category	SAF	Product Type	Consumer Exposure Level mg/cm <sup>2</sup> /day	IFRA Category 5 Consumer Exposure	Limitation
Category 10	100	Facial Cream/Make-up	3.17	4.2	A
Category 11	100	Hand Cream	4.2		A
Category 10	100	0.1	Hard Surface Cleaners	Max conc ≤2.5%	
Category 11	10	0.00033	Candles		

## What are «Maximum Pragmatic Levels»?

- For weak sensitisers in certain categories where product exposure is low QRA calculation may lead to very high theoretical acceptable levels of use

### IFRA Category 10

**Citral WoE NESIL = 1400ug/cm<sup>2</sup>**

**SAF = 100**

**AEL = 14.0 ug/day**

**CEL = 100 ug/cm<sup>2</sup>/day**

**AEL/CEL = 0.14**

**Concentration giving AEL ≥ CEL: ≤ 14%**

**Maximum Pragmatic Level ≤2.5%**

- Pragmatic level defined as that  
«not exceeding the usual concentration of the fragrance compound in the finished product»
- If AEL < Maximum pragmatic level, the AEL takes precedence

# Data Needed For Product (Re-categorization)

## ■ Exposure Data

- Amount of fragrance in the product type?
- How much is used/use? How many uses/day?
- What is the surface area exposed?
- Will the fragrance come into direct contact with the skin? If not, please explain.
- Is the product rinsed off? If yes, should a retention factor be applied? Please explain.
- Is the product type an article? If yes,
  - Amount of fragrance applied to the product?
  - Amount of fragrance transferred from the product to the exposed area?

## Data Needed For Product (Re-)Categorization

- Form developed (IFRA IL 796)
- <http://www.ifraorg.org/Home/Science+Regulatory/Risk-Assessment/Quantitative-Risk-Assessment-QRA-/QRA-Downloads/page.aspx/116>
- or <http://www.rifm.org/pub/publications.asp>
- Information should either be sent to Anne Marie Api ([amapi@rifm.org](mailto:amapi@rifm.org)) or Matthias Vey ([mvey@ifraorg.org](mailto:mvey@ifraorg.org))
- Product Type
  - Name of Product Type
  - Description of the Product Type
  - Description of how the Product Type is Used
  - What, if any, instructions are given to the Consumer on the product label



## IFRA RIFM QRA Information Booklet Version 6.0

Revised July 2011

The purpose of this booklet is to provide basic guidance to fragrance suppliers and users on the implementation of the new Quantitative Risk Assessment (QRA) approach for fragrance ingredients. The Information Booklet was first issued on May 12, 2006 to provide assistance in implementing the 40<sup>th</sup> Amendment to the IFRA Code of Practice.

This booklet is a dynamic document that will change and require periodic updating to reflect the most up-to-date Amendments to the IFRA Code of Practice. As such, it will be important to check the issue date (located at the bottom of each page) of this booklet. The current version of the booklet is the sixth update (Version 6.0, May 2011) and can be found on both the IFRA and RIFM websites ([www.rifm.org/pub/publications.asp](http://www.rifm.org/pub/publications.asp) and [www.ifraorg.org](http://www.ifraorg.org), Science and Regulatory / Risk-Assessment section)

This Booklet (Version 6.0, July 2011) includes important updated information on:

- how new IFRA Standards will be set
- how existing IFRA Standards will be handled
- what should be expected in the 46<sup>th</sup> Amendment (Spring 2011) in terms of number of fragrance ingredients affected and the implementation time
- what will be considered for inclusion in future IFRA Amendments to the Code of Practice
- definition of the IFRA product categories
- guidance on preparing IFRA Certificates
- categorization of product types not previously included:
  - Air delivery systems
  - Waxes for mechanical hair removal
  - Lip wax
  - Body paint
  - Breath sprays
  - Concentrated aerosol air fresheners
  - Dry shampoo (waterless shampoo)
  - Fragranced bracelets
  - Wheat bags

## IFRA/RIFM INFORMATIONAL BOOKLET VERSION 6.0 (July 2011)

[www.rifm.org/pub/publications.asp](http://www.rifm.org/pub/publications.asp)

[www.ifraorg.org/news.asp](http://www.ifraorg.org/news.asp)

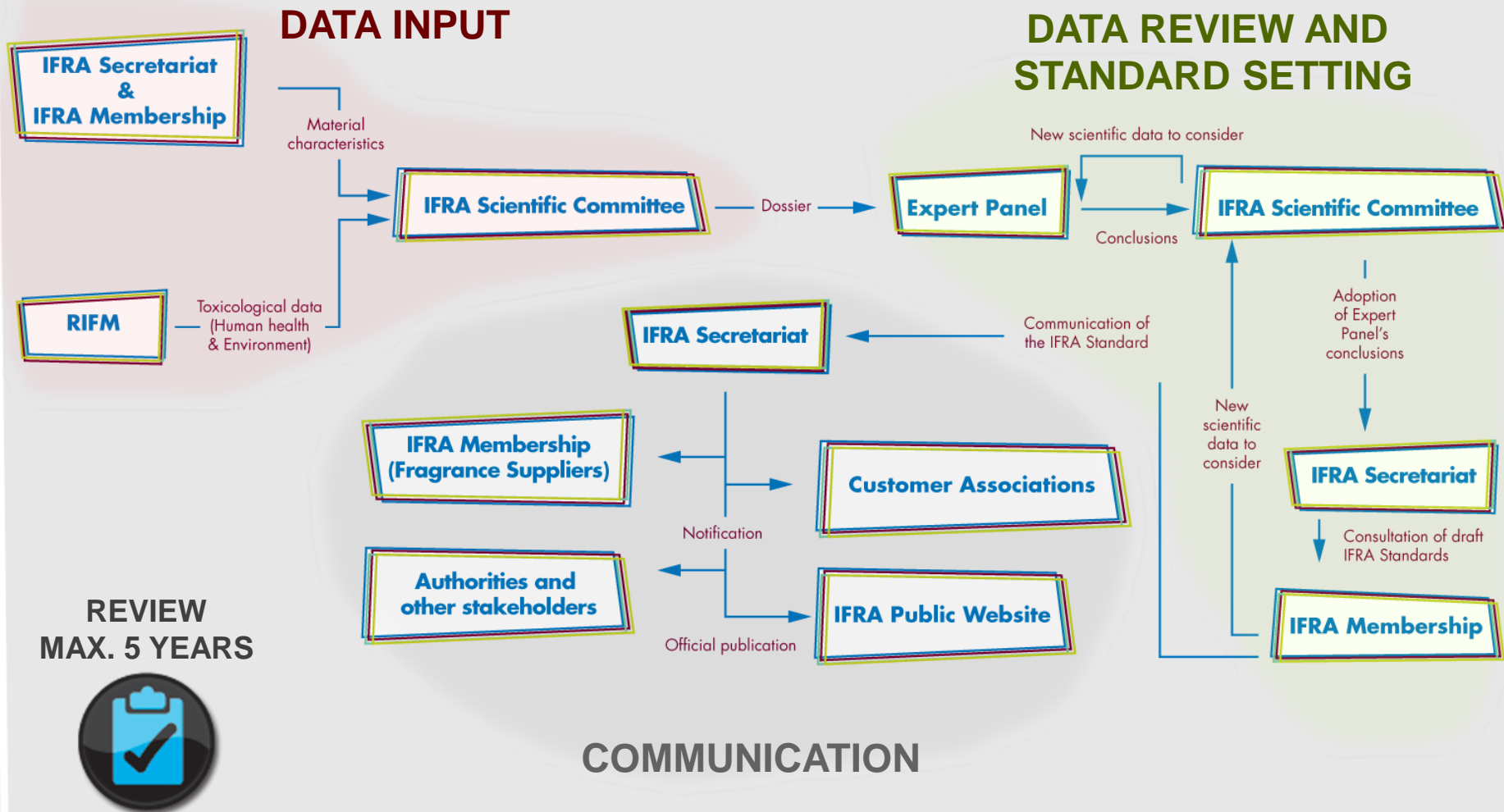
# IFRA/RIFM Informational Booklet

## Version 6.0 (July 2011)

- how new IFRA Standards will be set
- how existing IFRA Standards will be handled
- what should be expected in the 46th Amendment (Spring 2011) in terms of number of fragrance ingredients affected and the implementation time
- what will be considered for inclusion in future IFRA Amendments to the Code of Practice
- definition of the IFRA product categories
- guidance on preparing IFRA Certificates
- categorization of product types not previously included (e.g. Air delivery systems, Waxes for mechanical hair removal, Lip wax, Body paint, Breath sprays, Concentrated aerosol air fresheners, Dry shampoo (waterless shampoo), Fragranced bracelets, Wheat bags)



# IFRA Standards Process



# Evaluating and Integrating Future Change

- IFRA Standards will be adapted to any new data or developments of the QRA
- Looking to output and workplan from IDEA workshop(s) to shape any further changes
- With over 184 IFRA Standards implementing change would take some time

# Summary

- QRA has made a significant impact on how we manage fragrance safety and the IFRA Standards

But, still some areas to consider

- Workable number of Categories
- Use of pragmatic levels
- QRA refinements
- Integration of Aggregate Exposure data
- Scope – Products, Susceptible sub-populations,...



Givaudan<sup>®</sup>

ENGAGING  
THE  
SENSES