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Risk management by labelling 26 fragrances? Evaluation of Article 10 (1) of the seventh Amendment (Guideline 2003/15/EC) of the Cosmetic Directive

Ursula Klaschka*

University of Applied Sciences Ulm, Prittwitzstr. 10, D-89075 Ulm, Germany

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ABSTRACT

Background: Some fragrance compounds are severe contact allergens. According to the so-called “26 allergens rule” (Article 1 (10) of Directive 2003/15/EC) (EC, 2003), 26 supposedly allergenic fragrances must be listed on the containers of cosmetics products if they are present above certain mass percentages in the product. This declaration is meant to inform the consumer of potential risks of skin sensitizers in the products.

Objective: The objective of this paper is to validate whether “the 26 allergens rule” meets the expectations to improve consumer protection.

Methods: The method used for this validation was on one hand a reflection on the elements of the approach used in “the 26 allergens rule” and on the other hand a product analysis of 742 products by 4 large producers of cosmetic products on the German market.

Results: It was found that more than 50% of these cosmetic and washing and cleansing products contain at least one of the 26 substances above the thresholds for labelling and that there are 14% of all products which contain strong allergens. Many consumers apparently still buy these products. The indirect effect that producers reduce the amounts of these fragrances to avoid declaration seems to be small.

Discussion and recommendations: Several arguments were assembled which show that other instruments are needed to ensure consumer protection or protection of the environment. This paper recommends different approaches. The use of a list of single substances in such a directive is not in line with scientific standards. It is recommended to base decision making on comprehensive risk assessments or at least on valid and strong criteria. More parameters need to be involved, not only contact allergy. As illustrated in this article, the roles taken over by authorities and manufacturers in risk management of the “26 allergens” are relatively small compared with the responsibility carried by consumers. However, consumers are only able to take over their part properly if they are sufficiently trained and have the necessary infrastructure, capability and time to inform themselves. Regulations are not effective if they load the major responsibility for risk management on consumers, instead of on authorities and manufacturers. A successful risk management would include bans and restrictions of especially hazardous substances issued by governments, as well as efficient surveys to control the implementation of regulations by the responsible authorities. It would also include that producers meet the legal standards and take over voluntary action to make products safer. The evaluation of “the 26 allergens rule” is an example which can be transferred to other regulations and which could help to improve future regulatory approaches, with a focus on the roles authorities, manufacturers and consumers play in a promising risk management.

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Introduction

Fragrances are widely used in every day products. Most personal care, washing and cleansing products contain fragrances. 60% of fragrance products are used in washing and cleansing products,

including soap, 40% in cosmetics, toiletry and perfumery products (Bickers et al., 2003). If other uses are considered, too, a third is used in washing and cleansing products, a fourth in cosmetic products and the rest in other applications, such as candles, toys, fabric etc. with increasing tendency (Fragrance products information network, 2005). The number of fragrance compounds employed in everyday products is very large. The SCCP list (SCCP = Scientific Committee on Consumer Products) of perfume and aromatic raw materials contains 2750 entries (SCCNFP, 2000). The actual num-

* Tel.: +49 0731 5028456; fax: +49 0731 5028270.

E-mail address: Klaschka@hs-ulm.de.

Box 1: Contact allergy

Contact allergy is the result of two steps. In a first step, a chemical triggers the immune system specifically after skin contact leading to a systemic sensitization. This phase is called sensitization phase or induction, and is a lifelong acquisition. The second step is the outbreak of the disease symptoms that occur upon exposure to the substance that led to the sensitization. This second step is called elicitation. The sensitization by a certain chemical occurs usually at higher concentrations than the elicitation reactions in sensitized persons.

ber of fragrances used in every-day products is much larger, as also fragrances which do not appear on this list are used in cosmetics and other products. These numbers are growing, because scents play an important marketing factor leading to a strong pressure on manufacturers to create new odors and new scented products. Most consumers enjoy the agreeable psychoactive effect of fragrances and apparently do not suffer from any unwanted side effects. However, as the numbers and amounts of fragrance compounds employed increase, negative effects have to be addressed more and more (Straff, 2005; Umweltbundesamt, 2006). The main uptake routes by the consumer are via the skin, via inhalation or via ingestion of food. Fragrances can be responsible for deleterious health effects. Essential oils can impair the central nervous system, kidney and respiratory ducts and lead to severe poisoning after oral uptake. Asthma or migraine headaches, neurotoxicity, carcinogenicity, teratogenicity, endocrine disrupting activity or induction of psychological or other detrimental effects are also discussed in literature for single fragrance ingredients or for complex mixtures like natural oils (Anderson and Anderson, 1998; EC, 2002; Park et al., 2006; Straff, 2005; Umweltbundesamt, 2004a,b, 2006).

Contact allergy (Box 1) induced by fragrances has been a well-recognized problem for more than a decade. Around 2–4% of the German population suffer from contact allergy to fragrance compounds as estimated by tests with the fragrance mix 1 (composition see Table 2) (Schnuch et al., 2002). In the decades between 1980 and 2000 an increase in fragrance contact allergies was observed in many industrialized countries (Scheinman, 2002). The worldwide trends are compiled in Thyssen et al. (2007). Only recently the trend turned as far as contact allergy to the fragrance mix 1 is concerned. This decline of sensitization may be due to reduced exposure to these specific substances (Schnuch et al., 2004a,b). This observation dates before “the 26 allergens rule” came into force in 2005. Rastogi showed that new perfumes contained less substances of the fragrance mix 1, but other compounds (Rastogi et al., 2007b; Rastogi and Johansen, 2008). This hypothesis is strongly supported by the high frequency of contact allergies of more than 4% detected with the newly developed fragrance mix 2 (composition see Table 2 (5)) (Frosch et al., 2005). A recent study showed that contact allergy has followed a fluctuating trend over the years (Nardelli et al., 2008). It seems that the fragrances tested in the standard fragrance mixes may not be sufficient to identify all allergic reactions to fragrances in patients. There are new strong allergens, such as Majantol that has been used frequently and is not detected in patch tests with fragrance mix 1 or 2. As sensitized persons will suffer from contact allergy a lifelong and the disease often deteriorates over time with continued exposure, it is very important to protect especially children and young people from contact to relevant allergens to avoid sensitization and sensitized persons from contact with the allergens. But even in children's cosmetics and toys contact allergens are used in many products (Rastogi et al., 1999).

Legal action was taken for personal care products and cleansing products. One of the several European regulations concerning allergens in food, cosmetics or other consumer products (see Park et al.,

Box 2: “The 26 allergens rule”

Article 1(10) in Directive 2003/15/EC (EC, 2003), the 7th amendment of the Cosmetic Directive, lists 26 presumptive allergenic fragrances to be taken up in Annex III Part 1 (No. 67–92) of the EU Cosmetics Directive (EC, 1976). Annex III Part 1 is the “list of substances which cosmetic products must not contain except subject to restrictions and conditions laid down”. The restrictions in the case of “the 26 allergens” are identical for all 26 substances and are detailed under “other limitations and requirements”: “The presence of the substance must be indicated in the list of ingredients referred to in Article 6(1)(g) when its concentration exceeds: 0.001% in leave-on products, 0.01% in rinse-off products” (independent of the function in the product). There are no “Conditions of use and warning which must be printed on the label.” There are no restrictions for these 26 substances concerning the field of application and/or use and there is no maximum authorized concentration in the finished product in the “26 allergens rule”. For some of these compounds, there are restrictions in the Cosmetic Directive due to other reasons (see Table 2 (6)). This list of compounds (Table 2) was set up by the expert group for fragrances with possible allergenic potential of the SCCNFP (Scientific Committee on Cosmetics and Non-Food Products, now known as SCCP, which is a selected group of mainly toxicologists working at universities and authorities advising the European Commission) (SCCNFP, 1999). The regulations on fragrances in cosmetic products were taken over for washing and cleansing products by Regulation EG/648/2004 (EC, 2004, 2006a). The presence of any of these “26 allergens” must be indicated in the list of ingredients of washing and cleansing products when its concentration exceeds 0.01%.

2006) is “the 26 allergens rule” for fragrances (Box 2). This article will focus on this rule. It is designed to help the consumers to identify cosmetic products which contain any of these 26 presumptive allergens above a certain concentration. The full names and additional information on the 26 substances are given in Table 2. The evaluation of the implementation and success of this specific legal tool is a helpful example for the improvement of risk management. Each element of “the 26 allergens rule” will be questioned item by item, as illustrated in Table 1.

The evaluation of “the 26 allergens rule” is urgent as the amounts used and applications as well as the public interest are increasing. A revision of “the 26 allergens rule” was asked for several times, e.g. after the public consultation in November 2006. This evaluation could also contribute to an improved implementation of current new regulations and methods. The EU Cosmetics Directive was replaced by the new European Cosmetics Regulation KOM(2008)0049 (EC, 2008b) which will come into force in 2012, and the European chemical regime is being changed considerably by the European Regulation concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) (EC, 2006b). In addition, the methods for evaluation and risk assessment have been improved lately (Special Issue on QRA Regulatory Toxicology and Pharmacology, 2008; Api and Vey, 2008; Api et al., 2008).

Results: Stepwise evaluation of “the 26 allergens rule”*Question 1: Selection of 26 substances*

Have these 26 substances proved to be the most relevant fragrances causing contact-allergy reactions?

The 26 substances are the result of a SCCNFP draft opinion (SCCNFP, 1999) adopted in 1999 and were taken up in the EU Directive. “Certain substances have been identified as important cause

Table 1
This table illustrates the method how “the 26 allergens rule” was examined. Column 1 lists the elements of Article 1 (10) of Directive 2003/15/EC. These elements give rise to concrete questions (column 2) which were answered in detail in the text (Chapter 3) and in brief in column 3. Column 4 summarizes the recommended alternatives to the elements of “the 26 allergens rule” which are also described in detail in the text.

Article 1 (10) of Directive 2003/15/EC	Questions	Answers in brief	Alternatives
The list contains 26 fragrance substances.	1. Have these 26 substances proved to be the most relevant fragrances causing contact-allergy reactions or other hazards?	No. Data show that the list contains strong contact-allergens, but also very weak ones. Other strong allergens are not in the list.	Cut off criteria or risk assessments applicable to all substances are preferable to a list of substances. Regulations need to be based on comprehensive risk assessments including toxicological and ecotoxicological aspects, not only skin sensitization.
The restrictions for these 26 substances do not concern the field of application and/or use and do not fix a maximum authorized concentration in the finished product.	2. Is it justified to have no restriction concerning the field of application and/or use and no maximum authorized concentration in the finished product?	No. It is questionable whether very strong contact-allergens are allowed in leave-on products at all.	Strong allergens should be banned or used only below maximum concentrations in the products.
The restrictions are identical for all 26 substances. ... and are detailed under “other limitations and requirements”. “The presence of the substances must be indicated in the list of ingredients referred to in the Article 6(1)(g). ... when its concentration exceeds – 0.001% in leave-on products, – 0.01% in rinse-off products.”	3. Is it justified to restrict all 26 substances in the same way? 4. Are these substances listed on the containers of the products? 5. Are these threshold values based on scientific evidence?	No. The allergenic potentials of the 26 substances are so different that the restrictions would have to be differentiated. Yes. The number of products with these fragrances listed on their labels is very large. However, labelling does not reduce the sensitization potential of the respective product. No. The properties of the 26 substances are very different. These thresholds do not protect sensitized persons, as they do not indicate whether a certain allergen is absent. They also do not protect healthy persons from sensitization as the concentrations are not required to stay below the sensitizing thresholds.	Strong allergens should undergo stronger restrictions than weak allergens. Health protection of consumers could be improved by a larger selection of products without strong allergens for sale and by clear signals on the products if sensitizers are present. Different threshold values need to be derived on the basis of the effect values of each substance. Labelling could help sensitized and healthy persons to make their choice.

of contact allergy reactions in fragrance-sensitive consumers.” (2003/15/EC Preamble (15)). This was not a truly scientifically based decision, as the methods used for identification of allergens were and still are under debate. The European test guideline for skin sensitization B6 L 142/202 says, “There is no single test method which will adequately identify all substances for sensitizing human skin and which is relevant for all substances.” Majantol (CAS 103694-68-4) is an example which was not detected as allergen in tests with guinea pigs, but turned out to be an important allergen for humans (Schnuch et al., 2009). Also the human repeat insult patch test is not easy to conduct and interpret (McNamee et al., 2008). The predictive standard animal tests for sensitization e.g. the local lymph node assay needs to be complemented by the data obtained in epidemiological studies to accomplish a reasonable risk assessment and management.

Table 2 shows that the allergenic potential of the 26 fragrance compounds listed in EEC 2003/15/EC is not consistently evaluated by the various expert groups. The multicentre project IVDK (Information Network of Departments of Dermatology) analyzed the contact allergy potency of the 26 fragrance compounds listed in “the 26 allergens rule” in detail in an extended patch test with more than 21,000 patients (Schnuch et al., 2007). They found out that some of these fragrances are important allergens (Group I), some are clearly allergenic, but less important in terms of sensitization frequency (Group II) and some are (extremely) rare sensitizers or even non-sensitizers (Group III) (Table 2 (2)). The IKW (German Cosmetic, Toiletry, Perfumery and Detergent Association) issued an evaluation of the allergenic potential which is also taken up in Table 2 (3). All ingredients of the fragrances mix 1 and fragrance mix 2, standard mixtures used to detect contact allergy, are part of the list (Table 2 (5)).

11 of the 26 substances are produced at a level of more than 1000 tons per year in the European Union (Table 2 (9)). Most HPVCs of this list are considered as less important in terms of sensitization frequency (Group II) or as rare sensitizers or even non-sensitizers (Group III) (Schnuch et al., 2007), but high exposure might lead to a high prevalence of an effect. The only strong allergen produced at high production volumes is Cinnamal. The production volumes and application fields (Table 2 (9, 10)) might give an idea about the use pattern and the probability of contact with a certain chemical. A decent exposure assessment would be needed for each substance (Basketter et al., 2008a; Park et al., 2006).

The R-phrases (Table 2 (7)) show that most of these 26 substances are classified and labelled as dangerous substances according to Guideline 67/548/EWG. However, not all of them are classified with R43 (may cause sensitization by skin contact), not even oak moss extract and tree moss extract which are considered as very strong allergens (Schnuch et al., 2007). ECETOC (2003) suggests that substances with a skin sensitization potency, also a weak one, should be classified R43 and carry the symbol Xi. Most classifications in Table 2 (7) are self classifications by the producers and several compounds are classified differently by various producers. The self classifications are meant to be identical for a chemical substance and depend on its properties only. Apparently, either producers rely on different data bases or they apply the classification and labelling criteria differently. The finding of the multitude of R-phrases shows a big lack of consistency in fragrance regulations and makes it even more difficult for manufacturers and end-users to handle these chemicals.

Most substances of this list are classified as WGK 1 or WGK 2 compounds according to the Water Hazard Classes (Table 2 (8)) indicating for most of these substances a negative impact on the aquatic environment. The information about ecotoxicological standard assays (Table 2 (8)) shows that there are not many test results publicly available for most of these substances to be able to assess their ecotoxicological properties.

Table 2

Fragrance compounds of the “26 allergens rule” as listed in the directive with their INCI-names and CAS numbers. Column 2 gives synonyms for these compounds, among them also IUPAC names and commonly used names. The next 4 columns (footnote (1) to (4)) are a synopsis of the various classifications of the allergenic properties of these fragrances by various expert groups based on different methods. Some fragrances are subject to further restrictions according to the Cosmetic Directive (EEC, 1976; SCCNFP, 2000) (6). The risk phrases according to Guideline 67/548/EWG (EEC, 1967) are compiled as indicated on Safety Data Sheets of producers (7). Producers do not always classify a substance in the same way, resulting in various R-phrases combinations (indicated with “Or”). Water hazard classes and indications whether data for standard ecotoxicological data are publicly available give some information about the ecotoxicological properties (8). Ranges of production volumes (9) and usage examples are given in the last two columns (for further specifications see footnotes and text) (n.d. = no data).

INCI-name listed in guideline CAS No	Synonyms	Classif. by SCCNFP (1)	Allergen group (Schnuch) (2)	Allergenic potential (IKW/IVK) (3)	Human threshold values (4)	Fragr. mix 1/mix 2 (5)	Restrictions according to Cosmetic Directive (6)	Classification and labelling (7)/data on ecotoxicity (8)	HPVC/ LPVC (9)	Examples for occurrence and usage
Amyl cinnamal 122-40-7	2-(Phenylmethylene)-heptanal 2-Benzylidene-heptanal	List A	III	Very weak	23622	1	–	R36/37/38 Xi WGK 2 –	L	Soap, cleansing products
Benzyl alcohol 1100-51-62		List A	III	Rare	n.d.	–	Authorized use in solvents, perfumes and flavourings at a maximum concentration 1% in the finished product	R20/22 Xn WGK 1 Fish, <i>Daphnia</i> , Algae, Bacteria	H	Preservative, Solvent
Cinnamyl alcohol 104-54-1	3-Phenyl-2-Propen-1-ol Styryl Carbinol	List A	II	Not very potent	4724	1	Maximum level 0.8% in the finished product	R22-36/38-43 Xn or R22-36/37/38 Xn or R22-43 Xn WGK 2 –	L	Cosmetics, laundry detergents, soap
Citral 5392-40-5	3,7-Dimethyl-2,6-octadienal mixture of <i>cis</i> - and <i>trans</i> -isomers (Neral and Geranial, respectively)	List A	II	Very weak	775	2	Only in conjunction with 25% its weight of <i>D</i> -Limonene or mixed with citrus terpenes or alpha-pinene.	R38-43 Xi WGK 1 Fish, <i>Daphnia</i> , Algae, Bacteria	H	Cosmetics, flavour in food
Eugenol 97-53-0	2-Methoxy-4-(2-propenyl)-phenol	List A	II	Very weak	5905	1	–	R22-36/37/38-42/43 Xn Or R22-38-43 Xn Or R22-36/38-43 Xn WGK 1 Fish	L	Toothpaste, mouth wash, perfume, soap, antiseptics
Hydroxycitronellal 107-75-5	7-Hydroxy-3,7-dimethyloctanal	List A	I	Not very potent	2953	1	Maximum level 1% in the finished product	R38-41 Xi WGK 1 <i>Daphnia</i> , Algae	L	Cosmetics, perfumes, soaps, insecticides, antiseptics
Isoeugenol 97-54-1	2-Methoxy-4-(prop-1-enyl)phenol Propenylguaicol	List A	I	Potent	250	1	Maximum level 0.02% in the finished product	R22-36/37/38-43 Xn Or R22-36/37/38 Xn Or R22-38 Xn WGK 2 <i>Daphnia</i>	L	Essential oils, perfumes, cosmetics, soaps, detergents
Amylcinnamyl alcohol 101-85-9	2-Pentyl-3-phenylprop-2-en-1-ol	List A	II	Rare	23622	–	–	R36 Xi WGK 3 –	n.d.	Perfumes, soaps, cosmetics
Benzyl salicylate 118-58-1	Benzyl-2-hydroxybenzoate	List A	III	Rare	n.d.	–	–	R36/37/38 Xi WGK 2 –	H	Cosmetics, essential oils
Cinnamal 104-55-2	3-Phenyl-2-propenal	List A	I	Potent	591	1	Only in conjunction with 50% its weight of Eugenol or <i>D</i> -Limonene or other substances preventing sensitization	R36/37/38-43 Xi Or R38-43 Xi WGK 1 Fish	H	Cosmetics

Coumarin 91-64-5	1-Benzopyran-2-one <i>cis-o</i> -Coumarinic acid lactone	List A	II	Rare	n.d.	2	–	R22 Xn Or R 22 × 40 Xn Or R20/21/22- 36/37/38-40 Xn WGK 1 Fish, <i>Daphnia</i>	L	Cosmetics, perfumes, pesticides
Geraniol 106-24-1	(<i>E</i>) 3,7-Dimethyl-2,6- octadien-1-ol	List A	II	Rare	3875	1	–	R36/37/38 Xi Or R38-43 Xi WGK 1 Fish	H	Perfumes, skin care
Hydroxy-methylpentyl- cyclohexene Carboxaldehyde 31906-04-4	Lylal 4-(4 Hydroxy-4- methylpentyl)-3- cyclohexene-1- carbaldehyde Hydroxy-isohexyl 3-cyclohexene carbox-aldehyde	List A	I	Not very potent	4000	2	–	R43 Xi WGK 2 –	L	Cosmetics
Anisyl alcohol 105-13-5	4-Methoxybenzyl alcohol <i>p</i> -Anisyl alcohol	List B	III	Rare	3448	–	–	R22-36/37/38 Xn WGK 1 Fish	L	Perfume, flavor
Benzyl cinnamate 103-41-3	Benzyl-3-Phenyl-2- propenoate	List B	II	Rare	4720	–	–	R51/53 N WGK 2 <i>Daphnia</i>	L	Perfumes, cosmetics
Farnesol 4602-84-0	3,7,11-Trimethyl-2,6,10- dodecatrien-1-ol	List B	I	Very weak	2755	2	At least 96% pure	WGK 2 Fish, <i>Daphnia</i>	n.d.	Deodorants,
2-(4-tert-Butylbenzyl) propionaldehyde 80-54-6	Lilial Butylphenyl- methylpropional <i>p</i> -tert-Butyl- α - methylhydrocinnamal 4-(1,1-Dimethylethyl)- α - methylbenzenepropanal	List B	II	Very weak	29525	–	–	R22-38-51/53 Xn,N WGK 2 Fish, <i>Daphnia</i> , Bacteria	H	Cosmetics, washing products
Linalool 78-70-6	3,7-Dimethyl-1,6- octadien-3-ol	List B	III	Rare	13793	–	–	R 36/37/38 Xi WGK 1 Fish, <i>Daphnia</i> , Algae, Bacteria	H	Perfume
Benzyl benzoate 120-51-4		List B	III	Rare	20690	–	Maximum authorized concentration 0.5% (calculated as benzoic acid) in the finished product	R22 Xn WGK 2 Fish, <i>Daphnia</i> , Bacteria	H	Antiparasitic insecticide, perfumes, plasticizer
Citronellol 106-22-9	3,7-Dimethyl-6-octen-1- ol	List B	II	Rare	n.d.	2	–	R38-43-51/53 Xi N or R36/37/38 Xi or R36/38-43-51/53 Xi N WGK 1 Fish, <i>Daphnia</i> , Algae, Bacteria	H	Essential oils, deodorants, midge spray

Table 2 (Continued)

INCI-name listed in guideline CAS No	Synonyms	Classif. by SCCNFP (1)	Allergen group (Schnuch) (2)	Allergenic potential (IKW/IVK) (3)	Human threshold values (4)	Fragr. mix 1/mix 2 (5)	Restrictions according to Cosmetic Directive (6)	Classification and labelling (7)/data on ecotoxicity (8)	HPVC/LPVC (9)	Examples for occurrence and usage
Hexylcinnamaldehyde 101-86-0	Alpha-Hexylcinnamaldehyde; 2-Benzylideneoctanal; Alpha-hexyl-beta-phenylacrolein; Jasmonal H; H.C.A.	List B	III	Rare	23622	2	–	R36/37/38 Xi or R34 C WGK 2	H	Essential oils
D-Limonene	(R)-p-Mentha-1,8-diene	List B	III	n.d.	n.d.	–	To be used in conjunction with antioxidants, upper limit of peroxides content 20 mmoles/liter	R10-38-43-50/53 Xi, N WGK 2 Fish, <i>Daphnia</i>	H	Cosmetics, flavoring, botanical insecticide, cleaning products
5989-27-5	1-Methyl-4-(methylethylene)cyclohexene	List B	III	Very weak	n.d.	–	Maximum level 0.002% in the finished product	R22, R 36/37/38 Xn or R22-38 WGK 1 or 2	n.d.	Washing products
Methyl heptin Carbonate 111-12-6	Alpha-Isomethylionone, Gamma Methylionone, isomethyl-alpha Ionone, 3-methyl-4-(2,6,6-trimethyl-2-cyclohexenyl)-3-buten-2-one, Methyl-gamma-ionone	List B	III	Rare	70866	–	Upper limit 2% pseudoionone and pseudomethylionones as contaminants	R20/21/22 R 36/37/38 Xn	n.d.	Cosmetics, perfumes
127-51-5	Raldeine gamma lraldeine gamma							or no R-Phrases WGK 2		
Oak moss extract 90028-68-5	<i>Evernia prunastri</i> extract	List B	I	Potent	700	1	Maximum level 0.1% in the finished product	R 11 F WGK 1	n.d.	Shaving products, deodorants
Tree moss extract 90028-67-4	<i>Evernia furfuracea</i> extract	List B	I	Potent	n.d.	–	Maximum level 0.1% in the finished product	R 11 F WGK 1	n.d.	Shaving products, deodorants

(1) Classification by SCCNFP. *List A*: Fragrance chemicals, which according to existing knowledge are most frequently reported and well-recognised consumer allergens. *List B*: Fragrance chemicals, which are less frequently reported and thus less documented as consumer allergens (SCCNFP, 1999).

(2) Groups of allergens (Schnuch et al., 2007). *Group I*: important allergens. *Group II*: Clearly allergenic, but less important in terms of sensitization frequency. *Group III*: (extremely) rare sensitizers or even non-sensitizers.

(3) Classification of allergenic potential by the IKW (German Cosmetic, Toiletry, Perfumery and Detergent Association): potent–not very potent–weak–very weak–rare (Pleschka, 2007).

(4) Human sensitization thresholds for allergens obtained by combining data from datasets of human thresholds and local lymph node assays EC3 (in $\mu\text{g}/\text{cm}^2$) (Basketter et al., 2008b; Wijnhoven et al., 2008).

(5) Fragrance mixes 1 and 2 are used for diagnosing fragrance contact allergy by patch testing.

1–substance in fragrance mix 1: Composition of fragrance mix 1: Amyl cinnamal 1%, Cinnamyl alcohol 1%, Cinnamal 1%, Eugenol 1%, Geraniol 1%, Hydroxycitronellal 1%, Isoeugenol 1%, Oak moss 1%, Sorbitan sesquioleate (as emulsifier) 5%.

2–substance in fragrance mix 2: Composition of fragrance mix 2: Citronellol 0.5%, Lylal 2.5%, Hexylcinnamal 5.0%, Citral 1.0%, Coumarin 2.5%, Farnesol 2.5% (Frosch et al., 2005).

(7) Classification and Labelling according to Guideline 67/548/EWG (EEC, 1967). R10: Flammable; R11: Highly flammable; R22: Harmful if swallowed; R34: Causes burns; R36: Irritating to eyes; R37: Irritating to respiratory system; R38: Irritating to skin; R41: Risk of serious damage to eyes; R43: May cause sensitization by skin contact; R20/22: Harmful by inhalation and if swallowed; R20/21/22: Harmful by inhalation, in contact with skin and if swallowed; R36/38: Irritating to eyes and skin; R36/37/38: Irritating to eyes, respiratory system and skin; R42/43: May cause sensitization by inhalation and skin contact; R51/53: Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

(8) Data on ecotoxicity: Fish, *Daphnia*, Algae, Bacteria experimental data of standard tests publicly available (The validity of the data could not be verified).

(–) No experimental data of standard tests publicly available.

WGK Water Hazard Classification (according to the German Administrative Regulation on the Classification of Substances Hazardous to Waters into Water Hazard Classes) (Anon., 2005).

(9) High Production Volume Chemicals (HPVC, more than 1000 tons per year in the EU) or Low Production Volume Chemicals (LPVC, less than 1000 tons per year in the EU) according to data by the European Joint Research Centre European Chemicals Bureau (<http://ecb.jrc.ec.europa.eu/>).

These results strongly suggest that the list of substances in “the 26 allergens rule” is not satisfactory as it subsumes substances with very different properties and the expert classifications are far from being unanimous. Such a list would have to be updated regularly according to the scientific progress. For many fragrance compounds the publicly available data basis to assess their effects on health and environment is very thin (own unpublished data collection for the 2750 substances of the SCCNFP list (2000)). Rohde (2001) states that the number of fragrances that are not classified and labelled as dangerous substances decreases as more information on their toxicological and ecotoxicological properties is available. Therefore, it is likely that a lot more fragrances give rise to concern and the number of sensitizing fragrances known today is underestimated. It must also be asked whether it is useful to have a special regulation that concentrates on the effect of contact allergy exclusively. Fragrances can be taken up in the human body also by other routes and exert different unwanted effects. Regulations should preferably be based on a comprehensive risk assessment including human health and environmental aspects and not on one single end point only.

Question 2: Field of application and maximum concentrations in products

Is it justified to have no restriction concerning the field of application and/or use and no maximum authorized concentration in the finished product?

Some of the fragrance substances of “the 26 allergens rule” are regulated in other areas in the Cosmetics Directive as compiled in Table 2 (6). Only for some of the strong allergens belonging to Group I, there are maximum threshold values in the final products, e.g. hydroxycitronellal may only be used in cosmetics up to a maximum level of 1% in the finished product, oak moss up to 0.1%. But there are no thresholds in “the 26 allergens rule” itself and there are also no references to the thresholds defined elsewhere.

The chemical analysis of perfumes performed by Rastogi found very high concentrations of some contact allergens, such as Lyril, isoeugenol, atranol and chloroatranol in some samples (Rastogi et al., 2007a,b). One third of the analyzed deodorants contained Lyril at higher concentrations than recommended by the SCCP. This is legally in agreement with “the 26 allergens rule”, but it does not protect consumers.

“The 26 allergens rule” as it is now is designed to protect consumers who are already fragrance-sensitive, and who receive help to avoid the contact with the allergens at higher concentrations if they read the ingredient lists and do not use the respective products (IKW, 2004). But “The best way to prevent sensitization is to minimize exposure to sensitizing materials” (Scheinman, 2002). Why are healthy consumers not also protected and why is their sensitization not avoided by reducing the exposure to all strong sensitizers? It must be questioned whether there are no maximum authorized concentrations in the finished products depending on the sensitization potential of each substance.

The hazard depends on the potency of a substance and the exposure situation. The distinction between rinse-off and leave-on products is rather rough and not sufficiently based on scientific evidence. In addition, this distinction ignores the possible respiratory uptake of fragrances in rinse-off products, which can worsen symptoms in sensitized persons.

Question 3: Same treatment of all 26 allergens

Is it justified to treat all 26 substances in the same way?

It is obvious that these chemicals have very different physico-chemical and physiological properties. The development of the dermal sensitization quantitative risk assessment (QRA) developed by IFRA and discussed by SCCP (Scientific Committee on

Consumer Products) (SCCP, 2008) shows that each substance asks for a specific approach. Therefore, it does not make sense to treat substances with strongly different properties in the same way.

Question 4: Labelling

Are these substances listed on the products?

The main purpose of the “the 26 allergens rule” is to inform the consumers that a certain allergen is contained above a certain concentration. There might be an indirect effect of “the 26 allergens rule” if manufactures want to avoid labelling and reduce the amount of the 26 substances at levels below the thresholds that require labelling.

An analysis of the lists of ingredients on the containers helped to answer this question. 742 cosmetic and washing and cleansing products produced by four big manufacturers for the German market were checked as to whether the substances of the “26 allergens rule” are listed (Table 3). These producers offer information about their products on their homepages with lists of ingredients as required on the container. The information about fragrances in these products was collected in 2008 and 2009. Spot checks showed that the declarations in the internet coincided with those on the containers of the products on the shelves of the retailers. Products by some companies where the luxurious graphic design of their homepage impeded the access for standard personal computers could not be analyzed.

More than 50 per cent of the products contain at least one of the “26 allergens”. More than two thirds of products where any of the “26 allergens” is listed contain strong or medium contact allergens. More than 10% of all products analyzed contain strong allergens (Group I), but there are only few cases where more than one strong allergen is named in the list of ingredients. The need for declaration of these compounds does apparently not lead to their complete reduction below the level requiring labelling.

The ingredient list of some products comprises up to 13 different substances of the “26 allergens rule”. Apparently, consumers of these brands do not avoid products with these declarations.

The policies of manufactures seems to be different as can be seen e.g. by comparison of company A with company B. Company A apparently has changed their products to reduce the listing of the “26 allergens”, whereas company B seems to have other priorities and tolerates that more than every fourth of their products contain a strong contact allergen. Even products recommended for sensitive skin may contain strong or medium contact allergens. More than 10% of all products do not contain a perfume preparation and most of them do also not contain any of the substances of “the 26 allergens rule”. The number of perfume free products varies very much from company to company.

Many names on the products which contain perfume imply the association of a pleasant odour or fresh and clean air (“fresh as an orchid”, “fresh as a lemon”, “cherry flowers”, “lotus” and “lavender”, “dainty fresh”, “day at the sea”, “freshness of spring”, “fresh wind”, “mountain fresh”, “fresh as an apple”, “sea”, “meadow”, “lemon”, “freshness of April”, “summer wind” (translated by the author)), showing the importance of scents for marketing.

This analysis showed that the substances of “the 26 allergens rule” are listed on the containers. There were 103 products out of 742 which contain strong allergens (Group I), and around the same amount that contain substances with low allergenic potential (Group III), which shows that producers do not seem to use preferentially substances with low allergenic potential. “The 26 allergens rule” does not seem to be a strong incentive for producers to reduce the amount of the 26 substances to avoid declaration. Many consumers apparently still buy these products. The products evaluated here originate from big, well-known companies. It can-

Table 3

The declaration of fragrances on the containers or on the manufacturers' homepage was analyzed for cosmetics and washing and cleansing products on the German market produced by four companies. The fragrances named in the list of ingredients were grouped according to their allergenic potentials described by Schnuch et al. (2007). The product data were raised between July 2008 and June 2009. The product spectrum has been changing over time in every company, therefore the numbers vary accordingly. Especially, in company A, a considerable change concerning the listing of the "26 allergens" could be observed. Therefore, the data are given for company A for 2008 and for 2009 separately. The ingredient lists for some products had been available in 2008, but were so no longer in 2009, some products were taken from the market and new products appeared.

Companies	A	B	C	D	Total
Number of products checked	90	307	275	70	742
Number of products where at least one of the 26 allergens is listed	2008: 27 2009: 4	130	191	57	2009: 382 (51%)
Number (and rounded percentage) of products where at least one of the 26 allergens which are strong allergens (I) according to Schnuch et al. (2007) is listed (Names of the strong allergens)	2008: 3 2009: 1 (1%) (farnesol)	82 (27%) (hydroxycitronellal, farnesol, hydroxyisohexyl 3-cyclohexene carboxaldehyde)	17 (6%) (hydroxyitronellal, cinnamal, hydroxyisohexyl 3-cyclohexene carbox-aldehyde)	3 (4%) (hydroxy isohexyl 3-yclohexene carboxaldehyde)	2009: 103 (14%)
Maximum number of strong allergens listed on one single product	1	3	2	1	3
Number of products where no strong allergen (I), but at least one of the medium allergens (II) according to Schnuch et al. (2007) is listed. (Names of the medium allergens)	2008: 3 2009: 1 (coumarin)	34 (cinnamyl alcohol, citral, citronellol, coumarin, eugenol, geraniol)	113 (cinnamyl alcohol, citral, citronellol, coumarin, eugenol, geraniol)	28 (citral, citronellol, coumarin, eugenol, geraniol)	2009: 176 (24%)
Products where no strong (I) or medium (II) allergen, but at least one of the weak or no allergens (III) according to Schnuch et al. (2007) are listed	2008: 21 2009: 2	14	61	26	2009: 103 (14%)
Maximum number of substances of "the 26 allergens rule" listed on one product	2008: 4	13	7	11	13
Products recommended for sensitive skin, which listed at least one substance of "the 26 allergens rule"	2008: 19 2009: 4	2	3	0	2009: 9
Products recommended for sensitive skin, which listed at least one strong (I) or medium (II) allergen	2008: 6 2009: 2	0	1	0	2009: 3
Maximum number of substances of "the 26 allergens rule" listed on one product recommended for sensitive skin	2008: 5 2009: 4	7	4	0	7
Products where 'perfume' is not listed in the list of ingredients.	49	37	8	0	94 (13%)
Products where 'perfume' is not listed in the list of ingredients but which contain a substance of the "26 allergens".	2008: 11 2009: 1	0	0	0	2009: 1

not be excluded that the situation is very different for no-name products or imported brands.

A Danish market study of deodorants found out that in almost 70% of the deodorants investigated one or more of the 26 fragrances that are regulated for labelling, were present according to the ingredient lists on the products. Chemical analysis of a selection of products demonstrated that the labelling on the respective products complied with the presence of the respective fragrance ingredients. The same study found out that potent fragrance allergens are wide-spread in perfumes and less so in deodorants of the Danish market (Rastogi et al., 2007a).

The German Allergy and Asthma Association (Deutscher Allergie- und Asthmabund, DAAB) recommends a list of 83 cosmetics and washing and cleansing products that supposedly do not contain any fragrances (DAAB, 2009). The presence of perfume and of “the 26 allergens” was checked on the ingredient lists of these products. 11 products could not be included in the assessment, because they had similar, but not identical names compared to the DAAB list or were no longer for sale. The ingredient lists of 72 products could be found at the retailer, in the internet or upon request by E-mail at the retailers. Perfume was listed on 15 products (i.e. 21%). Among these the following members of “the 26 allergen rule” Coumarin (Group II), Hexyl Cinnamal (Group I), Linalool (Group III), Limonene (Group III) were listed on one product. This indicates that recommendations even by organizations like the DAAB need to be checked by the consumer on the product itself, as the names and compositions of cosmetic products seem to undergo a frequent change. The European Consumer Centre Austria estimated that 25% of cosmetic products are replaced or changed per year (Europäisches Verbraucherzentrum Wien, 2009).

Question 5: Threshold values for labelling

Are the threshold values based on scientific evidence?

According to “the 26 allergens rule” “the presence of the substances must be indicated in the list of ingredients . . . when its concentration exceeds – 0.001% in leave-on products – 0.01% in rinse-off products.” The labelling on the container tells that the respective allergen is present above a certain threshold value, but “the 26 allergens rule” does not help consumers who want to avoid certain substances completely, as they are not listed on the containers if they are present below these threshold concentrations.

When the SCCNFP selected the 26 substances, the scientific data did not permit to perform a quantitative risk assessment with dose–effect relationships. The correlations between extrapolations from animal or in vitro tests with effects on humans were not satisfying. Additionally, the variability of human data was very high. Under these circumstances safe threshold could not be derived. The identical thresholds used for all substances in “the 26 allergens rule” were a pragmatic solution for a problem that could not be solved at that time.

Since then test systems and risk assessment methods have been improved considerably. The new quantitative exposure-based QRA (Quantitative Risk Assessment) proposed by RIFM (Research Institute for Fragrance Materials, Inc.) and reviewed by REXPAN (RIFM Expert Panel) can be considered as big progress compared to the former qualitative approach (Api and Vey, 2008; Api et al., 2008). It is now generally accepted that sensitization and elicitation are threshold based events, the threshold for sensitization lying below the threshold for elicitation (Basketter et al., 2005, 2008a; Wijnhoven et al., 2008). Sensitization thresholds vary by five orders of magnitude for various fragrances, even for the small number of the 26 “allergens” they differ by more than two orders of magnitude (see Table 2 (4)) (Basketter et al., 2008b). Therefore, identical thresholds for all 26 substances have no scientific justification. It is evident that the thresholds for labelling a fragrance compound

on the container in the “26 allergens rule” do not correspond to threshold limits for sensitization or elicitation.

Even if the limits for labelling were derived according to the best scientific methods they would not indicate safe levels for the consumers. Exposure in everyday life might still be considerable even if the concentrations in cosmetic products stay below the threshold values and are not listed on the containers, as there are multiple applications of fragrances in so-called “air fresheners” or scented products of any kind (cigarettes, candles, fabric, cat litter, stationery and so on), see also market analysis (Wijnhoven et al., 2008). The exposure of the consumer resulting from all products which contain fragrance ingredients via various routes needs to be considered in an aggregate exposure assessment (Park et al., 2006; Wijnhoven et al., 2008). In addition, it is known that combined exposure of an allergen with a detergent e.g. in washing liquids can increase the allergic reaction (Heydorn et al., 2003). Also various fragrance substances show cross-reactions to each other. Schnuch et al. (2007) described e.g. that patients with positive patch reaction to Lyrar react frequently positive to hydroxycitronellal, or patients with positive patch reaction to isoeugenol react frequently positive to balsam of Peru or oak moss. For some fragrances it is known that their metabolites have a higher sensitization potential than the original substance. This is true e.g. for D-Limonene with a low allergenic potency that can be oxidized by air to strong allergens (e.g. Karlberg et al., 1994; Matura et al., 2005; Skold et al., 2008).

The limits used in the 26 allergens rule might help sensitized people to avoid elicitation by some substances, but they certainly do not help to avoid elicitation at concentrations below the limits requiring labelling and they also do not help to avoid new sensitizations. For all these reasons, thresholds for fragrances in cosmetics can not be considered as safe limits. The levels or even the applicability of threshold values in “the 26 allergens rule” must be debated under all these aspects again.

Discussion

Right to know—Does it make the products safer?

Pros and Cons of “the 26 allergens rule”

“The 26 allergens rule” demonstrates that the cosmetics industry takes over more responsibility for the application of allergenic fragrances than producers of other products where no labelling is required. Stricter rules in cosmetics are reasonable as many of them are used and applied to the body surface daily. The restriction of “the 26 allergens rule” is easy to imply, as it addresses only one endpoint and as it applies the same thresholds for all 26 substances. No detailed risk assessment is required, and no dose–effect relationships need to be established. Action was taken at an early stage, and “the 26 allergens rule” is a convenient system, which did not ask for a change in the composition of cosmetic products and still helps the consumer to reduce exposure to some allergens. Every customer can look for the respective fragrance ingredients on the product itself. The INCI-names used on the containers are international standards, with the aim to facilitate identification of a substance by consumers. However, many of the INCI-names do not give a clue about the chemical nature of the substance, so that even chemists who are not familiar with cosmetics need additional investigations to understand the ingredient list on a container.

“The 26 allergens rule” has clearly some drawbacks.

As illustrated in chapter 3 the allergenic potential of the 26 fragrance compounds is not consistently evaluated and it is not scientifically justified to use the same concentration thresholds for all 26 substances. General criteria would be preferable to a list of substances. A regulation that contains a list of substances needs to be updated regularly following the scientific progress. It might also

be questioned whether it is useful to set up a regulation for a single end point only. The instrument of comprehensive risk assessment as an integrated approach proved to be a useful tool. Risk assessments must address all effects on human health, not only contact allergy. As cosmetics are discharged into waste water mainly, the environmental risk and the aspect of indirect reuse may also not be ignored (Knacker et al., 2006). All various applications of a certain fragrance compound need to be considered in such a risk assessment. Degradation products and metabolites must also be taken into account. A comprehensive risk evaluation of substances needs to be effectuated before they are used in consumer products. If the substitutes applied by a producer to avoid labelling are more toxic the regulation is clearly contraproductive (Schnuch et al., 2009). For example Rastogi found that some isoeugenol derivatives smell like isoeugenol and could be used as substitutes, as they are not restricted and do not need to be declared on the container. But they can be the cause for elicitation in isoeugenol-sensitized persons (Rastogi and Johansen, 2008). The “26 allergen rule” needs to be supplemented by a regulation that substitutes of the “26 allergens” must be less toxic. If any of the 26 allergens is not listed on the container, it does not mean that it is not present at all, but only that it is present below the respective threshold. “The 26 allergen rule” does not help people to avoid a certain fragrance completely.

A very interesting questionnaire study performed by Noiesen et al. (2007) showed how difficult or even impossible it is even for informed patients with allergic contact dermatitis to take advantage of “the 26 allergens rule”. Most of these patients consulted the ingredient lists on the label before they bought a product. Some of the INCI names are difficult to understand and very difficult to remember to make a sensible decision in the shop after reading the ingredient list on the container. A big effort and a great deal of knowledge are required by a customer to be able to use the INCI names properly, a great demand that cannot be asked from people of lower educational levels. More than half of the patients in this survey did not trust the indications on the labels. This might be due to the fact that the sensitizing substances can legally be present in products below the concentrations requiring labelling. This low concentration may be sufficient for some patients for elicitation reactions. Therefore, these patients are not protected by “the 26 allergens rule” as it does not help to identify products which are free of these 26 substances.

Authorities–manufacturers–consumers: Who carries the responsibility for risk management?

Authorities and control. Directive 2003/15/EC which subsumes “the 26 allergens rule” has „as its main objective the protection of public health“(Preamble (1)). The tool of “the 26 allergens rule” for the protection of the public health is to inform the consumer about the presence of 26 fragrance ingredients in the product if present above a certain level. Member states have the duty to control compliance of products with Directive 2003/15/EC (Article 2). The number of cosmetic products on the market is very large and authorities need sufficient manpower for the control of “the 26 allergens rule”. Some national authorities verify compliance in random samples, such as the Ministry of Food and Rural Area of Baden-Württemberg (2005), the Dutch Food and Consumer Products Safety Authority or the Danish EPA (see RIVM Report by Wijnhoven et al., 2008).

In all three studies most but not all products complied with “the 26 allergens rule”. Some consumer products contained sensitizing compounds which were not listed on the containers. In the Dutch study 7 out of 21 products were not labelled, but contained at least one of the 26 fragrances above 0.01 wt% (Wijnhoven et al., 2008). In one product, the manufacturer used a fragrance substance as preservative, not as scent, and therefore he did not indicate it on the container. If such products are sold as “free of preserva-

tives”, this clearly misleads consumers. All these results show how important it is to guarantee the independent surveillance of such a regulation.

Manufacturers. Manufacturers could design the composition of their products independently of “the 26 allergens rule” and label the product as required (strategy of company B in Table 3). The compliance with “the 26 allergens rule” does not render the products less toxic, but informs the consumers. Labelling improves health protection only, if the consumers change their behaviour. If a company takes consumer choice seriously, they might want to avoid labelling by reducing the amount of the 26 substances in the product below the levels requiring labelling or even to zero (strategy of company A in Table 3). In this case, “the 26 allergens rule” leads indirectly to a reduction of the “26 allergens”, but it does not offer any incentive for the producer to avoid any other additional hazardous ingredients. The listing of the ingredients on the container can therefore not be regarded as a real use restriction.

Consumers. The main burden for risk management by “the 26 allergens rule” is on the consumers’ shoulder. As the main purpose of “the 26 allergens rule” is to inform the consumers, they must have enough knowledge to understand this information and take over their responsibility to select products that contain the respective allergen in lower concentrations. Sensitized people depend on this information to avoid elicitation, but also healthy customers should be able to reduce the probability to become sensitive. Most consumers are not informed about this right to know and can not use this information diligently, not even informed patients with allergic contact dermatitis (Noiesen et al., 2007). Most consumers trust the manufacturers of cosmetics and authorities and believe that the products are safe. Many consumers associate exclusively positive effects with agreeable odors and are not prepared to accept that these chemicals might also be the cause for negative health effects. A regulation which depends on the autonomous role of the informed consumer would only work, if a very effective campaign had been launched to inform consumers about this regulatory change, especially as it is difficult to teach this complicated matter. Some of the long chemical INCI names are discouraging for the interested consumer (Noiesen et al., 2007). One example is Lylal which is listed mostly as Hydroxy-methylpentyl-cyclohexene carboxaldehyde on the containers. The pure listing of hazardous substances on the containers is not clear enough for the public, but should at least be supplemented by warnings signals. In the actual situation, consumers need to invest considerable time and a lot of effort to be capable to understand the regulations and to protect their own health.

These arguments question very strongly whether “the 26 allergens rule” is a useful means for risk management.

Conclusion and recommendations

Actions to be taken by authorities, manufacturers and consumers

The data and reflections compiled here support the conclusion by Wijnhoven et al. (2008) “... the current legislation is not sufficient to prevent the occurrence of contact dermatitis and a better control of the exposure to sensitizers in consumer products is needed”.

“The 26 allergens rule” has many drawbacks and needs revision that should be initiated by the European Commission. The data and arguments in this article are meant to support this revision process as they demonstrate that other solutions would be more purposive for risk management than “the 26 allergens rule”.

Test strategies and evaluation methods need to be improved and implemented in the European regulations

The work of the ECETOC and OECD expert groups on sensitization hazards (ECETOC, 2003; OECD, 2008) will help to improve the test strategy, to harmonize evaluation methods and to reduce the discrepancies of expert judgements in the identification of contact allergy hazards. For ethical reasons quantitative risk assessments must not require data obtained from healthy humans who risk to be sensitized in the tests. The results of the ECETOC and OECD working groups should be used to revise European regulations such as “the 26 allergens rule” and replace lists of restricted sensitizers by clear criteria applicable to any compound. It would be preferable to base a regulation concerning one toxicological end point on clear criteria applicable to any substance under concern instead of a list of potential allergens that would need to be updated regularly along with the scientific progress. A minimum data requirement would be suited better for pollution control and regulation of substances than a list of compounds (see also Montforts and de Knecht, 2002). Of course, criteria and methods will also need to undergo redefinition according to the progress of knowledge, but not as frequently as the update of lists of substances. Strong allergens used in every day consumer products should be classified according to Directive 67/548/EEC (EEC, 1967), respective EU Regulation 1272/2008 (EC, 2008a) by authorities to end the actual heterogeneous self classifications (Table 2 (7)).

Some substances need to be banned, others may only be used below a maximum level

Strong allergens need to be banned completely from consumer products, because also very low concentrations below the amount requiring labelling can induce elicitation. Maximum levels need to be set up for less potent allergens to protect consumers from sensitization. Especially, for all substances, where neither dose–effect relationships nor an aggregated risk assessment were elaborated, the thresholds must be as low as possible for precautionary reasons. Regulations for fragrances in other consumer products are still needed.

Surveillance is indispensable

The use of fragrances in products is largely self-regulated by industry. The International Fragrance Association (IFRA) together with the Research Institute for Fragrance Materials (RIFM) assure that their testing guarantees a safe use of fragrances by the customer and for the environment (Bickers et al., 2003; IFRA, 2009; RIFM, 2009). IFRA publishes general guidelines, the “Code of Practice” and standards for the use of ingredients. These recommendations are considered as mandatory for the producers, but IFRA has no means to control or enforce the implementation. To ensure the safety of products sufficient independent market surveillance controls are necessary.

Contact allergy is one out of many toxic effects of fragrances that need attention and more public data are needed

The health issues of fragrances do not only concern skin safety. Out of the many toxic effects a fragrance might have the effect as skin irritant or sensitizer might be deduced directly after application of a product, whereas other systemic effects can hardly be related to the contact with a certain substance. But these effects might be even more relevant for the consumer. Some fragrances exert e.g. effects on the respiratory and digestive tracts or neurologic effects. The regulation of a few substances due to their potency for skin sensitization creates a sort of pseudo-safety. Due to the current regulatory situation the publicly available data basis is very thin. Standardized laboratory data for fragrance ingredients may be available for short-term effects, in some occasions also for long-term effects (Daughton and Jones-Lepp, 2001; Daughton

and Ternes, 1999; Klaschka and Kolossa-Gehring, 2007; Ternes et al., 2003). The number of classified fragrances is rising as more information about their effects is gathered (Rohde, 2001) which shows that their ecotoxicological and toxicological hazards might still be underestimated. More data and more information on toxicological and ecotoxicological effects of fragrances and applicable regulations must be made publicly available. The new internet service offered by the European Commission on Cosmetic Ingredients CosIng (<http://ec.europa.eu/enterprise/cosmetics/cosing/>) is a start, but not sufficient, as it does not even contain e.g. information on classification and labelling. The current version of European Regulation on Chemicals REACH (EC, 2006b) might lead to a better data basis for some fragrances produced at a high tonnage, but will probably not improve the data situation of most fragrances (due to low production volumes, low amounts in products, many producers, natural compounds, imported scented products (see Klaschka and Kolossa-Gehring, 2007)). If not enough data are available, the classification of a substance as PBT (persistent, bioaccumulating and toxic) is not possible and it is not considered further according to REACH, even if it may be of high toxicological or ecotoxicological impact. In addition, many fragrances are natural substances and can still be substances of concern. The situation of fragrances can be regarded as a motive to rethink the regulation of substances with a high toxicological or ecotoxicological impact which are produced at low amounts and the regulation of natural compounds in REACH. One major innovation in REACH is the shared responsibility and the improved information flow along the production chain from the producer to the end user. This is a similar situation as in the case of “the 26 allergens rule”. The end users can only exert their responsibility if they have invested time, energy and used their brains to acquire enough knowledge about the chemicals, their properties and possible alternatives. If the consumers are left alone – like in the case of “the 26 allergens rule” – this purpose of REACH will fail and the information flux will not lead to a more responsible use of chemicals. Therefore, the recommendations given here could be considered in the other regulations on fragrances and in the revision of REACH. Furthermore, it would be recommendable to harmonize the various European regulations for fragrance compounds which are so far different depending on their use in cosmetics, washing and cleansing products, food or consumer products.

Producers can improve their products and make them less hazardous

Producers have the best knowledge about the properties of their products and can optimize their products. One optimization aim should be to reduce the hazard of a product by respecting relevant regulations and by going beyond them on a voluntary basis. Hazardous chemicals in a product should only be substituted, if the properties of the new ingredients are well known and are clearly less noxious. More unscented cosmetic products and washing and cleaning products should be available on the market at reasonable prices.

The information for consumers must be improved

The ingredient lists on the product should contain information about all known fragrance ingredients. The message should be made public that some fragrances are identified as very important sensitizing or toxic culprits in every day products. Toxic ingredients such as sensitizers must be marked with a warning signal or a description of the potential effects (such as on tobacco product containers in the EU).

Eco-labelling of products would be a start

There are already criteria for the European Eco-label for scented product groups, such as soaps, shampoos and hair conditioners

(EC, 2007). They contain restrictions concerning the use of nitro-musk and polycyclic musk compounds and the requirement that the fragrances follow the Code of Practice of IFRA. The IFRA's Code of Practice asks for a quantitative assessment for dermal sensitizers (QRA). But it remains unclear what result of the QRA would be acceptable for the fragrances in the products with an Eco-label.

The weighing of risks versus benefits is clear-cut in the case of fragrances as they are not necessary for human survival. Noxious fragrances should be replaced in products by less dangerous ones. Many caveats were illustrated here for “the 26 allergens rule” which show why this is not a satisfactory tool for risk management.

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