

Fragrance Hypersensitivity: EU vs North America

Are there differences in prevalence?
or

Trying to make sense of the contradictory
and unknown!





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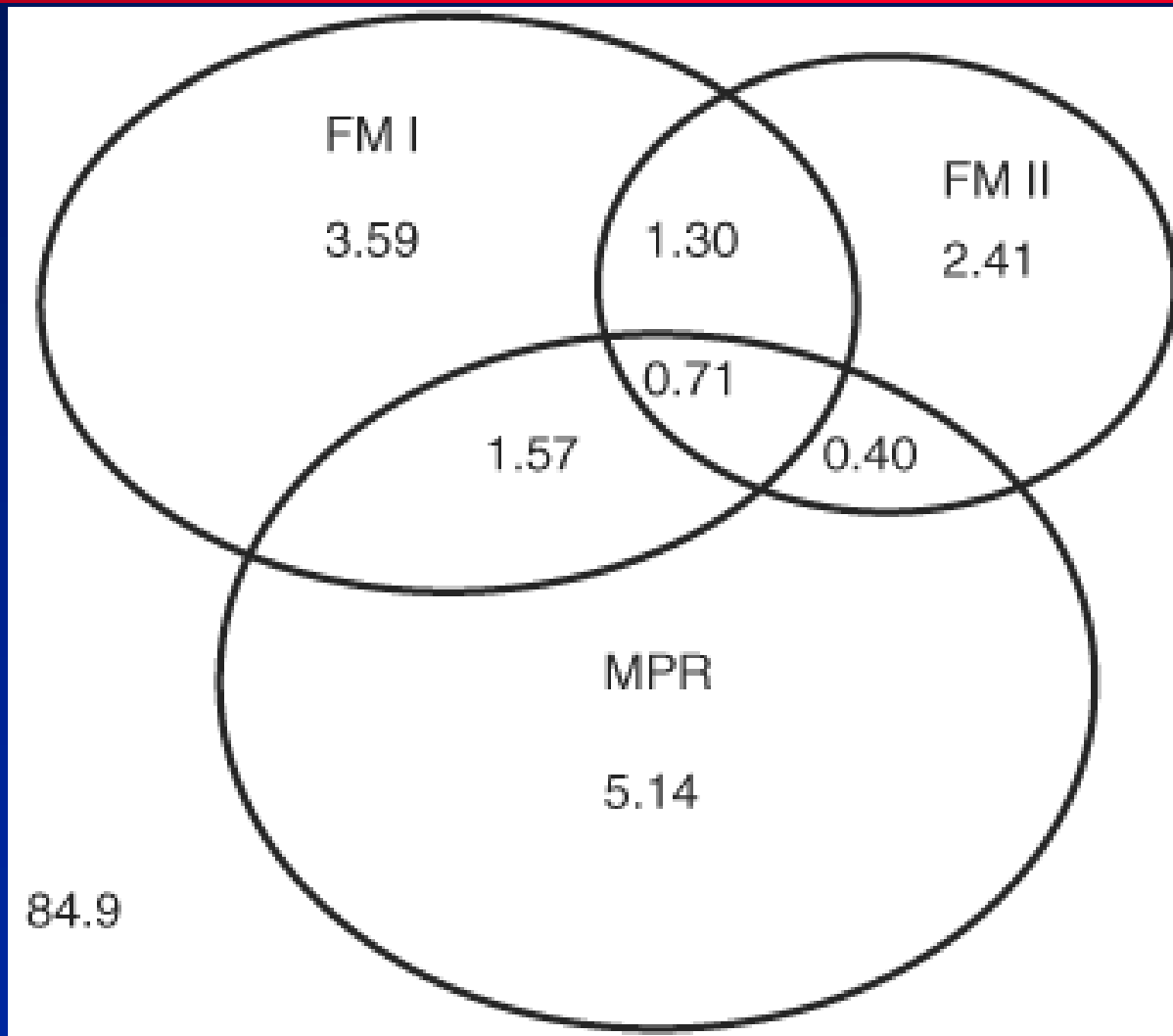
Conflicts of Interest

- Expert Panel Member, RIFM 
- My travel to this meeting is courtesy of RIFM 
- I like my cologne – especially on crowded subways 
- I have no known allergy to fragrances 
- I am speaking on behalf of myself –
 - This talk was prepared by me
 - I am not representing RIFM
 - I am not representing Columbia University Medical Center

Standard Fragrance Screening Allergens

- Fragrance mix 1: oak moss, geraniol, eugenol, isoeugenol, cinnamal, cinnamyl alcohol, α -amylcinnamal, hydroxycitronellal
- Fragrance mix 2: HICC, citral, farnesol, coumarin, citronellol, α -hexylcinnamal
- Balsam of Peru: resin obtained from bark of *Myroxylon pereirae* – multiple flavor/fragrance allergens
- Colophonium (rosin): resin obtained from pines and other conifers produced by heating fresh liquid resin to vaporize the volatile liquid terpene components consisting of different resin acids, especially abietic acid

Overlap of Fragrance Screening Allergens



Uter, et al.
Contact Dermatitis
2010; 63: 254-261

National Variations in Fragrance Responses in Dermatitis Patients: 2007 - 2008

Country	AU	DK	FI	GE	IT	LI	NE	PO	SP	SW	UK	NA
# tested	678	1318	760	2694	2938	680	2168	789	1845	2402	8909	5085
FM1 (%+)	10.4	6.0	6.1	6.4	4.2	3.7	7.3	6.1	4.9	7.7	7.2	9.4
M. Pereira (%+)	10.6	3.0	6.9	7.6	1.6	8.3	4.2	5.0	5.0	7.6	5.2	11.0
FM2 (%+)	7.9	3.0	3.6	4.3	nr	2.6	6.4	2.5	1.9	5.5	3.2	3.6
Colophony (%+)	6.1	2.6	4.5	4.3	1.5	4.8	2.6	1.6	1.8	2.8	2.7	2.8

Uter, et al. Contact Dermatitis 2012; 67: 9-19
Fransway, et al. Dermatitis 2013; 24: 10-21

Regional variations:

- Variation in product usage & allergen exposure
- Differences in proportion of occupational cases seen
- Access to care / patch testing
- Inter-individual variations in patch test readings

Relevance of Reactions: FM I Dermatitis Patients (n=?)

Initial patch reaction	Relevance			Negative to all ingredients (n=22)
	Initial positive result (n=138)	Repeat positive result (n=121)	Repeat positive to ≥ 1 ingredient (n=99)	
?+	25.0% (40) ^{a,b}	43.5% (23)	54.5% (11)	52.1% (12)
+	40.5% (42) ^b	40.5% (42)	46.9% (32)	23.8% (10)
++	71.4% (28)	71.4% (28)	71.4% (28)	0
+++	75.0% (28)	75.0% (28)	75.0% (28)	0

^a 39.5% of ?+ not reduplicated

^b 59.4% of fragrance reactions were ? or +

Devos, et al. Dermatitis 2008; 19: 43-47

Final Interpretation of Fragrance Reactions

Substance	N	RXNS (n)	Final Interpretation				Relevance (%)			
			+++ N (%)	++ N (%)	+ N (%)	+/- N (%)	Definite	Probable	Possible	Past
Fragrance mix I, 8.0% pet.	4232	511	95 (18.6)	140 (27.4)	216 (42.3)	59 (11.5)	12 (2.3)	152 (29.7)	309 (60.5)	11 (2.2)
Myroxylon Pereirae, 25.0% pet.	4234	333	37 (11.1)	64 (19.2)	168 (50.5)	63 (18.9)	3 (0.9)	122 (36.6)	173 (52.0)	9 (2.7)
Fragrance mix II, 14.0% pet.	4237	218	17 (7.8)	42 (19.2)	124 (56.6)	35 (16.0)	5 (2.3)	79 (36.1)	122 (55.7)	3 (1.4)
Colophonium (rosin), 20.0% pet	4236	96	39 (40.6)	22 (22.9)	31 (32.3)	4 (4.2)	2 (2.1)	19 (19.8)	37 (38.5)	24 (25.0)

Preliminary data, NACDG, 2011-2012

FM I (+) reactions

- 2632 patients tested from 01/01/1994 – 06/30/2014
 - 248 (9.4%) w/ ?, +, ++, or +++ reactions
 - 238 (9.0%) w/ +, ++, or +++ reactions
 - 105 (4.0%) w/ ++ or +++ reactions
 - 62 of 143 ? And + patients tested to individual components of FM I
 - All ? Reactors Tested (n = 4), negative
 - 10 / 58 (17.2%) + reactors, negative
 - 21 (0.80%) with IR responses
 - » Unpublished data, Belsito

FM1(+); Constituent (-)

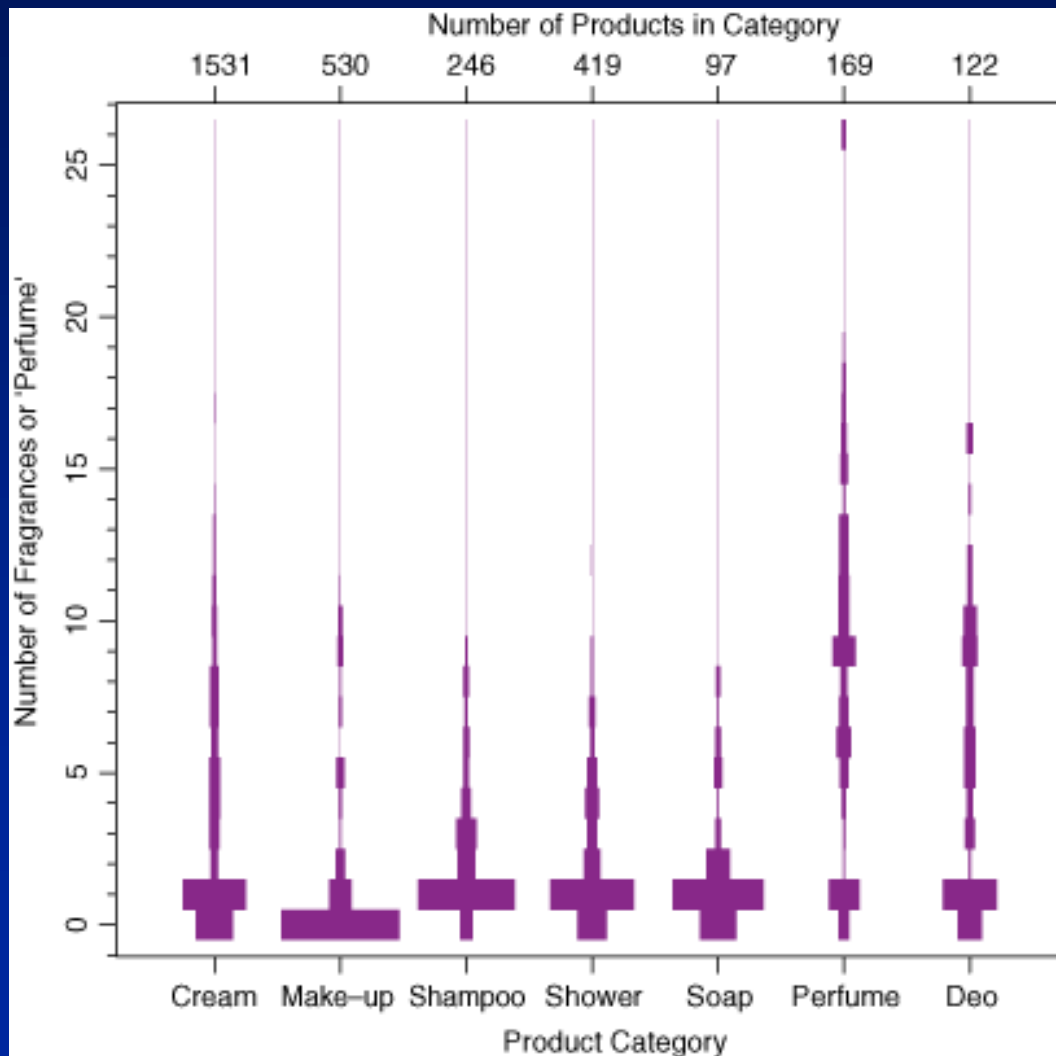
The Dilemma

Significant number of subjects (n = 131/940; 13.9%) reacted negatively to the breakdown constituents but positively to FM 1

- false-positive reaction to the mix
- each constituent acts as an irritant, which lowers the elicitation threshold for other allergens when tested in combination
- false-negative reactions to the individual constituents of the FM, because the the skin penetration of FM 1 is increased by the emulsifier sorbitan sesquioleate
- different evaporation potentials of components than of the mixture
 - cinnamal and cinnamyl alcohol were more stable when analyzed as ingredients in FM 1 than when analyzed in individual preparations
- fragrance mixtures have increased potency in sensitization and elicitation of contact allergic reactions as compared with isolated fragrances
 - mixtures of fragrances, i.e. FM 1 and FM 2, not only reflect normal exposure to perfumes, but also provide the optimal stimulus to the immune system

» Nardelli, et al. Contact Dermatitis 2013; 68: 307-13

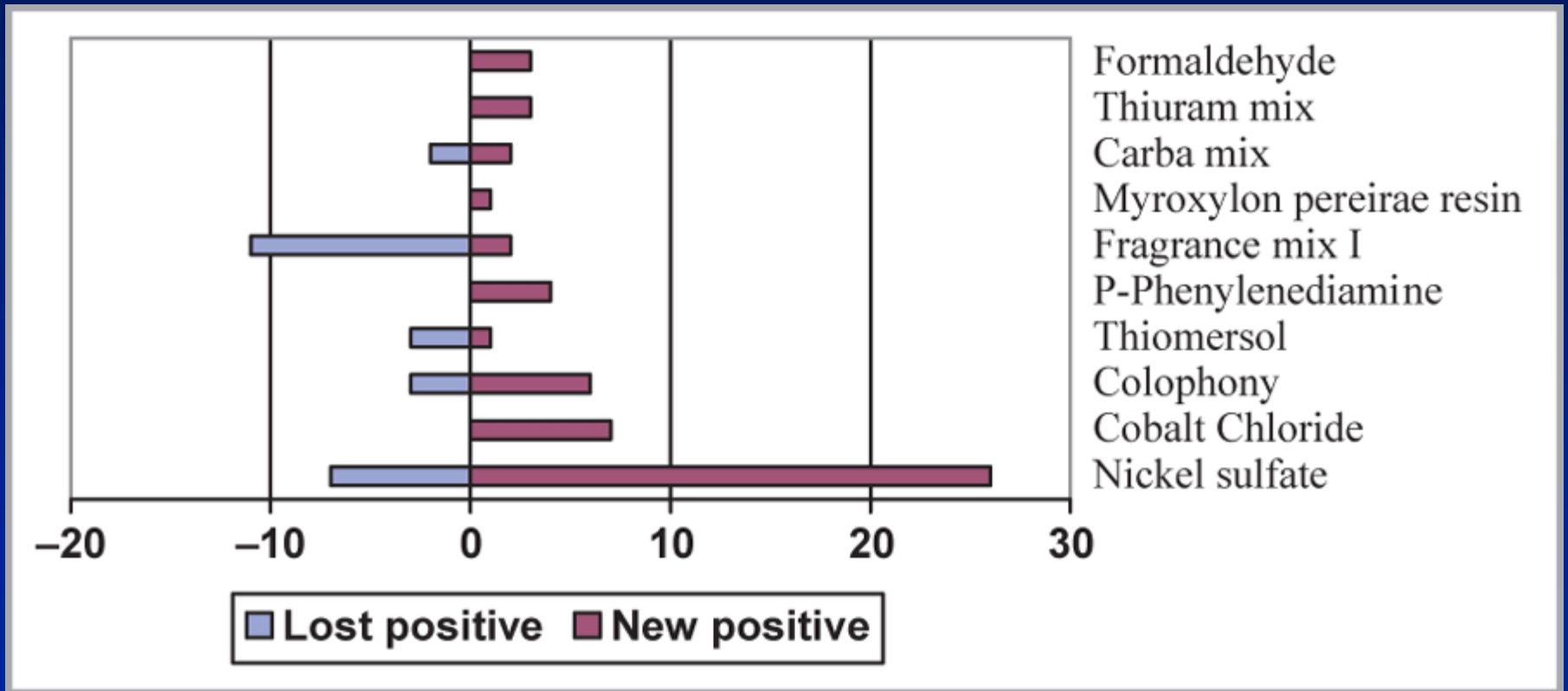
Fragrance Combinations in Consumer Product



Germany: stratified
random sample;
presence of 26
fragrances requiring
labelling

Uter, et al.
Contact Dermatitis
2013; 69: 335-41

Persistence of Positive Patch Tests: 2010 v. 1995, population cohort, n=403)



Mortz, et al. Br J Dermatol 2013; 168: 318-25

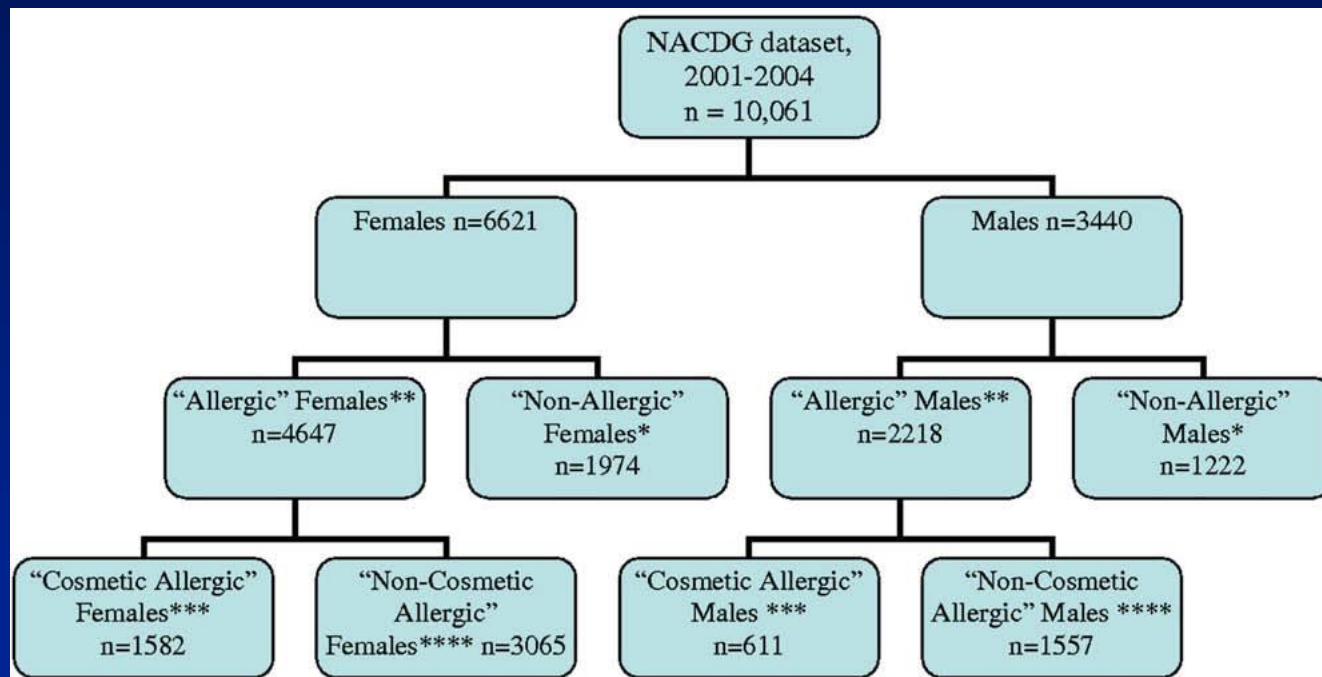
Persistence of Positive Patch Tests: 2010 v. 1995, population cohort, n=403

Number of positive patch test reactions in 1995 and 2010 and the number of positive reactions reproduced for the individual allergens in TRUE Test panel 1 and 2 together with lost and new positive reactions (n = 403)

	+ in 1995	+ in 2010	Reproduced positive, n (%)	Lost positives	New positives
Nickel sulfate	31	50	24 (77)	7	26
Fragrance mix I	11	2	0	11	2
Colophony	5	8	2 (40)	3	6
Myroxylon pereirae	3	2	2 (67)	1	0

Mortz, et al. Br J Dermatol 2013; 168: 318-25

North American Contact Dermatitis Group 2001-2004



23.9% Females &
17.7% Males
w/ cosmetic allergy

Warshaw, et al.
J Am Acad Dermatol
2009; 60: 23-38.

Allergen	% Females with allergy to cosmetic source N = 1582	% Males with allergy to cosmetic source N = 611
Myroxylon pereirae, 25%	19.1	22.6
Fragrance mix 1, 8%	19.1	21.1

North American Contact Dermatitis Group 2001-2004

Dermatitis patients (n = 10,061)

		Patients w/ diagnosis of allergic contact dermatitis (n = 6815; 67.7% of patients tested)	
Allergen	Total allergic N (%)	% allergy related to cosmetic	% allergy unrelated to cosmetic
Quaternium-15, 2% pet	917 (9.1%)	22.1%	9.3%
M. pereirae, 25% pet	977 (9.7%)	20.1%	14.6%
Fragrance mix I, 8% pet	917 (9.1%)	20.1%	10.3%

Pratt, et al. Dermatitis 2004; 15: 1 – 8;

Warshaw, et al. Dermatitis 2008; 19: 129-36;

Warshaw, et al. J Am Acad Dermatol 2009; 60: 23-38.

Cosmetic Sources of Allergy: North America, 2001 - 2004

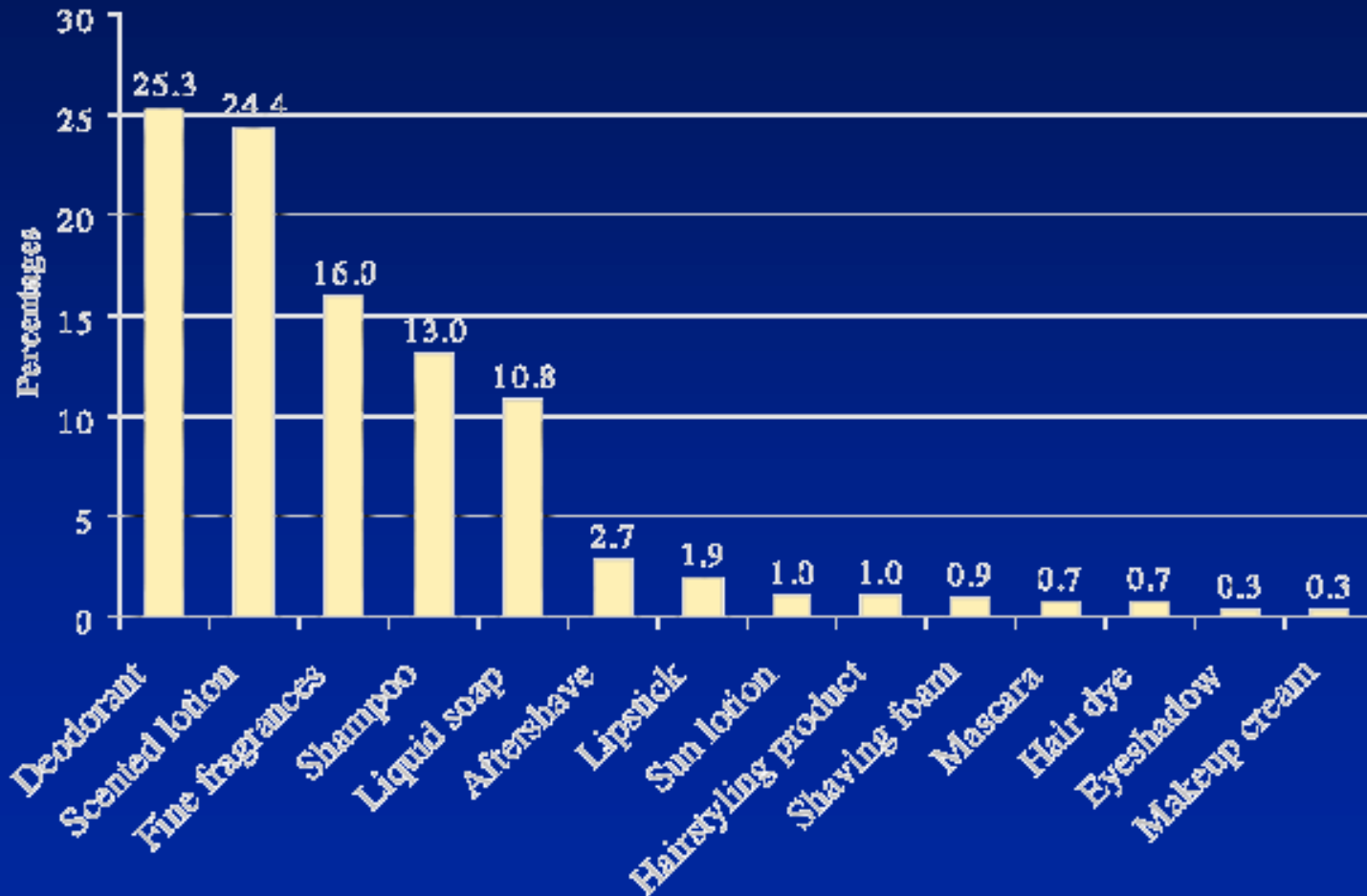
Cosmetic product types associated w/ patch test reactions in patients w/ cosmetic ACD – not necessarily FM I / II or M. pereirae reactions
(Warshaw, et al. J Am Acad Dermatol 2009; 60: 23-38)

Product category	<u>Females</u>		<u>Males</u>	
	No. of patients with positive allergic reaction to source (% all females allergic to cosmetics, n = 1582)*	No. of currently relevant reactions in category/total category reactions (%)	No. of patients with positive allergic reaction to source (% all males allergic to cosmetics, n = 611)*	No. of currently relevant reactions in category/total category reactions (%)
Cosmetic, NOS	1072 (67.8)	1871/2003 (93.4)	467 (76.4)	973/1025 (94.9)
Moisturizers	529 (33.4)	901/946 (95.2)	306 (50.1)	658/680 (96.8)
Hair care products	475 (30.0)	495/607 (81.2)	134 (21.9)	142/161 (88.2)
Nail products	171 (10.8)	167/211 (79.2)	7 (1.2)	16/17(94.1)
Perfumes and fragrances	132 (8.3)	156/191 (81.7)	58 (9.5)	73/88 (83.0)
Make-up	88 (5.6)	121/124 (97.6)	0	0 (0)
Skin cleansers	64 (4.1)	79/82 (96.3)	59 (9.7)	74/77 (96.1)
Oral care products	12 (0.8)	17/17 (100)	5 (0.8)	6/6 (100)
Deodorants/antiperspirants	7 (0.4)	8/8 (100)	20 (3.3)	27/31 (87.1)

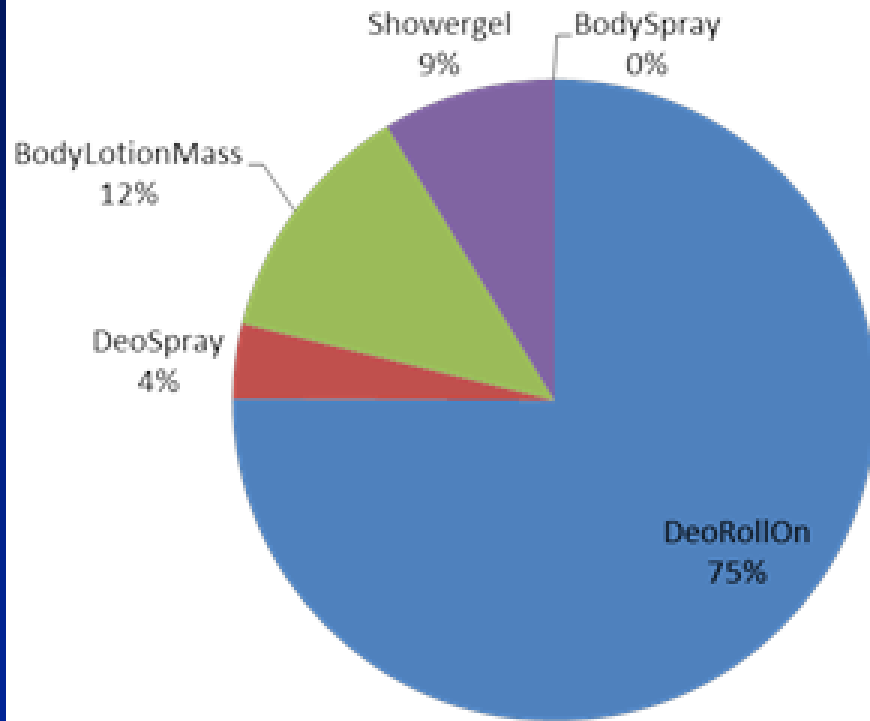
NOS, Not otherwise specified.

*Totals greater than 1582 and 611, respectively, because a single patient could have several reactions, each to a different category of cosmetics.

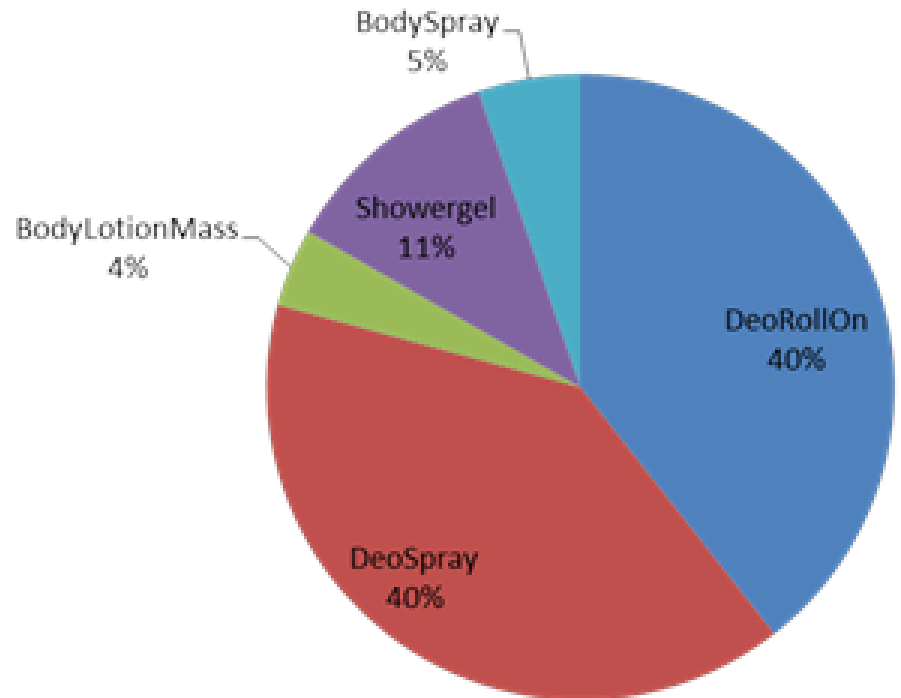
Cosmetic Sources of Fragrance Allergy: Denmark, 2005 - 2009



HICC: US vs EU



HMPCC (QRA) US



HMPCC (QRA) EU

Occupational Contact Allergy to Fragrance Mix 1?

IVDK, 1992 – 1998; 57,779 patients tested to FM I; 1454 tested more than once & assigned highest reactivity to FM I

ISCO-88	Job title/group	n	%*	+ to +++ (%)	++ to +++ (%)
2230, 3231	Geriatric nurse	322	1.209	17.4	6.2
3226	Masseur, physiotherapist	287	2.921	16.4	5.9
8120	Metal furnace operator, melter, caster, drawer	119	1.097	16.0	5.9
7320	Potter, glass maker, or blower	70	0.879	15.7	8.6
5141	Cosmetologist	139	12.981	14.4	2.9
5121†	Household worker (including housewife)	6820	NC	13.9	4.7
6110, 6120, (6200, 9211)	Agricultural labourer	333	3.187	13.8	4.2
5220, 5230, 9110	Salesperson	1013	0.616	13.3	4.5
2300	Teaching professional	1498	1.583	13.1	3.9
7311	Precision mechanic	153	1.593	13.1	3.9
7430, (5200)	Textile worker or salesperson	408	1.936	13.0	5.1
3131, 7344, 8224	Photographer, laboratory worker	108	3.375	13.0	1.9
1000, 4000, and others	Office worker	7779	1.043	12.2	4.2
5123	Waiter, bartender, etc	471	1.404	12.1	3.6
4211, 4212	Cashier	125	1.119	12.0	4.8
(5220, 5230), 6113	Florist, gardener	468	1.578	12.0	4.9
9151, 9322, 9333	Package and transport labourer	488	0.389	11.9	3.7
7311, 7343, 7346	Printer, typesetter, and related	187	1.076	11.8	4.8
7213	Sheet metal worker	78	0.629	11.5	3.8
2142–2147	Engineer	1279	0.716	11.5	4.1

Crude prevalence rates for occupations “above average” as derived by Poisson regression analysis of 52 occupations/occupational groups

- No statement regarding source of exposure
- No statement as to relevance of reaction

Uter, et al. Occup Environ Med 2001; 58: 392-8.

Occupational Contact Allergy to Fragrance Mix 1?

IVDK, 1992 – 1995; n = 2192 workers in medical profession; overall, no increase in FMI reactions and significantly decreased M. *Pereirae* reactions in female HCWs vs. controls; by subanalysis within medical profession

Allergens	Nurses (f)	Receptionists (f)	Med. lab. Workers (f)	Dental Nurses (f)	Dental Techn. (f+m)	Dentists (f+m)	Physicians (f+m)	Masseurs (f+m)
Nickel	1.1 0.98 - 1.23	1.3* 1.04 - 1.62	0.9 0.7 - 1.16	1.0 0.74 - 1.36	0.9 0.64 - 1.27	0.9§ 0.47 - 1.7	0.7* 0.5 - 0.97	1.1 0.8 - 1.5
Fragrance	1.2* 1.05 - 1.43	1.1 0.76 - 1.57	1.0 0.67 - 1.48	0.9 0.55 - 1.47	0.6 0.3 - 1.2	0.8§ 0.3 - 1.9	0.9 0.6 - 1.3	1.5* 1.04 - 2.16
Thiomersal	2.8* 2.4 - 3.3	1.02 0.65 - 1.59	2.6* 1.85 - 3.66	2.6* 1.72 - 3.93	1.3 0.69 - 2.42	5.3*§ 3.19 - 8.8	3.2* 2.28 - 4.49	2.3* 1.43 - 3.7
Thiuram	2.8* 2.16 - 3.63	1.9* 1.1 - 3.3	1.5 0.8 - 3.6	1.8* 1.02 - 3.19	1.6 0.72 - 3.57	4.8*§ 2.39 - 9.6	3.1* 2.07 - 4.65	1.9 0.85 - 4.24
Glutardialdehyde	4.5* 3.31 - 6.13	3.5* 1.97 - 6.23	1.7 0.69 - 4.17	10.1* 6.12 - 16.66	2.6§ 0.65 - 10.43	2.6§ 0.65 - 10.43	0.6 0.19 - 1.88	1.1§ 0.27 - 4.44
Glyoxal	4.1* 2.35 - 7.15	3.7*§ 1.3 - 10.57*	2.3*§ 1.4 - 3.9	5.2*§ 1.82 - 14.86	-	-	-	-
Formaldehyde	2.0* 1.29 - 3.09	1.1 0.49 - 2.46	2.0* 1.09 - 3.64	0.7 0.26 - 1.87	1.3 0.42 - 4.04	0.8§ 0.1 - 5.69	0.6 0.22 - 1.6	2.1* 1.0 - 4.42
Benzalkonium	1.5 0.92 - 2.44	0.4§ 0.07 - 2.86	0.8§ 0.2 - 3.23	2.1§ 0.67 - 6.58	-	1.5§ 0.21 - 10.68	1.3§ 0.4 - 4.1	0.6§ 0.1 - 4.3

- No statement regarding source of exposure
- No statement as to relevance or intensity of reaction

Occupational Contact Allergy to Fragrance Mix 1?

St. John's Institute, London, 1984 – 1998, n =14,052

Occupation	Females			Males		
	n	FM1 (+), n	FM1 (+), %	n	FM1 (+), n	FM1 (+), %
Retired	885	128	14.5	1017	118	11.6
Service industry	118	13	11.0	285	20	7.0
Storekeeper	65	7	10.8	127	9	7.1
Health care	779	81	10.4	154	18	11.7
Florist	119	12	10.1	107	7	6.5
Teacher	370	37	10.0	119	6	5.0
Foodhandler	66	6	9.1	96	10	10.4
Supervisor	58	4	6.9	72	9	12.7
Hair/beauty	437	25	5.7	50	5	10.0

No statement regarding source of exposure

No statement as to relevance or intensity of reaction

- Buckley, et al. Occup Med 2002; 52: 13-16

Occupational Contact Allergy to Cosmetics

occupationally relevant cosmetic (? contribution of fragrance) allergy; NACDG, n=10,061; % = % of all occupational cases for the given gender; n = 94 women & 31 men)

Occupation	Female N (%)	Male N (%)
Cosmetologist	49 (52.1)	9 (29.0)
Healthcare	15 (16.5)	3 (9.7)
Food worker	5 (5.5)	1 (3.2)
Student	4 (4.2)	0
Secretarial	4 (4.2)	1 (3.2)
Manager	2 (2.2)	2 (6.5)
Mechanic	1 (1.1)	2 (6.5)
Machinist	1 (1.1)	3 (9.7)
Engineer (industrial/electrical)	0	2 (6.5)
Janitor	1 (1.1)	1 (3.2)

not adjusted for % of given occupation among tested population and no statistical significance can be associated w/ data

- Warshaw, et al. J Am Acad Dermatol 2009; 60: 23 - 38

Top 10 Allergens in HCWs

2632 patients tested for suspected ACD:
01/01/1994 – 06/30/2014

Allergen	HCW Total (N)	HCW Total (%)	NHCW Total (N)	NHCW Total %	P-Values
quaternium-15	29	17.6	136	5.7	≤ .001
nickel sulfate	23	13.9	242	9.9	0.177
thiuram mix	23	13.9	63	2.6	≤ .001
carba mix	20	12.1	64	2.6	≤ .001
thimerosal	18	11.0	15	0.6	≤ .001
fragrance mix	16	9.7	195	8.0	0.566
cobalt chloride	15	9.1	125	5.1	0.061
formaldehyde	14	8.5	104	4.3	0.029
balsam of Peru	13	7.9	144	5.9	0.421
benzalkonium chloride	11	6.7	39	1.6	≤ .001

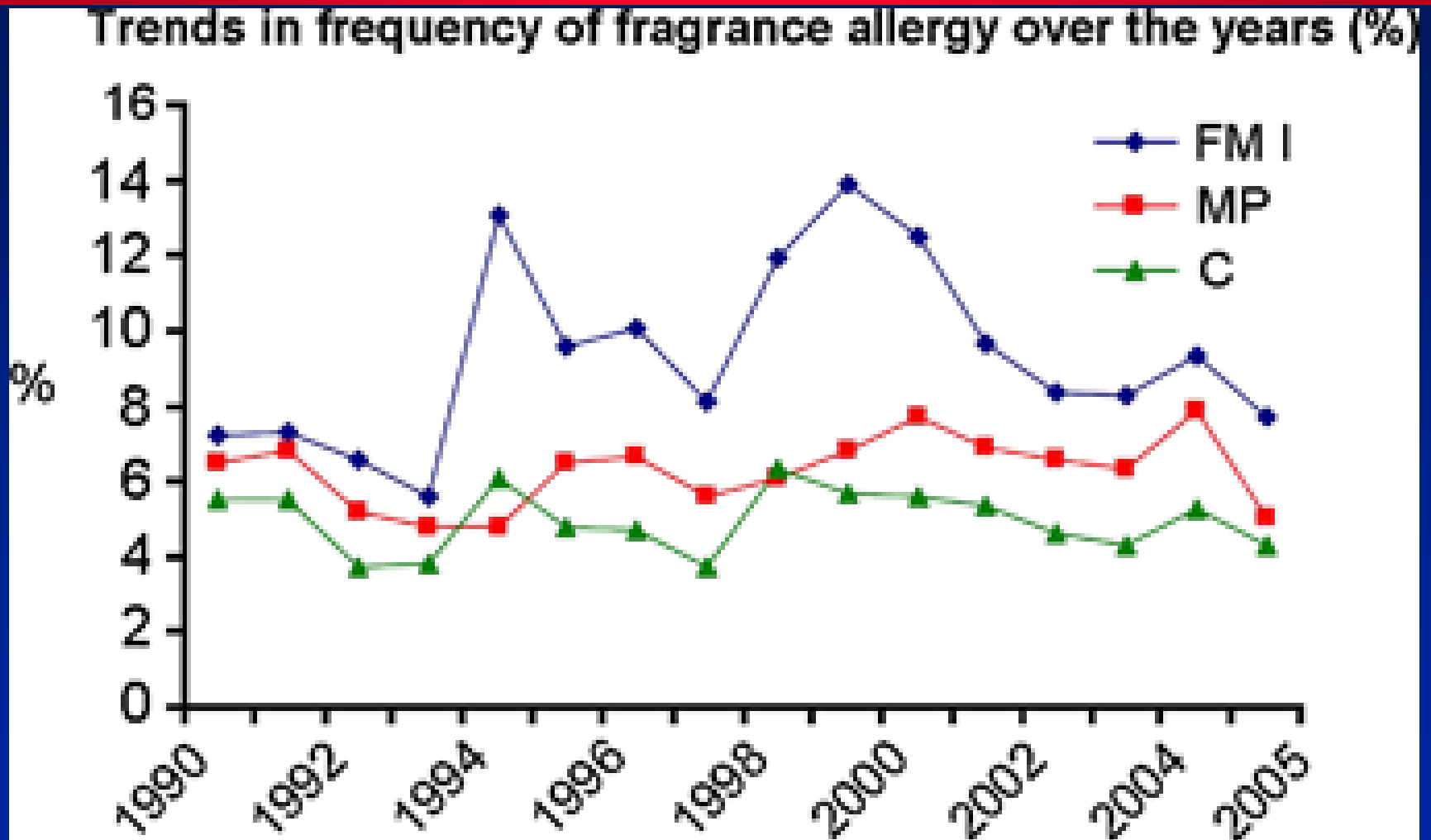
Kadivar & Belsito, Occupational Dermatitis in Health Care Workers Evaluated for Suspected Allergic Contact Dermatitis. Submitted.

Top 10 Relevant Allergens in HCWs

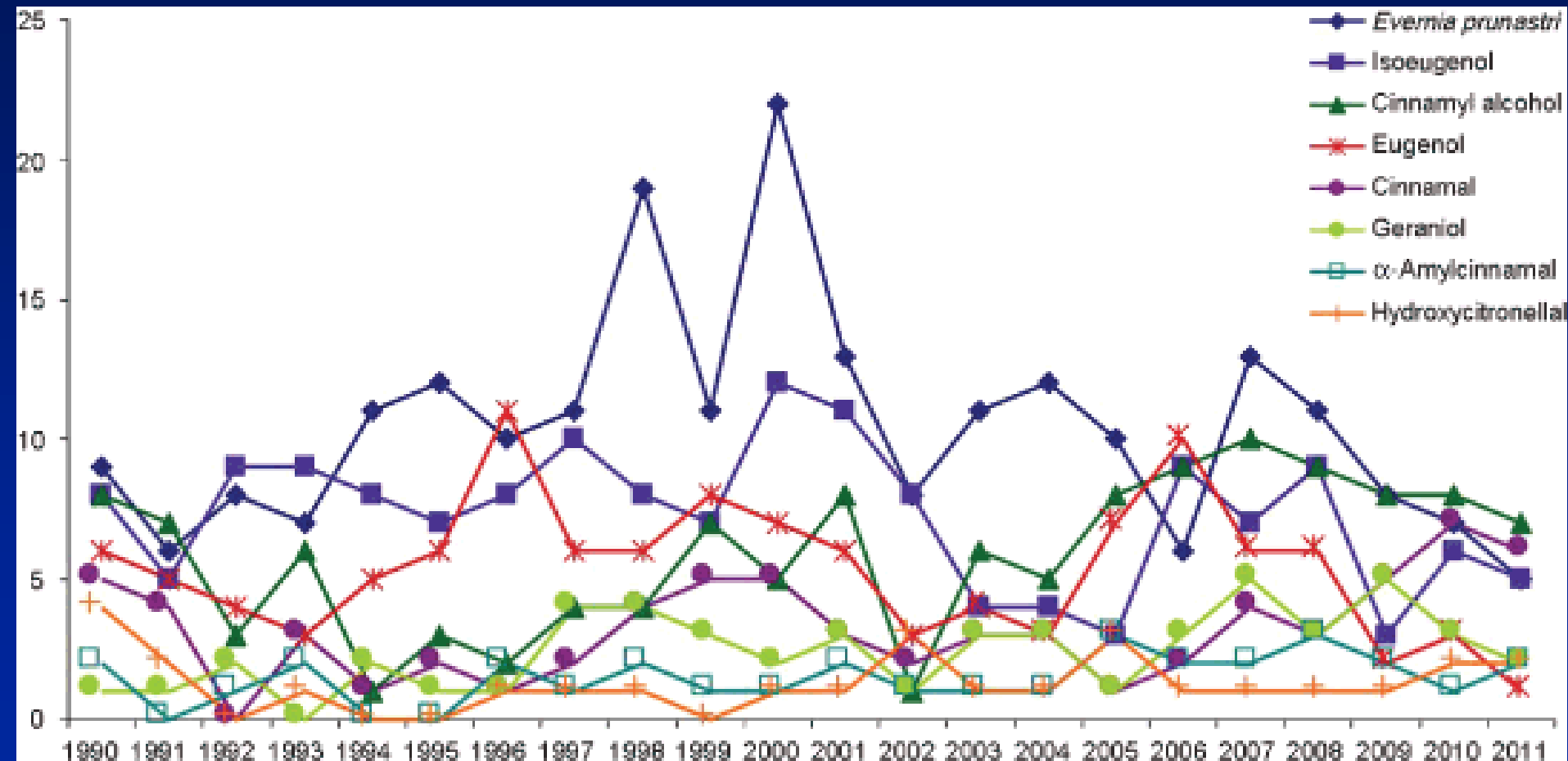
Allergen	HCW Total Relevant (N)	HCW Total Relevant %	NHCW Total Relevant (N)	NHCW Total Relevant %	P-Value
quaternium-15	24	14.5	125	5.1	≤ 0.001
nickel sulfate	15	9.1	217	8.9	1.000
thiuram mix	20	12.1	61	2.5	≤ 0.001
carba mix	18	10.9	63	2.6	≤ 0.001
thimerosal	17	10.3	15	0.6	≤ 0.001
fragrance mix	8	4.8	185	7.6	0.291
cobalt chloride	10	6.1	124	5.1	0.729
formaldehyde	11	6.7	102	4.2	0.211
balsam of Peru	10	6.1	138	5.6	0.969
benzalkonium chloride	9	5.5	38	1.6	0.001

Kadivar & Belsito, Occupational Dermatitis in Health Care Workers Evaluated for Suspected Allergic Contact Dermatitis. Submitted.

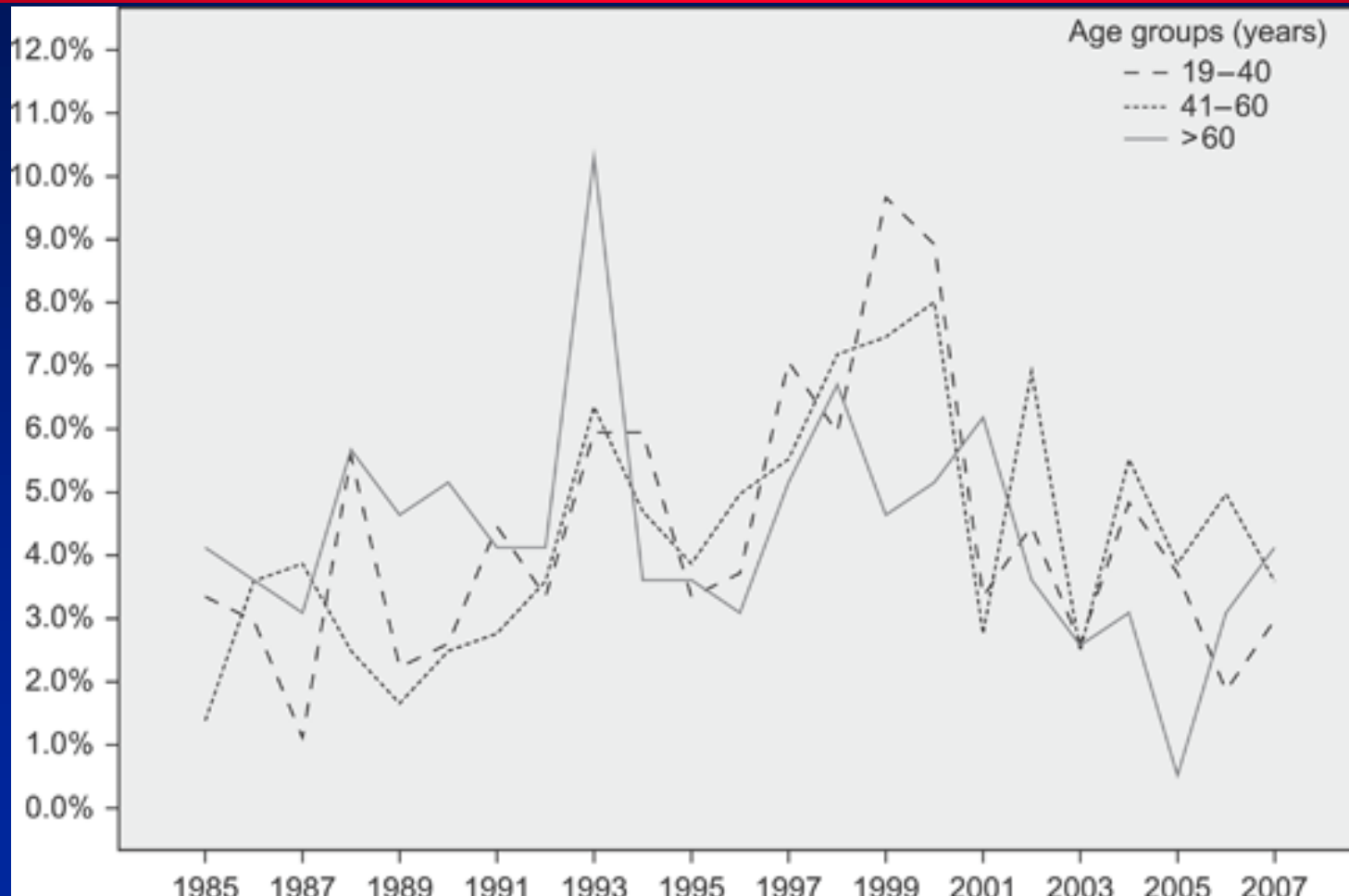
Fragrance Allergen Trends: Leuven, Belgium



FM I Constituent Trends: Leuven, Belgium



FM I Trends: Gentofte Hospital, Denmark



The decline was significant in women but not men.

Thyssen, et al. Contact Dermatitis 2008; 59: 238-44

Fragrance Allergen Trends: North America

	2009-2010 Pos (%)	2007-2008 Pos (%)	2005-2006 Pos (%)	2003-2004 Pos (%)	2001-2002 Pos (%)
Fragrance mix I 8% pet.	8.5	9.4	11.5	9.1	10.2
Myroxylon pereirae 25% pet	7.2	11.0	11.9	10.6	11.5
Fragrance mix II 14% pet.	4.7	3.6	-	-	-
Colophony 20% pet.	2.7	2.8	2.2	2.8	2.7

FM II Reactions in Dermatitis Patients

- 4.5% Denmark, n= 12,302, 2005 – 2008
 - Heistenberg, et al. Contact Dermatitis 2010; 63: 270-6
- 4.9% IVDK, n= 40,709, 2005 – 2008
 - Uter, et al. Contact Dermatitis 2010; 63: 254-61
- 3.6% North America, n= 5,085 , 2007 – 2008
 - Fransway, et al. Dermatitis 2013; 24: 10-21

Belsito, et al.

Dermatitis 2006; 17: 21 - 8

- pts w/ eczema undergoing patch testing for diagnostic purposes
- all tested to NACDG standard tray (Chemotechnique Diagnostics, AB, Malmö, Sweden)
- at discretion of physician, pts also tested to HICC (5%, 1.5% & 0.5%) in petrolatum w/ 0.2% BHT (International Flavors & Fragrances, Union Beach, NJ)

Belsito, et al.

Dermatitis 2006; 17: 21 - 8

- 1603 patients evaluated, 6 centers, 01 Jan, 2003 – 31 Dec, 2003:
 - Belsito: Kansas City, KS - n= 81
 - Fowler: Louisville, KY - n = 460
 - Sasseville: Montreal, PQ - n= 443
 - DeLeo: New York, NY - n = 276
 - Marks: Hershey, PA - n = 253
 - Storrs: Portland, OR - n = 90

Belsito, et al.

Dermatitis 2006; 17: 21 - 8

- 7/1603 (0.4%) read as allergic to HICC, 5%
 - 1 definite; 3 probable; 2 possible; 1 unknown
 - 5 reacted to HICC, 1.5%
 - 3 reacted to HICC, 0.5%
 - 3 had a + to FM; 2 had a + to BP (both + to FM)
 - none reacted to other fragrances (1 w/ ? Jasmine)
- 1/1603 w/ ? reaction
 - negative to 1.5% & ? to 0.5% (relevance = unknown)
- No IR rxns

Belsito, et al.

Dermatitis 2006; 17: 21 - 8

- 0.4% + to 5% HICC (R = 85.7%)
- 0.3% + to 1.5% HICC (R = 63.6%)
- 0.2% + to 0.5% HICC (R = 100%)
 - no evidence of IR at any doses
 - 5% seems to give best predictive results
 - both pts + to 5% and - to 1.5% & 0.5% w/ + relevance
 - 1 pt ? to 1.5% but + to 5% and 0.5% w/ + relevance
 - 3/7 (42.9%) pts reacted to $\geq 0.5\%$ HICC
 - no historical data for these allergens in North America
 - incidence rate significantly lower than that reported from Europe

HICC: Usage Data: US vs EU, 2003

NAME	Number of Fragrance Compounds Containing the Ingredient	97.5%ile of Compounds Containing the Ingredient
HMPCC (Underarm products, Europe)	834	8.6700
HMPCC (Underarm products, US)	66	4.8900
HMPCC (Hydroalcoholics, Europe)	2617	8.5800
HMPCC (Hydroalcoholics, US)	474	8.6000

Data courtesy of Matthias Vey, PhD, Scientific Director,
International Fragrance Association

Proposed Studies

- Differences in product types containing HICC & concentrations of use for HICC between the European countries and North America should be further explored to investigate the wide range in reported DTH to HICC:

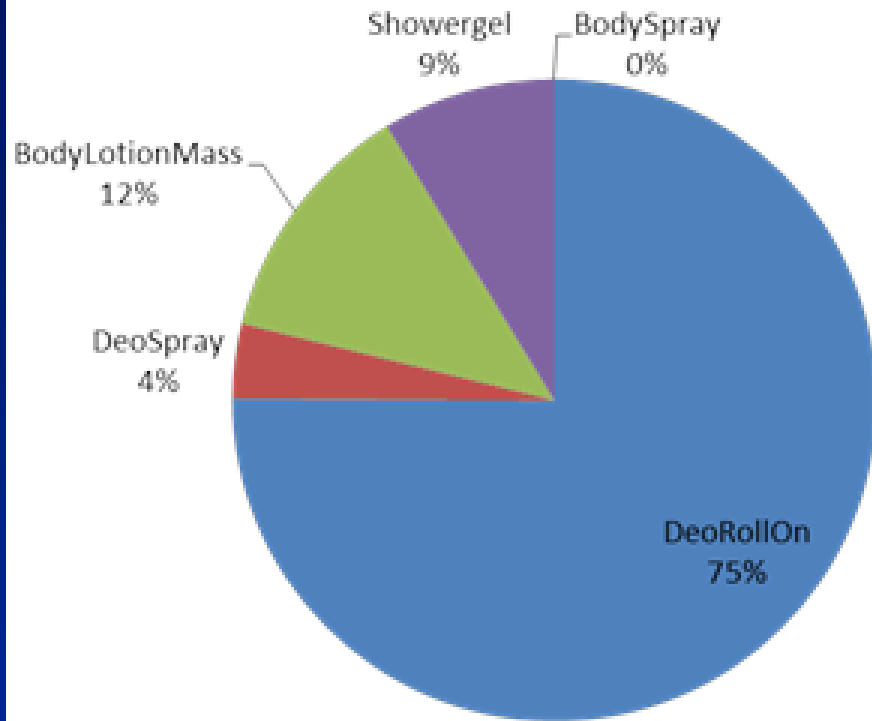
- North America: 0.4%

VS

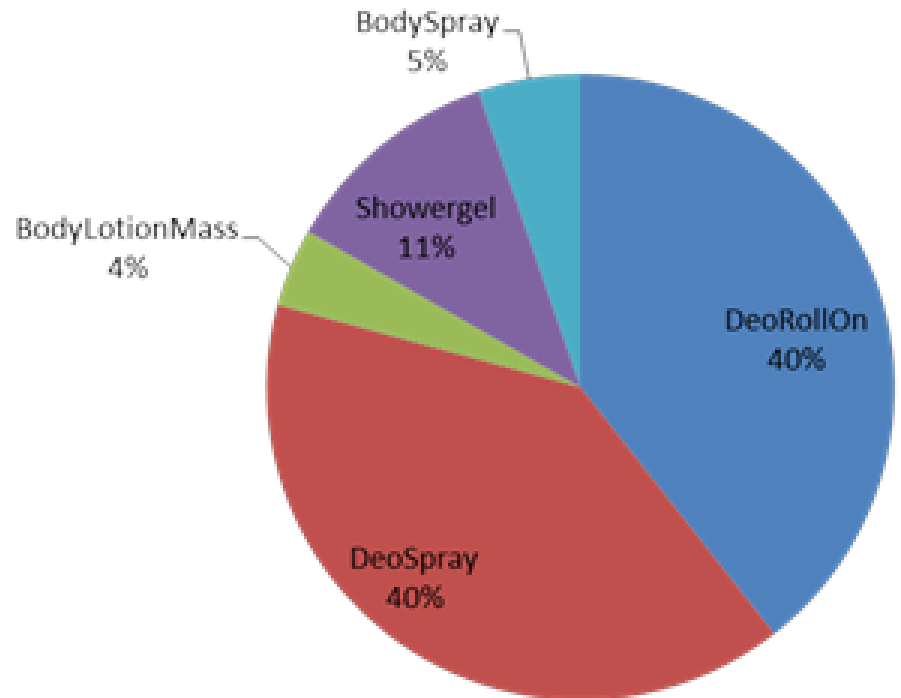
- | | |
|------------------|---------------------|
| – London: 1.2% | -- Copenhagen: 2.6% |
| – Dortmund: 1.4% | -- Malmö: 3.0% |
| – Odense: 2.4% | -- Leuven: 17.0% |

» Frosch, et al. Br J Dermatol 141: 1076, 1999

HICC: US vs EU



HMPCC (QRA) US



HMPCC (QRA) EU

Proposed Studies

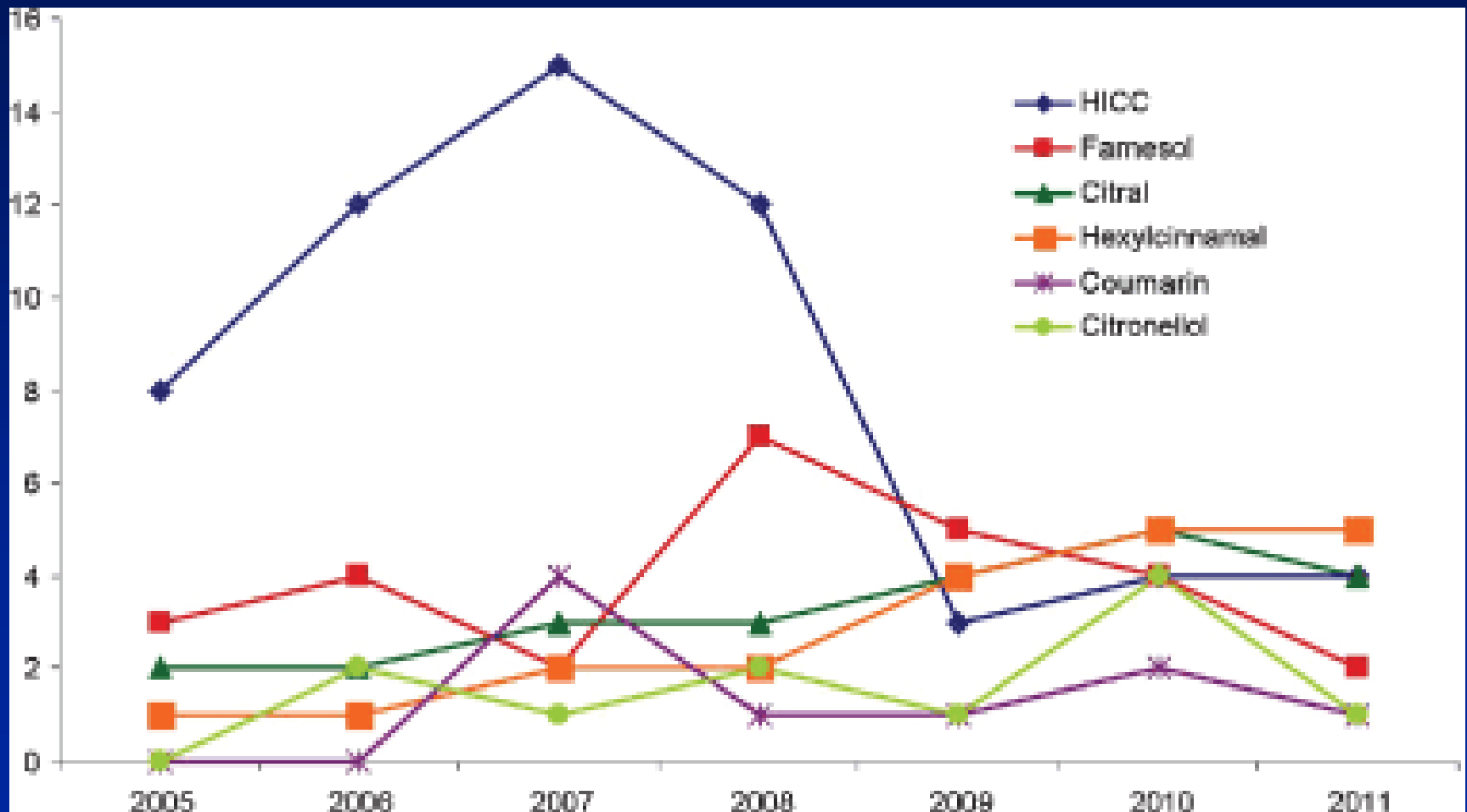
- Studies in North America are needed to assess for changing incidences in DTH to HICC
 - test w/ 5% in pet w/ 0.2% BHT
 - 5% in pet w/out BHT
 - 0.2% BHT control
- 2007: FM II added to standard tray
 - 5/6 centers same; Belsito to KS to NY; added NH, NY x 2, FL, OH, MN, CA, ON
 - Incidence of reactions:
 - 3.6% (2007 – 2008)
 - 4.7% (2009 – 2010)
 - 4.3% (2011- 2012 -- preliminary)

Final Interpretation of FM II Reactions

Belsito data, unpublished: FM II, 1/1/07 – 6/30/14

- 40/1093 (3.7%) FM II = ?, +, ++ or +++
 - 3/1093 (0.3%) = ?
 - None tested to components
 - 21/1093 (1.9%) = +
 - 4/6 positive to component: HICC (2); citral (1), coumarin (1)
 - 16/1093 (1.5%) = ++, +++
 - 12/12 positive to component
 - HICC (5), citral (3), coumarin (2), citronello (1), α -hexylcinnamal (1)
- 4/1093 (0.4%) FM II = IR

FM II Constituent Trends: Leuven, Belgium



HICC Trends: EU

- Prevalence in Denmark – initially reported as declining but corrected to unchanged
 - Heisterberg, et al. Contact Dermatitis 2012; 67:49 – 51.
- Prevalence in Germany, Austria, Switzerland (IVDK) – decreasing
 - Schnuch, et al. Contact Dermatitis 2012; 67: 47 – 49.

Declines in Fragrance Allergy

Fragrance Ingredient	Fragrance Mix (FM) I or II	Standard Implementation Completed ¹	Potential Implementation for Product Shelf Life ²
Amyl cinnamal	FM I	2009	2014
Cinnamyl alcohol	FM I	2009	2014
Cinnamal	FM I	2009	2014
Geraniol	FM I	2009	2014
Hydroxycitronellal	FM I	2009	2014
Eugenol	FM I	2009	2014
Isoeugenol	FM I	2009	2014
Evernia prunastri Oakmoss absolute	FM I	2011	2016
Hydroxyisohexyl-3-cyclohexene carboxaldehyde (HICC)	FM II	2010 ³ ; 2011 ⁴	2015; 2016
Citronellol	FM II	2009	2014
Coumarin	FM II	2010	2015
Farnesol	FM II	2008	2013
α -Hexylcinnamal	FM II	2009	2014
Citral	FM II	2008	2013

¹Standards were implemented first for new fragrance compounds and then for existing fragrance compounds. The date reflects when restrictions on all fragrance compounds would have been implemented.

²This includes 12-18 months to get the “new” products to the store shelves and up to 36 months for the shelf life of the “old” products. How long a cosmetic product in the end might remain in the hands of the final consumers is not possible to assess.

³Standard based on QRA.

⁴Standard incorporating elicitation information.

Fragrance Allergy

North America vs. Europe

- Where have we been?
- Where are we?
- Where do we want to be?

