

ORIGINAL ARTICLE

Patch test results with patients' own perfumes, deodorants and shaving lotions: results of the IVDK 1998–2002¹

W Uter,*† J Geier,‡ A Schnuch,‡ PJ Frosch§

† Department of Medical Informatics, Biometry and Epidemiology, University of Erlangen-Nürnberg, Waldstr. 6, D-91054 Erlangen, Germany

‡ Information Network of Departments of Dermatology (IVDK) at the University of Göttingen, von-Siebold-Str. 3, D-37075 Göttingen, Germany

§ Department of Dermatology, University of Witten/Herdecke and Klinikum Dortmund gGmbH, Beurhausstr. 40, D-44137 Dortmund, Germany

Keywords

clinical epidemiology, contact allergy, fragrance, patch testing

*Corresponding author, Department of Medical Informatics, Biometry and Epidemiology, D-91054 Erlangen, tel. +49 91318522750; fax +49 91318522721; E-mail: wolfgang.uter@rzmail.uni-erlangen.de

Received: 27 February 2006,
accepted 11 April 2006

DOI: 10.1111/j.1468-3083.2006.01973.x

Abstract

Objective Assessment of the value of patch testing patients' own perfumes, eau de toilette, deodorants and shaving lotions with regard to diagnosing contact allergy to fragrances, and an analysis of the spectrum of concurrent patch test reactions to single fragrance allergens.

Study design Data of the Information Network of Departments of Dermatology (IVDK; www.ivdk.org) regarding patch test results with above products brought in by the patient, considered as possible cause of contact dermatitis, were retrospectively analysed. Between 1998 and 2002, 1468 patients were patch tested with 2557 single products (deodorants, $n = 1094$; eau de toilette, $n = 598$; perfume, $n = 530$; and pre- or after-shave, $n = 325$; remainder not classifiable), mostly 'as is'.

Results Positive reactions were observed in 129 patients (to 191 products). In 58 of these patients, no further patch test reactions to the fragrance mix (FM-I), *Myroxylon pereirae* resin (balsam of Peru) or 4-(4-hydroxy-4-methyl-pentyl)-3-cyclohexencarboxaldehyde (e.g. Lyrall®) were found. A strong association between contact sensitivity to the above commercial allergens and positive reactions to products was observed. Some single compounds such as ylang-ylang oil, propolis and especially oak moss absolute are important allergens in the 'perfume-positive' subgroup, but less in a subgroup positive to own deodorants.

Discussion Patch testing this scope of products, brought in by the patient, can be regarded as a simple, safe and effective method to diagnose clinically relevant contact sensitization – the more so, as the composition of such products is ever-changing, and the sensitivity of established 'screening allergens' is thus insufficient.

¹Centres contributing patch test results with patients' own products (in alphabetical order): Aachen (H. Dickel, S. Erdmann), Berlin B.-Frank. (B. Tebbe, R. Treudler), Berlin Charité (T. Zuberbier, M. Worm), Dortmund (P.J. Frosch, C. Pirker, R. Herbst), Dresden (G. Richter, R. Aschoff), Duisburg (J. Schaller), Erlangen (M. Fartasch, M. Hertl, V. Mahler), Essen (U. Hillen), Gera (J. Meyer), Göttingen (Th. Fuchs, J. Geier), Graz (W. Aberer, B. Kränke), Hamburg (M. Kiehn, R. Weißbecher), Heidelberg (A. Schulze-Dirks, U. Jappe, M. Hartmann), Jena (A. Bauer, W. Wigger-Alberti, M. Kaatz, S. Schliemann-Willers), Kiel (J. Brasch), Lübeck (J. Grabbe), Mannheim (Ch. Bayerl), Marburg (I. Effendy, H. Löffler), München Schwabing (M. Agathos), München TU (J. Rakoski), Nürnberg (I. Müller), Tübingen (G. Lischka), Ulm (H. Gall †, P. Gottlöber, G. Staib, R. Hinrichs, H. Pillekamp), Würzburg (J. Arnold, A. Trautmann)

Introduction

Fragrances are ubiquitous in human everyday life. Probably due to such exposure, contact allergy to fragrances is not uncommon, according to both population-related^{1,2} and clinical studies.^{3,4} Contact allergy against perfumes, which are often a mixture of hundreds of single fragrance compounds, is usually diagnosed with the 'fragrance mix', which will be called 'fragrance mix I' (FM I), for better distinction with the newly developed 'fragrance mix II' (FM II). The FM I is a mixture of one natural compound, oak moss absolute, and isoeugenol, hydroxycitronellal, cinnamic aldehyde (INCI: cinnamal), cinnamic alcohol

(INCI: cinnamyl alcohol), eugenol, alpha-amyl cinnamic aldehyde (INCI: amylcinnamal) and geraniol as synthetic fragrances, at a concentration of 1% each. Hence, the total concentration is 8% (in petrolatum), with sorbitan sesquioleate added as dispersing agent. However, the FM I may yield both false-positive and false-negative results (as any allergen), both if compared to test results with its single constituents,⁵ and if validated against a past history of fragrance intolerance. In order to compensate the unsatisfactory sensitivity of the FM I in the diagnosis of contact allergy to currently used fragrances, an additional FM II was developed (14% in petrolatum). The FM II contains 4-(4-hydroxy-4-methyl-pentyl)-3-cyclohexene carboxaldehyde (INCI: hydroxy-methylpentylcyclohexene carboxaldehyde, e.g. Lyrall) at 2.5%, citral at 1%, farnesol and coumarin at 2.5% each, citronellol at 0.5% and α -hexyl-zimtaldehyd (INCI: hexylcinnamaldehyde) at 5%.⁶ According to first experience, the FM II detects a relevant number of additional cases of fragrance contact allergy.⁶ In addition, the European Standard Series⁷ and the standard series of the German Contact Dermatitis Research Group (DKG, www.ivdk.org/dkg/dkgblo.html) include balsam of Peru (INCI: *Myroxylon pereirae*, 25% petrolatum). While prior to the introduction of the FM I, *M. pereirae* was considered an important screening fragrance allergen, it is nowadays considered less significant, due to its limited sensitivity.

In the past decade, conspicuous trends in sensitization to FM I and its compounds, *M. pereirae* and oil of turpentine, have been reported, suggestive of a changing exposure in the population.⁴ Indeed, chemical analyses of current perfumes have confirmed changes in the composition of these products.⁸ The changing composition of perfumes and related products, together with the observation that the sensitivity of screening allergens, even if improved, is far from 100%, point to the important role of patch testing those perfumes, deodorants, shaving lotions or other perfumed products, which the patient suspects to have caused dermatitis to close a potential diagnostic gap. Compared to other products such as cutting fluids or synthetic resins, the patch testing of perfumes and related products is relatively simple.⁹ The present analysis addresses results with perfumes, deodorants, and shaving lotions brought in by the patients and patch tested in the departments of the Information Network of Departments of Dermatology (IVDK, www.ivdk.org) between 1998 and 2002.

Methods

The methods and objectives of the contact allergy surveillance network IVDK have been described before.¹⁰ In brief, the patch test results along with a standardized set of demographic and clinical data of all patients attending one of the participating centres are collected. The procedure

follows current international guidelines¹¹ further amended by the German Contact Dermatitis Research Group (DKG),¹² of which all IVDK partners are members. All data are transmitted in an anonymous, electronic format to the data centre in Göttingen twice a year and quality controlled.¹³

The present analysis focuses on the subset of those patients in whom own perfumes, deodorants, and after- or pre-shaves have been patch tested. This was the case in 1468 of the 48 381 patients patch tested in the 5-year period. As outcome, reactions on the third day of reading of the patch test (day 3) are considered. In addition to the above products, test reactions to commercial allergens were analysed in terms of sensitization prevalence standardized for age and gender.¹⁴ In addition, the difference of sensitization prevalence to commercial allergens between those patients reacting positively vs. those not reacting to their own products was statistically tested with logistic regression analysis, adjusted for age and gender; *P*-values < 0.05 were regarded significant. In view of the exploratory nature of this analysis, no alpha adjustment techniques were employed. For data management and analysis, the statistical software package SAS (version 8.1, SAS-Institute, Cary, NC, USA) was used.

Results

Results of patch testing own perfumes, deodorants and shaving lotions

In the study period, 40 centres participated in the IVDK network, which more or less regularly include patients' own products in the patch test programme. However, in 12 centres, no perfumes and related products had been tested, and in another nine centres this was an exception (< 1% of all patients). In contrast, 13.3% of all patients in the Dortmund department had been tested with such products, followed by Tübingen (12.0%), Göttingen (8.9%) and a number of other departments.

In good accordance with current recommendations,⁹ 95.8% of all 2557 products tested in the 1468 patients had been tested as is (i.e. undiluted). Thirty-five products had been diluted to 10%, and 14 to 1% by adding water, while 13 products were tested as 1% in ethanol. Other dilutions or diluents had been used only in single cases (data not shown).

Although 172 of the 191 positive test reactions occurred after testing undiluted products, a number of diluted products also caused positive patch test reactions. Among the 191 positive reactions observed in 129 patients, 71.7% were scored as weak positive (+), 12.0% as positive (++) and 6.3% as strong positive (+++). In addition to positive test reactions, doubtful (erythematous) test reactions were observed after applying 93 products, a 'soap effect'

Table 1 Patch test method and result (reading 72 h after start of exposure: day 3) with deodorants, perfume, eau de toilette and shaving lotions. Occurrence of several products (including different categories) per patient is possible

	Undiluted				10 to < 100%				< 10%			
	<i>N</i> _(test)	?/IR	+	++/+++	<i>N</i> _(test)	?/IR	+	++/+++	<i>N</i> _(test)	?/IR	+	++/+++
Deodorants	1069	43	57	15	19	1	5	1	6	–	–	–
Eau de toilettes	593	33	35	10	1	–	–	–	4	–	–	–
Perfumes	466	31	27	11	25	2	5	1	39	–	4	–
Shaving products	307	19	11	5	10	1	2	–	8	1	1	–

after 16 products, and irritant reactions with erosions or bullae after applying 3 of the 2557 products (0.12%).

A look at different categories of products revealed that deodorants had been tested most often ($n = 1094$), followed by eau de toilette ($n = 598$) and perfume or eau de toilette ($n = 530$), while shaving lotions – mostly after-shave, less frequently preshave – had been tested 325 times. Ten products could not be classified. While 72.3% of the patients had been tested with just one product, or several products of the same category, different product categories had been tested in 406 patients, yielding positive reactions to more than one category in 18 cases. Details are presented in Table 1.

All patients had also been tested with commercial test series. Positive reactions to such allergens were observed in 876 patients (59.7%). In the subset of 129 patients reacting positively to their own product(s), 103 (79.8%) also reacted to some commercial allergen. However, if only commercial fragrance allergens² are considered, this proportion was 73/129 (56.6%). In other words, contact sensitivity to fragrances was detected by testing own products only in 56 patients. If only the screening fragrance allergens in the standard series as tested during this period are considered (FM I, *M. pereirae*, Lyrall), 71/129 patients were positive to these, while 58/129 were detected only by testing own products. If oil of turpentine as fragrance allergen *sensu lato* is additionally considered, 76/129 were positive to at least one of the four allergens, i.e. 53/129 cases were detected only by testing own products.

Positive reactions to commercial fragrance allergens

Contact allergy to fragrance allergens tested as commercial test preparations are presented in Table 2 for the subgroup

²FM I, MP, Lyrall, benzyl salicylate, clove oil, orange oil, lemon oil, vanillin, the FM I compounds, benzaldehyde, benzyl cinnamate, cedar wood oil, eucalypt oil, laurel oil, lemongrass oil, oil of bergamot, spearmint oil, salicyl aldehyde

of patients tested with deodorants, and in Table 3 for the subgroup tested with perfume, eau de toilette or shaving lotions, the latter excluding 13 patients with positive reactions also to deodorants. In both subgroups, the analysis was stratified into patients reacting positively to their product vs. patients not reacting positively to their own product.

The FM I is the overall most important allergen; however, evidently, in more than half of the patients with positive reactions to their product, no positive reaction to the FM I was observed. Among the constituents of the FM I, oak moss absolute, hydroxycitronellal and isoeugenol rank as most frequent allergens, while the other constituents caused positive reactions less frequently: overall, alpha-amyl cinnamic aldehyde and cinnamic aldehyde three times each, and geraniol, cinnamic alcohol and eugenol two times each. The comparison of the two subsets – deodorant positive vs. other positive – is remarkable in that the pattern of allergens, and partly the frequency of positive reactions, is quite different:

- The prevalence of contact sensitization to main allergens such as the FM I, oil of turpentine, Lyrall and hydroxycitronellal is much higher in the perfume subgroup, compared to the deodorant subgroup.
- Some allergens such as ylang-ylang oil and oak moss absolute are significant allergens only in the perfume subgroup.
- Conversely, contact allergy to *M. pereirae* had been diagnosed more frequently in the deodorant subgroup

Discussion

The unprecedented analysis presented provides an assessment of the value of patch testing patients' own perfumes and related products suspected to have caused allergic contact dermatitis, based on a large clinical database. The fact that patients' own products are recorded electronically (if at all) as free text, necessitating rather laborious post hoc classification, may explain the scarcity of similar reports.¹⁵ In addition, from a perspective of clinical epidemiology, our analysis illustrates the possible role

Table 2 Pattern of concomitant positive reactions to commercially available fragrance allergens in 'deodorant-positive' vs. 'deodorant-negative' patients. Sensitization prevalence is standardized for age and gender with accompanying 95% confidence interval (CI)

	%	Deodorant positive (n = 66)				Deodorant negative (n = 855)			
		N _(test)	N _(pos)	% pos	95% CI	N _(test)	N _(pos)	% pos	95% CI
Fragrance mix I	8	61	25	38.0*	(24.1–51.9)	805	125	15.0	(12.5–17.5)
Balsam of Peru (<i>Myroxylon pereirae</i>)	25	60	17	22.9*	(12.7–33.1)	806	79	9.1	(7.2–11.0)
4-(4-Hydroxy-4-methyl-pentyl)-3-cyclohexencarboxaldehyde (e.g. Lyrall)	5	26	7	24.5*	(7.6–41.4)	345	14	4.2	(1.9–6.4)
Oil of turpentine	10	61	5	5.7	(0.9–10.5)	808	31	3.8	(2.5–5.2)
Hydroxycitronellal	1	33	4	6.5	(0.7–12.3)	204	9	4.3	(1.5–7.1)
Isoeugenol	1	33	4	6.5	(0.7–12.3)	204	15	7.2	(3.6–10.8)
Cinnamic aldehyde	1	29	3	11.3*	(0–24.1)	133	2	1.1	(0–2.7)
Geraniol	1	29	2	8.3	(0–20.4)	141	0	0.0	(0.0–2.1)

*Significant difference ($P < 0.05$) adjusted for age and gender. All allergens in petrolatum.

Table 3 Pattern of concomitant positive reactions to commercially available fragrance allergens in 'shaving product/eau de toilette/perfume positive' (excluding 16 patients with positive reactions to deodorants also) vs. 'negative' patients. Sensitization prevalence is standardized for age and gender with accompanying 95% confidence interval (CI)

	%	Shaving product/eau de toilette/perfume positive (n = 63)				Shaving product/eau de toilette/perfume negative (n = 819)			
		N _(test)	N _(pos)	% pos	95% CI	N _(test)	N _(pos)	% pos	95% CI
Fragrance mix I	8	56	32	57.1*	46.2–68.1	764	108	13.9	11.4–16.4
Balsam of Peru (<i>Myroxylon pereirae</i>)	25	56	13	13.9*	7.3–20.4	766	74	8.8	6.8–10.7
Oil of turpentine	10	56	11	21.8*	7.0–36.5	768	20	2.5	1.4–3.6
4-(4-Hydroxy-4-methyl-pentyl)-3-cyclohexencarboxaldehyde (e.g. Lyrall)	5	20	8	58.3*	37.5–79.0	310	4	1.3	0–2.7
Oak moss absolute	1	28	8	22.1*	7.0–37.2	153	14	8.8	4.2–13.4
Hydroxycitronellal	1	31	4	15.5*	0.7–30.3	210	4	1.4	0–2.8
Ylang-ylang oil	10	7	3	16.3 ^{n.c.}	2.0–30.5	43	2	5.0	0–11.3
Propolis	10	42	3	3.8*	0–8.1	577	6	1.0	0.2–1.8

*Significant difference ($P < 0.05$) adjusted for age and gender. All allergens in petrolatum. n.c., not calculable.

of single fragrance compounds available as commercial allergen in the different product categories (deodorants vs. other products).

Our results support evidence from case reports and case series that have repeatedly illustrated the usefulness of patch testing various kinds of products brought in by the patient (for an overview of the technique, see Frosch *et al.*⁹). Although the breakdown testing of the single constituents of a product, after observing a positive reaction to the product in the first place, is a highly desirable standard, it is often just not feasible in case of perfumes and similar products, due to their complexity. Still, the patient benefits from testing perfume products suspected to have caused dermatitis, because a past episode of allergic contact dermatitis will be explained, identifying a certain

product as culprit. Our data demonstrate that diagnostic success often relies on the testing of own products, because potentially relevant commercial allergens tested negative, which has been found previously.¹⁶ The variation between centres regarding the proportion of patients patch tested with own perfumes and related products was remarkable. In view of the simple technique, practical problems are probably less relevant than different research interests of the participating centres (as in the case of the Dortmund department), or a particular demographic profile of patients.¹⁷ However, in view of the ubiquity of fragrances, and the relative frequency of fragrance contact allergy, a certain share of underdiagnosed cases could be suspected in those departments not using this valuable adjunct to routine patch testing.

As products are only tested if they have been suspected to have caused allergic contact dermatitis, test reactions deemed allergic can regularly be considered clinically relevant. This is not necessarily the case if commercial allergens tested positive: unless declared on the package, single ingredients have to be identified using chemical analysis,^{8,18} which is surely beyond routine for most departments. In this context, the declaration of at least 26 important fragrance allergens¹⁹ may help patients and dermatologists to identify and avoid, respectively, these fragrance allergens.

Perfumes and related products have been largely patch tested as is (undiluted), in accordance with current recommendations.⁹ The fact that strong positive reactions were rarely observed supports this standard. Not infrequently, doubtful reactions were observed on the first or second day of reading, which turned into unequivocally positive reactions on day 3, or faded to negative (results not shown). Hence, as in the case of commercial allergens, patch tests with such products should be read at least until day 3, according to international standards.¹¹ In case perfumes and related products are suspected to cause skin irritation, the risk of irritant patch test reactions can be reduced by letting the volatile compounds evaporate (waiting 5 min after application of perfume into the chamber) prior to applying the patches on the back.¹⁶

Looking at commercial allergens, the high frequency of contact sensitization to the FM I illustrates the still outstanding importance of this screening allergen. However, the overall sensitivity, as validated against positive reactions to perfume products, is only 49% (exact 95% CI: 39–58%). Comparing deodorants with other products, the lower sensitivity of the FM I in the former category may indicate either a spectrum of contact allergens less well represented by the FM I, or additional ‘competing’ allergens in deodorants, such as preservatives or emulsifiers. However, in this and other comparisons between the two subgroups ‘deodorants’ vs. ‘other’, a previous mixed exposure, and possibly sensitization, of the patients to products from both categories must be assumed. Consequently, the observed pattern of concomitant reactivity will not be exclusively ‘due to’ the one or the other product category, but merely represent a certain degree of association. Moreover, when comparing patch test (or possibly also clinical) reactions to complex products vs. single allergens, possible synergistic effects between combinations of allergens²⁰ in the products may be an additional cause of increased reactivity to products.

A major change of the pattern of exposure to fragrances has been the broad use of the synthetic fragrance 4-(4-hydroxy-4-methyl-pentyl)-3-cyclohexencarboxaldehyde (e.g. Lyrall), a well-known contact allergen,^{21,22} which had thus been included in the DKG standard series a few years

ago.²³ Despite the relatively limited number of patients tested – due to the addition of the compound only during the study period – the importance of this allergen is evident from our data, especially in the subgroup of patients sensitive to perfume/eau de toilette and shaving lotion. In contrast to this relatively new compound, *M. pereirae* is a traditional contact allergen, which, in our material, still has some significance, especially in the context of sensitivity to deodorants.

The allergenic potency of the eight single constituents of the FM I differs greatly, according to experimental results, and according to clinical data, taking different levels of approximate exposure into account.⁴ Even in the rather small subgroup of patients testing positive to various fragrance products, the three most important allergens, according to previous evidence,⁴ rank among the top allergens, namely, oak moss absolute, isoeugenol and hydroxycitronellal (Tables 2 and 3), while the other five are less important. The differences between deodorants and other products may reflect a partly different pattern of exposure to these allergens, e.g. pointing to 4-(4-hydroxy-4-methyl-pentyl)-3-cyclohexencarboxaldehyde as an important allergen in perfume, eau de toilette and shaving lotions, but not so much in deodorants, while isoeugenol seems to be an important allergen across the full range of products assessed here. Further allergens include the essential ylang-ylang oil, or, as natural mixes of allergens with compounds partly relevant for fragrance allergy, oil of turpentine and propolis, mainly in the subgroup of patients reacting to perfumes, eau de toilette or shaving lotions.

Conclusion

In summary, our analysis illustrates that patch testing of patients’ own fragrance products (i) is technically simple and carries little risk of serious side-effects, (ii) is, despite this, probably not sufficiently being used by a number of departments, in view of the fact that (iii) a notable number of cases with fragrance contact allergy are only identified using own materials, and not by using screening allergens such as the FM I, FM II, etc. The impact of the mandatory declaration of 26 single fragrances¹⁹ on the spectrum of exposure and subsequently on the pattern of contact sensitization is yet uncertain – it may well be that these compounds are going to be replaced by other compounds that need not be declared, except as ‘perfume’, because they have not (yet) surfaced as important contact allergens, which they may well be. At any rate, further, possibly massive changes in the pattern of exposure to fragrance compounds must be anticipated. As these cannot be balanced immediately by the development of new screening agents such as the FM II, the ever changing

exposure is another strong argument in favour of patch testing exactly those products which the patient suspects to have caused dermatitis.

References

- Nielsen NH, Linneberg A, Menné T *et al.* Allergic contact sensitization in an adult Danish population: two cross-sectional surveys eight years apart (the Copenhagen Allergy Study). *Acta Derm Venereol* 2001; **81**: 31–34.
- Schäfer T, Böhler E, Ruhdorfer S *et al.* Epidemiology of contact allergy in adults. *Allergy* 2001; **56**: 1192–1196.
- Johansen J, Menné T, Christophersen J, Kaaber K, Veien N. Changes in the pattern of sensitization to common contact allergens in denmark between 1985–86 and 1997–98, with a special view to the effect of preventive strategies. *Br J Dermatol* 2000; **142**: 490–495.
- Schnuch A, Lessmann H, Geier J, Frosch PJ, Uter W. Contact allergy to fragrances: frequencies of sensitization from 1996 to 2002. Results of the IVDK*. *Contact Dermatitis* 2004; **50**: 65–76.
- Schnuch A, Geier J, Uter W, Frosch PJ. Another look on allergies to fragrances: frequencies of sensitisation to the fragrance mix and its constituents. Results from the IVDK. *Exogenous Dermatol* 2002; **1**: 231–237.
- Frosch PJ, Pirker C, Rastogi SC *et al.* Patch testing with a new fragrance mix detects additional patients sensitive to perfumes and missed by the current fragrance mix. *Contact Dermatitis* 2005; **52**: 207–215.
- Bruze M, Goossens A, Gruvberger B. Recommendation to include methyl dibromo glutaronitrile in the European standard patch test series. *Contact Dermatitis* 2005; **52**: 24–28.
- Rastogi SC, Menné T, Johansen JD. The composition of fine fragrances is changing. *Contact Dermatitis* 2003; **48**: 130–132.
- Frosch PJ, Geier J, Uter W, Goossens A. Patch testing with the patients' own products. In: Frosch PJ, Menné T, Lepoittevin JP, eds. *Textbook of Contact Dermatitis*, 4th edn. Springer, Berlin, 2006: 929–941.
- Uter W, Schnuch A, Geier J, Frosch PJ. The epidemiology of contact dermatitis. The information network of departments of dermatology (IVDK) in Germany. *Eur J Dermatol* 1998; **8**: 36–40.
- Wahlberg JE, Lindberg M. Patch testing. In: Frosch PJ, Menné T, Lepoittevin JP, eds. *Contact Dermatitis*. Springer, Berlin, 2006: 365–390.
- Schnuch A, Aberer W, Agathos M *et al.* Leitlinien der Deutschen Dermatologischen Gesellschaft (DDG) zur Durchführung des Epikutantests mit Kontaktallergenen. *Hautarzt* 2001; **52**: 864–866.
- Uter W, Mackiewicz M, Schnuch A, Geier J. Interne Qualitätssicherung von Epikutantest-Daten des multizentrischen Projektes 'Informationsverbund Dermatologischer Kliniken' (IVDK). *Dermatol Beruf Umwelt* 2005; **53**: 107–114.
- Schnuch A. PAFS. population-adjusted frequency of sensitization. (I). Influence of sex and age. *Contact Dermatitis* 1996; **34**: 377–382.
- Uter W, Balzer C, Geier J, Frosch PJ, Schnuch A. Patch testing with patients' own cosmetics and toiletries – results of the IVDK, 1998–2002. *Contact Dermatitis* 2005; **53**: 226–233.
- Johansen JD, Frosch PJ, Rastogi SC, Menné T. Testing with fine fragrances in eczema patients: results and test methods. *Contact Dermatitis* 2001; **44**: 304–307.
- Schnuch A, Geier J, Uter W *et al.* National rates and regional differences in sensitization to allergens of the standard series. Population adjusted frequencies of sensitization (PAFS) in 40 000 patients from a multicenter study (IVDK). *Contact Dermatitis* 1997; **37**: 200–209.
- Frosch PJ, Rastogi SC, Pirker C *et al.* Patch testing with a new fragrance mix – reactivity to the individual constituents and chemical detection in relevant cosmetic products. *Contact Dermatitis* 2005; **52**: 216–225.
- The European Parliament and the Council of the European Union. Directive 2003/15/EC of the European Parliament and of the Council of 27 February 2003 amending Council Directive 76/768/EEC on the approximation of the laws of the Member States relating to cosmetic products. *Official J European Union* 2003; **L66**: 26–35.
- Johansen JD, Skov L, Volund A, Andersen K, Menné T. Allergens in combination have a synergistic effect on the elicitation response: a study of fragrance-sensitized individuals. *Br J Dermatol* 1998; **139**: 264–270.
- Johansen JD, Frosch PJ, Svedman C *et al.* Hydroxyisohexyl 3-cyclohexene carboxaldehyde- known as Lyrall: quantitative aspects and risk assessment of an important fragrance allergen. *Contact Dermatitis* 2003; **48**: 310–316.
- Frosch PJ, Johansen JD, Menné T *et al.* Lyrall is an important sensitizer in patients sensitive to fragrances. *Br J Dermatol* 1999; **141**: 1076–1083.
- Geier J, Brasch J, Schnuch A *et al.* Lyrall has been included in the patch test standard series in Germany. *Contact Dermatitis* 2002; **46**: 295–297.