

How to Measure the Effectiveness of the Dermal Sensitization QRA For Fragrance Ingredients

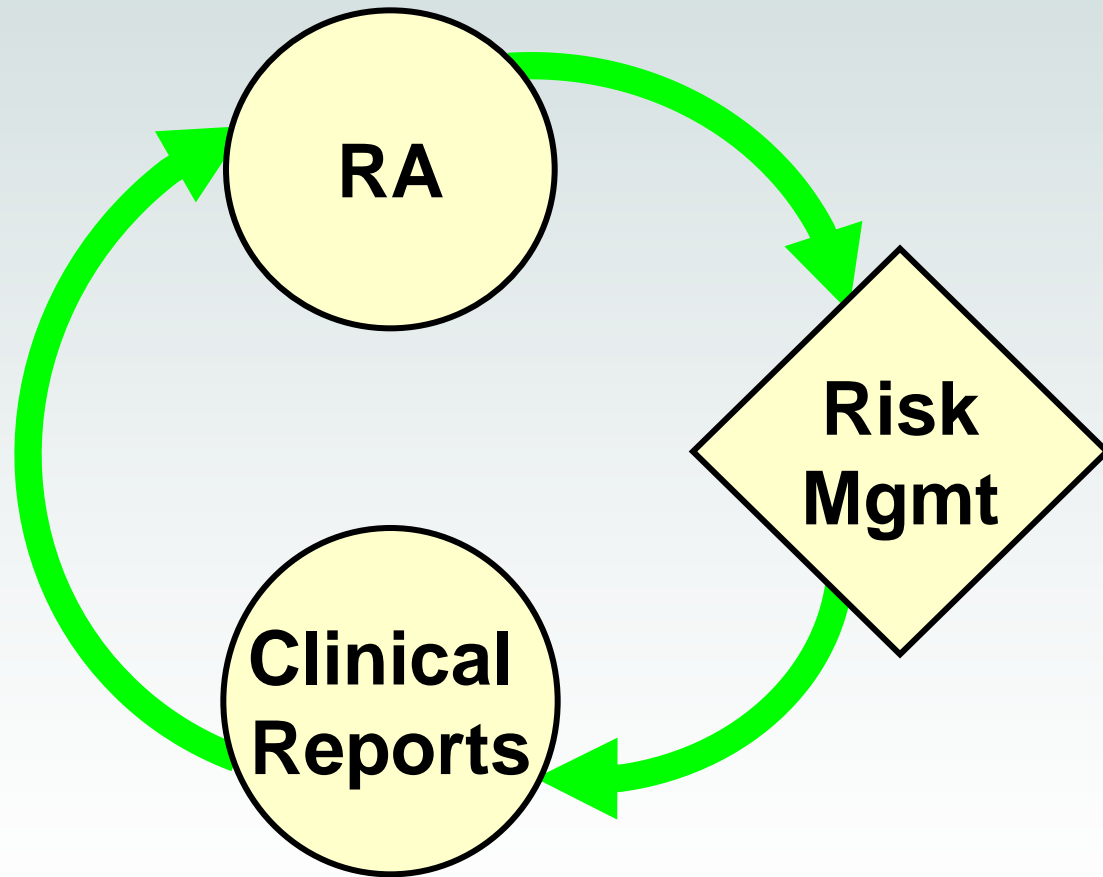
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IDEA Workshop
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QRA Dermal Sensitization: Does It Work?



- Evidence of proven effectiveness for other materials
- Need to build evidence in fragrance ingredients





Mortz et al., 2012

● British Journal of Dermatology

- study followed school age children who were studied 15 years ago.
- Most notable is that in 1995, 11 children reacted positively to FM 1. However, 15 years later in 2010, none of the 11 reacted to FM 1. Two new reactions were observed to FM 1.
- Authors concluded that sensitization can become lower over the years, but it was difficult to explain.
- In the intervening 15 years, significant changes to the use of the materials in FM 1 have occurred. Perhaps this may account for the changes.



QRA Dermal Sensitization

Fragrance Ingredient	Industry Survey or Limit Prior to QRA-based Standard	QRA –based Limit
Cinnamic Aldehyde	Skin level: 0.05%	↓Deo/AP: 0.02%
Citral	Hydroalcoholics: 1.7%	↓Hydroalcoholics: 0.6%
	Deo/AP: 0.05%	Deo/AP: 0.05%
Isoeugenol	Skin level: 0.2%	↓Hydroalcoholics: 0.02%

Patch Test Database

U. Hospital Leuven



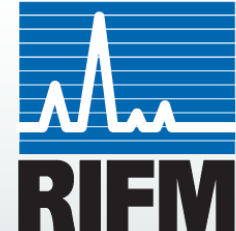
- **Api et al, Dermatitis, 21(4): 207-213, 2010**
 - **RIFM sponsored surveys 2000-2007**
 - **Identify product types containing specific fragrance ingredients**
 - **Of total patients, select those positive to Fragrance Mix and their own cosmetic products with fragrance-related contact allergic reactions**
 - **About 500 positive patch test to their own cosmetic products per year**
 - **About 250 have reactions related to specific fragrance ingredients**

Database U. Hospital Leuven 2000-2007



Fragrance Ingredient	Product Type	Positive Patch Test Reactions to Product Confirmed & Not Confirmed
Cinnamic Aldehyde	Deodorant	4
	Intimate Hygiene Wipes	1
	Hair Care	1
Citral	Hydroalcoholic	9
	Skin Care	2
	Deodorant	1
Isoeugenol	Hydroalcoholic	14
	Skin Care	4
	Deodorant	2
	Hair Dye	1

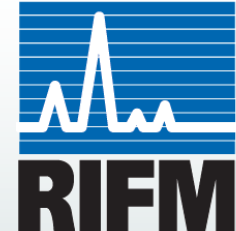
Database U. Hospital Leuven 2008-2012



Fragrance Ingredient	Total Positive Patch Test Reactions to Product Confirmed & Not Confirmed				
	2008	2009	2010	2011	2012
Amyl Cinnamic Aldehyde (2007)	0	3	1	0	0
Cinnamic Alcohol (2007/2008)	1	1	16*	0	2
Cinnamic Aldehyde (2007/2008)	0	1	4	0	3
Geraniol (2007)	8	8	7	0	2
Hydroxycitronellal (2007/2008)	1	6	5	0	3
Eugenol (2007/2008)	0	3	11	3	0
Isoeugenol (2007/2008)	1	1	2	0	0
Oakmoss absolute (2008)	2	10	6	4	2

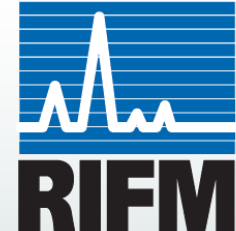
*Most often linked to ketoprofen photosensitivity

Database U. Hospital Leuven 2008-2012



Fragrance Ingredient	Total Positive Patch Test Reactions to Product Confirmed & Not Confirmed				
	2008	2009	2010	2011	2012
HMPCC (2007)	12	20	24	5	5
Citronellol (2007)	1	5	10	0	2
Coumarin (2008)	0	0	1	1	1
Farnesol (2006)	1	3	5	0	1
α -Hexylcinnamaldehyde (2007)	0	13	8	0	4
Citral (2006)	2	0	1	0	9

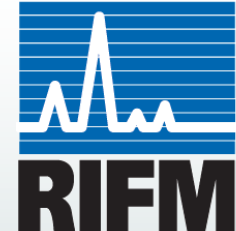
Database U. Hospital Leuven 2008-2012



Fragrance Ingredient	Total Positive Patch Test Reactions to Product Confirmed				
	2008	2009	2010	2011	2012
Amyl Cinnamic Aldehyde (2007)	0	1	0	1	0
Cinnamic Alcohol (2007/2008)	1	0	4*	0	2
Cinnamic Aldehyde (2007/2008)	0	0	1	0	1
Geraniol (2007)	8	4	4	0	2
Hydroxycitronellal (2007/2008)	1	4	2	0	0
Eugenol (2007/2008)	0	0	2	3	0
Isoeugenol (2007/2008)	1	0	0	0	0
Oakmoss absolute (2008)	0	2	2	0	0

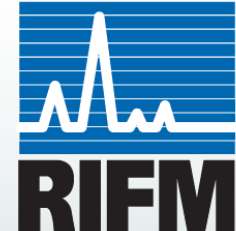
*Most often linked to ketoprofen photosensitivity

Database U. Hospital Leuven 2008-2012



Fragrance Ingredient		Total Positive Patch Test Reactions to Product Confirmed				
		2008	2009	2010	2011	2012
HMPCC	(2007)	12	12	13	5	5
Citronellol	(2007)	1	3	2	0	2
Coumarin	(2008)	0	0	0	1	1
Farnesol	(2006)	1	2	1	0	1
α -Hexylcinnamaldehyde	(2007)	0	10	5	0	4
Citral	(2006)	2	0	1	0	9

Database U. Hospital Leuven 2011-2012



Fragrance Ingredient	Product Type	Positive Patch Test Reactions to Product Confirmed	
Amyl Cinnamic Aldehyde	Shaving product	1	(2011)
Cinnamic Alcohol	Cleansing Product	1	(2012)
	Hair Care & Shampoo	1	(2012)
Cinnamic Aldehyde	Skin Care	1	(2012)
Geraniol	Skin Care	1	(2012)
HMPCC	Hydroalcoholic	1	(2012)
	Bath/Shower	1	(2012)
	Skin Care	1	(2012)
	Sun	1	(2012)
	Deo	1	(2012)

Database U. Hospital Leuven 2011-2012



Fragrance Ingredient	Product Type	Positive Patch Test Reactions to Product Confirmed	
Citronellol	Deo	2	(2012)
Coumarin	Sun	1	(2011)
	Skin Care	1	(2012)
Farnesol	Deo	1	(2012)
Eugenol	Hydroalcoholic	1	(2011)
	Sun	2	(2011)
α-Hexylcinnamaldehyde	Shaving Products	1	(2012)
	Bath/Shower	1	(2012)
	Deo	2	(2012)

Database U. Hospital Leuven 2011-2012



Fragrance Ingredient	Product Type	Positive Patch Test Reactions to Product Confirmed	
Citral	Bath/Shower	4	(2012)
	Cleansing Product	1	(2012)
	Hair/Shampoo	1	(2012)
	Deo	1	(2012)
	Skin Care	2	(2012)



Retrospective Studies

- **Difficult to impossible to accomplish in individual clinics**
- **Numbers of reactions are small**
- **Number of confirmed reactions are even smaller**
- **Totals are too small to be meaningful to make conclusions**
- **As such efforts are focused on prospective studies**



Prospective Study

- **Proposal: to develop a network and system of recording and sharing information from dermatology clinics as a potential method of determining the effectiveness of the QRA over a long time period (minimum 5 years and ideally much longer) could be judged against incidence (not prevalence)* of allergy to fragrance under an agreed scheme.**

Prospective Study

- ***It will not be feasible – neither using population-based, nor clinic-based studies – to measure *incidence*, as this would inevitably involve *repeated patch testing* of a cohort of individuals with the allergen(s) in focus. However, regarding new substances (not cross-reacting with existing ones), all prevalent cases can be regarded as incident. Moreover, a focus on contact allergy prevalence (=PT results) in younger patients with a shorter cumulative exposure history can approximate incidence so some extent.**



Prospective Study

- 1. Incidence of positive diagnostic patch test reactions to fragrance mixes**
- 2. Incidence of positive diagnostic patch test reactions to a specific fragrance ingredient**
- 3. Recording of body site of allergic contact dermatitis associated with 1 and 2 above**
- 4. Recording of product type presented by patient (including brand and batch number) [NEW]**



Prospective Study

- 5. Determination of clinical relevance of product to current or historic allergic contact dermatitis, with details on how relevance was examined**



Prospective Study

- 6. Provision of product sample for analysis - Try to determine the date at which each subject's allergy to X was discovered. While the date of discovery is not always related to the date of induction/acquisition of allergy, there is still a statistically greater chance that older dates of discovery will relate to pre-QRA induction and dates of discovery after (some years maybe) implementation of QRA restrictions, will reflect the impact of QRA**



Prospective Study

- 7. Provision of fragrance ingredients of a product (as far as these are not commercially available as PT allergens) for break-down testing in case of a positive reaction to the product.**

Next Steps

- **Draft a 'case record form' and some procedural layout (based on the present collection of ideas)**
- **Develop a protocol**
- **Find clinics interested in participating**

More Information



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