Perfume Allergies

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SCCS (2012)

Summary & Details:
GreenFacts

Level 2 - Details on Perfume Allergies

The answers to these questions are a faithful summary of the scientific opinion produced in 2012 by Scientific Committee on Consumer Safety (SCCS):
"Opinion on Fragrance allergens in cosmetic products"

The full publication is available at: https://copublications.greenfacts.org/en/perfume-allergies/
and at: http://ec.europa.eu/health/opinions/en/perfume-allergies/

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- Each question is answered in Level 1 with a short summary.
- These answers are developed in more detail in Level 2.
- Level 3 consists of the Source document, the internationally recognised scientific opinion which is faithfully summarised in Level 2 and further in Level 1.

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1. Introduction


Fragrance ingredients are found in cosmetics and other consumer products.
Source: Lilieks

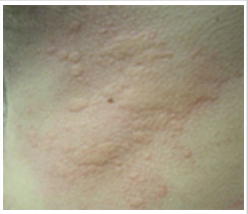
Fragrance substances are naturally or synthetically derived organic compounds with a characteristic, usually pleasant smell. They are ubiquitously found in perfumes and other perfumed cosmetic products, but also in detergents, fabric softeners and other household products where fragrances may be used to provide the consumer with a fresh smell or to mask unpleasant odours from raw materials. Fragrance substances are also used in aromatherapy and are sometimes present in herbal products. A fragrance formula ('perfume') may contain up to several hundred or more different ingredients. Special fragrance databases lists more than 2,587 fragrance ingredients used for perfuming.

Contact allergy to fragrance ingredients occurs when a susceptible individual has been exposed on the skin to the fragrance allergen, for example through their presence in a cosmetic product. It is a life-long, specifically altered reactivity of the immune system involving recognition of the fragrance allergen(s) by immune cells. Once a contact allergy has been developed, cells capable of recognizing and reacting towards the allergen will always be present in the immune system. As a consequence, symptoms of allergic contact dermatitis characterised by erythema ('redness'), swelling and vesicles occur upon re-exposure to the fragrance allergen in question. If exposure continues over a longer period of time, it may develop into a chronic condition with scaling and painful fissures of the skin. Allergic contact dermatitis to fragrance ingredients is most often caused by exposure to cosmetics and predominantly involves the face, armpits or hands. The disease can be severe and generalised, with a significant impairment of quality of life and potential consequences for fitness for work. Apart from allergic contact dermatitis, fragrances in perfumes and cosmetic products can also provoke irritant contact dermatitis, immediate contact reactions (contact urticaria), pigmented contact dermatitis or photosensitivity.

A 1999 opinion by the SCCNFP identified 26 substances that needed to be identified on the label of consumer products to help prevent allergic reactions. Since that time, the review of the clinical and experimental data published after 1999 revealed that many more fragrance substances have been shown to be sensitisers in humans.

2. What kind of skin problems are known to be caused by fragrance ingredients?

2.1 What is contact allergy?


Skin rashes can be caused by fragrance ingredients, but are usually not allergic reactions.
Source: James Heilman

Contact allergy to fragrance ingredients occurs when an individual has been exposed on the skin to a sufficient dose of a fragrance allergen, for example through its presence in the cosmetic product. It is a life-long, specifically altered reactivity of the immune system involving recognition of the fragrance allergen(s) by immune cells. Once a contact allergy has been developed, cells capable of recognizing and reacting towards the allergen will always be present in the immune system. As a consequence, symptoms - allergic contact dermatitis - may occur upon re-exposure to the fragrance allergen(s) in question.

Allergic contact dermatitis is an inflammatory skin disease characterised by erythema ('redness'), swelling and vesicles in the acute phase. If exposure continues, it may develop

into a chronic condition with scaling and painful fissures of the skin. Allergic contact dermatitis to fragrance ingredients is most often caused by fragranced cosmetic products and usually involves the face and/or hands. It may affect fitness for work and the quality of life of the individual. In the process of developing allergic contact dermatitis, a distinction between the induction ('sensitisation') and the elicitation 'reaction upon re-exposure to the allergen' phase is made.

2.2 What 'other' non-allergic reactions to fragrance ingredients are observed?

Apart from allergic contact dermatitis, fragrances in perfumes and fragranced cosmetic products may also provoke irritant contact dermatitis, immediate contact reactions (contact urticaria), pigmented contact dermatitis or photosensitivity. Irritant effects of some individual fragrance ingredients are known if humans are exposed to higher concentrations. Irritant contact dermatitis from perfumes is believed to be common, but there are no existing investigations to substantiate this. Some people complain about intolerance or rashes to perfumes/perfumed products but are shown to not be allergic by testing. This may be due to irritant effects or inadequate diagnostic procedures. Fragrances may cause a dose-related contact urticaria of the non-immunological type ('irritant contact urticaria').

Pigmented cosmetic dermatitis refers to increased pigmentation, usually on the face/neck, often following sub-clinical contact dermatitis. Moreover, it is also known that some substances provoke allergic reactions only in the presence of UV-light ('photo-contact allergy'). Nowadays, several substances of this type have either been banned or maximum use limits have been introduced to avoid photo-allergies in consumers. Hence, photo-allergic contact dermatitis is a relatively uncommon disease.

Fragrances are volatile and therefore, in addition to skin exposure, eyes, nose and the respiratory tract are exposed to the fragrance ingredients. It has been estimated that about 2–4% of the adult population is affected by respiratory or eye symptoms in this way. In addition to potential irritant reactions of the airways, it is known that exposure to fragrances may exacerbate pre-existing asthma.

2.3 How can contact allergies be diagnosed?

Contact allergy in humans to a specific perfume allergen is generally diagnosed by prognostic patch testing. This involves the application of small doses of the set of suspected allergens or the culprit product on a cotton patch either on the back or the upper arm of the patient for a period of 24 to 48 hours. In days after removal of the patch, exposed skin sites are visually examined by an expert, generally a dermatologist, for the occurrence of allergic reactions following topical exposure to the potential contact allergen. The whole process of identifying contact allergens is standardised. There are international guidelines for the application, reading and interpretation of the patch test.

2.4 How common is perfume allergy and can it be avoided?

Contact allergy to fragrance ingredients is relatively common disease. In Europe, it affects about 1 to 3% of the general population- and about 16% of eczema patients. Allergic contact dermatitis can be severe and widespread, with a significant impairment of quality of life and potential consequences for fitness for work. Thus, prevention of contact sensitisation to fragrances, both in terms of primary prevention ('limiting or eliminating exposure to allergens in the population') and secondary prevention ('avoiding re-exposure to specific sensitiser in clinically diagnosed individuals'), is an important objective of public health risk management measures. Means of limiting or eliminating exposure to limiting or eliminating exposure to fragrance allergens ('primary prevention') include

- *Prohibition* by regulatory measures or other means;
- *Restriction* of the maximum permissible concentration of an allergen, or critical component of natural mixtures according to different uses and product types;
- *Substitution* of the allergen with a suitable less or non-allergenic compounds;
- *(Re-)formulating* the fragrance or fragranced product with the aim of limiting or eliminating those substances for which a sensitising potential has been shown;
- *Deliberate avoidance* of the use of fragrances where they are not essential to the function or purpose of the finished product;
- *Information*, e.g. labelling so that the consumer may make an informed choice to avoid exposure to a particular ingredient.

In clinical dermatology, avoidance of re-exposure to an allergen is central to the care of sensitized patients. In this context, the valid diagnosis of sensitisation by patch testing with standardised material is a prerequisite of successful allergen avoidance. In addition to the correct clinical evaluation and diagnosis of contact allergy to a specific fragrance allergen, ingredient labelling of fragrance allergens is an important tool for clinicians to optimize the investigation of their patients with suspected fragrance allergy, as well as for fragrance allergic patients for avoiding products containing substances they have been shown to be allergic to. Both these aims are objectives of secondary prevention and seem to have been well accepted.

3. How can fragrance substance become skin allergens?

Allergenic fragrance substances are usually of low molecular weight chemicals that act as 'haptens'. This means that they provoke an immune reaction in the body only when attached to a carrier protein.

Some substances are allergenic as such, while others must be 'activated' before they become allergenic. Here, science distinguishes between prehaptens and prohaptens. A prehapten is a chemical that is itself non- or low-sensitising, but that is transformed into a hapten outside the skin by simple chemical transformation, for example oxidation by air or photo-activation in the presence of UV light. A pro-hapten is a chemical that is itself non- or low-sensitising but that is transformed into a more potent hapten in the skin ('bioactivation') usually via enzyme catalysis. It is not always possible to know whether a particular allergen that is not directly reactive acts as a prehapten or as a prohapten, or both. This is because air oxidation and metabolic bio-activation can often give the same product. Many fragrance substances can act as prehaptens or prohaptens, forming allergens which are more potent than the parent substance.

In the case of prehaptens, it is possible to prevent activation outside the body to a certain extent by different measures, for example preventing exposure to air during handling and storage or adding suitable antioxidants. In the case of prohaptens, the possibility to become activated is inherent to the molecule and activation cannot be avoided by extrinsic measures.

Cross- reactivity has been shown for certain alcohols and their corresponding aldehydes, for example between geraniol and geranial (citral) and between cinnamyl alcohol and cinnamal. Cross-reactivity is also expected between ester derivatives and their parent alcohols, as the esters will be hydrolysed by esterases in the skin. Esters of important contact allergens that can be activated by hydrolysis in the skin are isoeugenol acetate, eugenyl acetate and geranyl acetate, all of which are known to be used as fragrance ingredients.

4. What fragrance substances can be classified as skin allergens?

4.1 What sources of information have been taken into account for the SCCS opinion?

The present opinion by the Scientific Committee on Consumer Safety (SCCS) updates a 1999 opinion by the Scientific Committee on Cosmetic Products and Non-Food Products (SCCNFP) using a systematic and critical review of the scientific literature to identify fragrance allergens, including natural extracts, relevant to consumers. A well-defined search strategy was established to retrieve pertinent clinical/epidemiological and experimental studies. This was complemented, where necessary, with SAR modelling. The evidence was evaluated according to clearly defined criteria and the substances were then categorised as (i) **established contact allergens** (in humans or animals), (ii) likely contact allergens or (iii) **possible contact allergens**.

Category	Number of individual fragrences	Number of natural extracts	Lists of substances	Conclusion concerning labelling of consumer products
Established in humans	54	28	82 substances (13.1 [see Annex 2, p. 11])	Labelling recommended (see conclusion)
Established in animals	18	1	19 substances (13.2 [see Annex 1, p. 10])	Labelling recommended (see conclusion)
Likely	26		26 Substances (13.3 [see Annex 4, p. 14])	Labelling recommended (see conclusion)
Possible	35	13	48 substances (13.4 [see Annex 3, p. 13])	-

4.2 What are the findings from clinical and epidemiological studies?

Based on the results of clinical/epidemiological studies, the SCCS identified a total of 54 individual chemicals and 28 natural extracts (essential oils) that can be categorised as '**established contact allergens in humans**'. Of these, 12 are of special concern due to the high number of reported cases. One ingredient in particular stands out, hydroxyisohexyl 3-cyclohexene carboxaldehyde (HICC), having caused more than 1,500 reported cases of sensitisation in humans since the 1999 SCCNFP publication.

4.3 What are the findings from studies in animals?

Where human data are lacking or are considered to be insufficient, animal studies such as the local lymph node assay (LLNA) in the mouse or guinea pig assays (GPMT, Buehler test) can provide important information on the skin sensitising potential and potency of fragrance substances (other types of animal studies are also available). Results from animal testing (mainly LLNA) were available for approximately 70 fragrance substances. Based on this data and in combination with human evidence where possible, 18 individual chemicals and 1 natural extract were categorised by the SCCS as '**established contact allergens in animals**'.

4.4 Can the chemical structure of a substance help predict if it is an allergen?

The ability of a chemical to react with and bind to proteins in the skin, either directly or after activation, determines the chemicals' potential to be a skin sensitizer. The relationship between molecular structure and protein reactivity is based on well-established principles of mechanic organic chemistry and forms the basis for identifying structural alerts by existing structure activity relationship (SAR) computer models. While significant progress has been made in the area of SAR modelling, the computer-based methodology alone is not considered to be sufficient for the identification of skin allergens. Nevertheless, SAR can be used in combination with human and animal data to make useful predictions. Based on a combination of evidence, the SCCS determined 26 individual chemicals categorised as '**likely contact allergens**' and 35 individual chemicals plus 13 natural extracts categorised as '**possible contacts allergens**'.

5. How is the general public exposed to fragrance allergens?

There are various modes of exposure to fragrances, including not only products used for their scent, such as perfumes and eau de toilette, after shaves and deodorants, but also products where scent is an added feature, such as other cosmetic categories (for example wipes), topical pharmaceuticals, household products and products encountered in the occupational setting.

The general public is predominantly exposed to fragrance substances via their ubiquitous use in perfumes or perfumed cosmetic products, but also via their presence in and use of detergents, fabric softeners, and other household products. In the latter product types fragrances may be used to provide the consumer with a fresh smell or to mask unpleasant odours from raw materials. Fragrance substances are also used in aromatherapy and may be present in herbal products. A fragrance formula ('perfume') may contain up to several hundredsof different ingredients. Special fragrance databases lists more than 2587 fragrance ingredients used for perfuming.

Different routes of exposure are reflected by the areas of the body that are affected. Deodorants are for example associated with axillary dermatitis. However, while sensitisation and initial allergic reaction may follow a distinct pattern in affected area, less specific exposures, for example via hand creams or cleaning lotions may later be sufficient to cause allergic contact dermatitis.

6. What are the gaps in the current knowledge about perfume allergies?

Although the science has progressed, there are still gaps in clinical and epidemiological research. Amongst others, the SCCS opinion lists the following gaps:

- Clinical data on more fragrance substances are needed to assess more fully the epidemiology of fragrance contact allergy and pin-point the culprit substances for induction and elicitation of contact allergy in man. Data from a broader range of EU countries is needed, as difference in exposure and use habits are expected across Europe.
- Very little is known about susceptible groups of the population. Data are needed to qualify and quantify the increase in risk of susceptible groups in order to provide a better protection of all consumers.
- Aberrant enzyme activity in certain individuals, often related to genetic enzyme polymorphisms, may result in an increased or reduced risk of sensitisation to prohaptens in certain individuals or populations. More research into the role of relevant traits is needed.
- Dose-response data from clinical studies are available for only a few allergens. To establish individual safe levels, such data are required for all established allergens of concern and covering an appropriate range of product types.
- Data on human exposure to fragrances from the use of different product categories is very scarce and therefore does not provide an optimal basis of risk assessment. Exposure data on use for perfume/eau de cologne are for example lacking.
- Most experimental studies are done on individual fragrance ingredients, while exposure to allergens in cosmetic products is usually to mixtures of allergens. The risk of sensitisation and elicitation may depend on the mixture of substances, but very few studies on this exist.
- Screening in dermatitis patients should be performed with air-exposed samples of such fragrance substances that in experimental studies have been demonstrated to act as prehaptens.
- Patch testing should, if possible, be performed with the isolated true haptens formed from prehaptens and prohaptens to increase the possibility to diagnose allergy from these type of substances.
- There is a need for more experimental research to further establish the impact of the behaviour of fragrance substances when applied on the skin (including factors such as volatility, autoxidation, skin penetration, reactivity in skin and bio-activation).

Also, with regard to the animal data used in the opinion, several studies were of insufficient quality. Often, data on experimental results are not published but available only in company files and therefore not easily accessible.

Finally, applying only mechanism-based SAR as a tool in non-animal based risk assessment for skin sensitisation is of limited value for fragrance substances. This is due to major information gaps in the present model when addressing substances that act via activation, and the high incidence of such substances in fragrances.

Further experimental investigations of the sensitisation potential of fragrance substances are needed to determine the impact of the volatility of the substance as well as the effect of the vehicle on skin penetration/absorption and reactivity.

From a clinical perspective, it is important for the individual who is sensitised to one fragrance substance to know if they must also avoid other fragrance substances that can cause allergic contact dermatitis due to cross-reactivity. This is a field that has not been studied very much so far and needs to be focused on much more in the future.

7. Conclusion : are the current European regulations on fragrance allergens adequate?

7.1 Is the current list of possible allergens adequate ?

The SCCS opinion lists a number of individual substances and natural extracts considered as 'established contact allergens in humans, 'established contact allergens in animals' or 'likely contact allergens by combination of evidence'. The selection is made based on a comprehensive screen of available clinical and animal data, paired with computer-based SAR modelling where appropriate.

The SCCS considers that these substances represent those fragrance ingredients that the consumer should be made aware of when present in cosmetic products. Substances known to be transformed into known contact allergens (for example by hydrolysis of esters) should be treated as equivalent to these known contact allergens. The combined concentration of the alcohol and its ester must be considered regarding exposure. Important examples include isoeugenol and its esters, geraniol and its esters, eugenol and its esters, and linalool and its esters.

7.2 Is there a threshold of safe use for these allergens?

There are two components to the safety of fragrance ingredients in terms of contact allergy: (i) the need to eliminate or reduce **induction** of contact allergy (**primary prevention**), which, when it occurs, is lifelong and (ii) the need to eliminate or reduce **elicitation reactions** (**secondary prevention**) on the skin of those individuals who are already sensitised.

Based on available data, the SCCS could not establish thresholds of safe use for individual fragrance allergens. However, they concluded that a general level of exposure up to 0.8 $\mu g/cm^2$ (0.01%) may be tolerated by most consumers with contact allergy to fragrance ingredients. The SCCS considers that this level of exposure could be efficient in limiting elicitation unless there is substance-specific data, either experimental or clinical, to the contrary. Such a threshold based on elicitation levels in sensitised individuals will be sufficiently low to protect both sensitised individuals as well as most of the non-sensitised consumers from developing contact allergy.

It was not possible to provide a safe threshold for natural extracts of concern, as no specific investigations exist and the model providing the general threshold has been based on individual chemicals only. However the SCCS considers that the maximum use concentration applies to the above-identified fragrance allergens also when present in the natural extract. This will also reduce the risk of sensitisation and elicitation from natural extracts.

It is important to stress that this general threshold, although limiting the problem, does not preclude that the most sensitive segment of the population may react upon exposure to these levels. Hence, this threshold does not remove the necessity for providing information to the consumer concerning the presence of the fragrance substance in cosmetics.

In the case of hydroxyisohexyl 3-cyclohexene carboxaldehyde (HICC), the SCCS considers that the number of cases of allergy documented over the last decade is exceptionally high and that continued exposure by the consumer is not safe. Therefore, HICC should not be used in consumer products.

In accordance with the 2004 recommendation of the Scientific Committee on Consumer Products (SCCP), the SCCS is of the opinion that chloroatranol and atranol, the main allergenic constituents of *Evernia prunastri* (oakmoss) and *Evernia furfuracea* (treemoss), should not be present in products for the consumer.

7.3 Are there other substances that are relevant for consumers regarding perfume allergies?

Many fragrance substances can act as prehaptens or prohaptens, forming allergens which are more potent than the parent substance by abiotic and/or metabolic activation. Activation can thus increase the risk of sensitisation. Fragrances with published data showing the formation of sensitising compounds by autoxidation, bioactivation or both include:

- Limonene, linalool and linalyl acetate, known to be prehaptens and form sensitising compounds by air oxidation;
- Cinnamyl alcohol, eugenol, isoeugenol and isoeugenyl acetate, known to be prohaptens and form sensitising compounds by metabolic transformation;
- Geraniol and alpha –terpinene, known to be both prehaptens and prohaptens;
- Geranial (an isomer of citral) is a sensitser without activation but forms more potent sensitising compounds by air oxidation and also by metabolic transformation.

The SCCS is of the opinion that substances known to be transformed to known contact allergens should be treated as equivalent to these contact allergens. The same restrictions and other regulatory requirements should apply, unless specific data exist that allow for an individual assessment.

Annex

Annex 1:

Table 13-2: Fragrance substances categorised as established contact allergens in animals.

INCI name (or, if none exists, perfuming name according to CosIng)	CAS number	Human evidence: see text	EC 3 value (min; %)
Individual chemicals			
Allyl phenoxyacetate	7493-74-5	none	3.1
p-tert. -Butyldihydrocinnamaldehyde	18127-01-0	none	4.3
CYCLAMEN ALDEHYDE	103-95-7	none	22
Dibenzyl ether	103-50-4	none	6.3
2,3-DIHYDRO-2,2,6-TRIMETHYLBENZALDEHYDE	116-26-7	limited	7.5
trans-2-Hexenal	6728-26-3	none	2.6
2-Hexylidene cyclopentanone	17373-89-6	none	2.4
HEXYL SALICYLATE	6259-76-3	negative	0.18
p-Isobutyl-α-methyl hydrocinnamaldehdye	6658-48-6	none	9.5
Isocyclocitral	1335-66-6	none	7.3
α-Methyl cinnamic aldehyde	101-39-3	none	4.5
METHYLENEDIOXYPHENYL METHYLPROPANAL	1205-17-0	none	16.4
METHYLUNDECANAL	110-41-8	none	10
2-Methoxy-4-methylphenol	93-51-6	none	5.8
4-Methoxy-α-methyl benzenpropanal	5462-06-6	none	23.6
METHYL OCTINE CARBONATE	111-80-8	limited	2.5
Perillaldehyde p-Mentha-1,8-dien-7-al	2111-75-3	none	8.1
PHENYLACETALDEHYDE	122-78-1	limited	3
Natural extracts			
Jasminum Sambac Flower CERA / Extract / Water	91770-14-8	none	35.4

Source: SCCS, Opinion on Fragrance allergens in cosmetic products [see http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_o_102.pdf], pages 109-110

Annex 2:

Table 13-1: Established contact allergens in humans.

INCI name (or, if none exists, perfuming name according to CosIng)	CAS number	Human evidence: see text
Individual chemicals		
ACETYLCEDRENE	32388-55-9	+
AMYL CINNAMAL*	122-40-7	++
AMYL CINNAMYL ALCOHOL*	101-85-9	++
AMYL SALICYLATE	2050-08-0	+
trans-ANETHOLE	4180-23-8	+ (r.t.)
ANISE ALCOHOL*	105-13-5	+
BENZALDEHYDE	100-52-7	+
BENZYL ALCOHOL*	100-51-6	++
BENZYL BENZOATE*	120-51-4	++
BENZYL CINNAMATE*	103-41-3	++
BENZYL SALICYLATE*	118-58-1	++
BUTYLPHENYL METHYLPROPIONAL *	80-54-6	++
CAMPHOR	76-22-2 / 464-49-3	+ (r.t.)
beta-CARYOPHYLLENE (ox.)	87-44-5	Non-ox.: +, ox.: +
CARVONE	99-49-0 / 6485-40-1 / 2244-16-8	+ (r.t.)
CINNAMAL*	**104-55-2**	+++
CINNAMYL ALCOHOL*	**104-54-1**	+++
CITRAL*	**5392-40-5**	+++
CITRONELLOL*	106-22-9 / 1117-61-9 / 7540-51-4	++
COUMARIN*	**91-64-5**	+++
(DAMASCENONE) ROSE KETONE-4	23696-85-7	+ (r.t.)
alpha-DAMASCONE (TMCHB)	43052-87-5 / 23726-94-5	++
cis-beta-DAMASCONE	23726-92-3	+
delta-DAMASCONE	57378-68-4	+
DIMETHYLBENZYL CARBINYL ACETATE (DMBCA)	151-05-3	+
EUGENOL*	**97-53-0**	+++
FARNESOL*	**4602-84-0**	++ - +++
GERANIOL*	**106-24-1**	+++
HEXADECANOLACTONE	109-29-5	+ (r.t.)
HEXAMETHYLINDANOPYRAN	1222-05-5	++
HEXYL CINNAMAL*	101-86-0	++
HYDROXYISOHEXYL 3-CYCLOHEXENE CARBOXALDEHYDE (HICC)*	**31906-04-4 / 51414-25-6**	++++
HYDROXYCITRONELLAL*	**107-75-5**	+++
ISOEUGENOL*	**97-54-1**	+++
alpha-ISOMETHYL IONONE*	127-51-5	++
(DL)-LIMONENE*	**138-86-3**	++ (non-ox.); +++ (ox.)
LINALOOL*	**78-70-6**	++ (non-ox.) +++ (ox.)
LINALYL ACETATE	115-95-7	+ (non-ox.) ++ (ox.)
MENTHOL	1490-04-6 / 89-78-1 / 2216-51-5	++
6-METHYL COUMARIN	92-48-8	++
METHYL 2-OCTYNOATE*	111-12-6	++
METHYL SALICYLATE	119-36-8	+
3-METHYL-5-(2,2,3-TRIMETHYL-3-	67801-20-1	++ (r.t.)
CYCLOPENTENYL)PENT-4-EN-2-OL		
alpha-PINENE and beta-PINENE	80-56-8 and 127-91-3, resp.	++
PROPYLIDENE PHTHALIDE	17369-59-4	+ (r.t.)
SALICYLALDEHYDE	90-02-8	++

INCI name (or, if none exists, perfuming name according to CosIng)	CAS number	Human evidence: see text
Individual chemicals		
alpha-SANTALOL and beta-SANTALOL	115-71-9 and 77-42-9, resp.	++
SCLAREOL	515-03-7	+
TERPINEOL (mixture of isomers)	8000-41-7	+
alpha-TERPINEOL	10482-56-1 / 98-55-5	
Terpinolene	586-62-9	+
TETRAMETHYL ACETYLOCTAHYDRONAPHTHALENES	54464-57-2 / 54464-59-4 / 68155-66-8 / 68155-67-9	+
TRIMETHYL-BENZENEPROPANOL (Majantol)	103694-68-4	++
VANILLIN	121-33-5	++
Natural extracts		
CANANGA ODORATA and Ylang-ylang oil	**83863-30-3; 8006-81-3**	+++
CEDRUS ATLANTICA BARK OIL	92201-55-3; 8000-27-9	++
CINNAMOMUM CASSIA LEAF OIL CINNAMOMUM ZEYLANICUM BARK OIL	8007-80-5 84649-98-9	++ (r.t.)
CITRUS AURANTIUM AMARA FLOWER / PEEL OIL	8016-38-4; 72968-50-4	++
CITRUS BERGAMIA PEEL OIL EXPRESSED	89957-91-5	+ (r.t.)
CITRUS LIMONUM PEEL OIL EXPRESSED	84929-31-7	++
CITRUS SINENSIS (syn.: AURANTIUM DULCIS) PEEL OIL EXPRESSED	97766-30-8; 8028-48-6	++
CYMBOPOGON CITRATUS / SCHOENANTHUS OILS	89998-14-1; 8007-02-1; 89998-16-3	++
EUCALYPTUS SPP. LEAF OIL	92502-70-0; 8000-48-4	++
EUGENIA CARYOPHYLLUS LEAF / FLOWER OIL	**8000-34-8**	+++
EVERNIA FURFURACEA EXTRACT*	**90028-67-4**	+++
EVERNIA PRUNASTRI EXTRACT*	90028-68-5	+++
JASMINUM GRANDIFLORUM / OFFICINALE	**84776-64-7; 90045-94-6; 8022-96-6**	+++
JUNIPERUS VIRGINIANA	8000-27-9;	++
	85085-41-2	
LAURUS NOBILIS	8002-41-3; 8007-48-5; 84603-73-6	++
LAVANDULA HYBRIDA	91722-69-9	+ (r.t.)
LAVANDULA OFFICINALIS	84776-65-8	++
MENTHA PIPERITA	8006-90-4; 84082-70-2	++
MENTHA SPICATA	84696-51-5	++
MYROXYLON PEREIRAE	**8007-00-9;**	++++
NARCISSUS SPP.	diverse	++
PELARGONIUM GRAVEOLENS	90082-51-2; 8000-46-2	++
PINUS MUGO/PUMILA	90082-72-7 / 97676-05-6	++
POGOSTEMON CABLIN	8014-09-3; 84238-39-1	++
ROSE FLOWER OIL (ROSA SPP.)	Diverse	++
SANTALUM ALBUM	**84787-70-2; 8006-87-9**	+++
TURPENTINE (oil)	**8006-64-2; 9005-90-7; 8052-14-0**	++++
VERBENA ABSOLUTE	8024-12-2	++

Source: SCCS, Opinion on Fragrance allergens in cosmetic products [see http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_o_102.pdf], pages 106-109

Annex 3:

Table 13-4: Fragrance substances categorised as possible contact allergens.
Opinion on fragrance allergens in cosmetic products

INCI name (or, if none exists, perfuming name according to CosIng)	CAS number	Human evidence: see text	EC 3 value (min; %)	SAR
Individual chemicals				
CYCLOHEXYL ACETATE	622-45-7	limited	none	0
ETHYLENE DODECANEDIOATE	54982-83-1	limited	none	0
HYDROXYCITRONELLOL	107-74-4	limited	none	0
METHOXYTRIMETHYLHEPTANO L	41890-92-0	limited	none	0
METHYL p-ANISATE	121-98-2	limited	none	0
METHYL DIHYDROJASMONATE	24851-98-7	limited	none	0
PHENETHYL ALCOHOL	60-12-8	limited	none	0
PHENYLPROPANOL	122-97-4	limited	none	0
AMYLCYCLOPENTANONE	4819-67-4	negative	none	+
BENZYL ACETATE	140-11-4	negative	none	+
6-ETHYLIDENEOCTAHYDRO-5,8-METHANO-2H-BENZO-1-PYRAN	93939-86-7	negative	none	+
3α,4,5,6,7,7α-HEXAHYDRO-4,7-METHANO-1H-INDEN-5(OR 6)-YL ACETATE	54830-99-8	negative	none	+
alpha-IONONE	127-41-3	negative	none	+
beta-IONONE	79-77-6	negative	none	+
METHYL IONONE (mixture of isomers)	1335-46-2	negative	none	+
TERPINEOL ACETATE (Isomer mixture)	8007-35-0	negative	none	+
alpha-TERPINYL ACETATE	80-26-2	negative	none	+
CITRONELLYL NITRILE	51566-62-2	none	none	++
alpha-CYCLOHEXYLIDENE BENZENEACETONITRILE	10461-98-0	none	none	+
DECANAL	112-31-2	none	none	++
DIHYDROMYRCENOL	18479-58-8	none	none	+
3,7-DIMETHYL-1,6-NONADIEN-3-OL	10339-55-6	none	none	++
2-ETHYL-4-(2,2,3-TRIMETHYL-3-CYCLOPENTEN-1-YL)-2-BUTEN-1-OL	28219-61-6	none	none	+
GERANYL ACETATE	105-87-3	none	none	++
HEXAHYDRO-METHANOINDENYL PROPIONATE	68912-13-0	none	none	+
IONONE isomeric mixture	8013-90-9	none	none	+
ISOBERGAMATE	68683-20-5	none	none	+
METHYL DECENOL	81782-77-6	none	none	+
TRICYCLODECENYL PROPIONATE	17511-60-3	none	none	+
OXACYCLOHEXADECENONE	34902-57-3	none	none	++
VERDYL ACETATE	2500-83-6/ 5413-60-5	none	none	+
trans-beta-Damascone	23726-91-2	none	none	+
gamma-Damascone	35087-49-1	none	none	+
Citronellal	106-23-0	none	none	++
Phenethyl salicylate	87-22-9	none	none	++
Natural extracts				
ACORUS CALAMUS ROOT OIL	84775-39-3	Limited	none	
CEDRUS DEODARA WOOD OIL	91771-47-0	Limited	none	
CITRUS AURANTIUM AMARA LEAF OIL	72968-50-4	Limited	none	
CITRUS TANGERINA …	223748-44-5	Limited	none	
CYMBOPOGON NARDUS / WINTERIANUS HERB OIL	89998-15-2; 91771-61-8	Limited	none	
ILLICIUM VERUM FRUIT OIL	84650-59-9	Limited	none	
LAVANDULA SPICA	97722-12-8	Limited	none	
LITSEA CUBEBA	90063-59-5	Limited	none	

INCI name (or, if none exists, perfuming name according to CosIng)	CAS number	Human evidence: see text	EC 3 value (min; %)	SAR
Individual chemicals				
PELARGONIUM ROSEUM	90082-55-6	Limited	none	
SALVIA spp.	Diverse	Limited	none	
TAGETES PATULA	91722-29-1	Limited	none	
THYMUS spp.	84929-51-1	Limited	none	
VETIVERIA ZIZANOIDES	8016-96-4; 84238-29-9	Limited	none	

Source: SCCS, Opinion on Fragrance allergens in cosmetic products [see http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_o_102.pdf], pages 111-113

Annex 4:

Table 13-3: Fragrance substances categorised as likely contact allergens by combination of evidence.

INCI name (or, if none exists, perfuming name according to CosIng)	CAS number	Human evidence: see text	EC 3 value (min; %)	SAR
AMBRETTOLIDE	7779-50-2	limited	none	+
CARVACROL	499-75-2	limited	none	+
Citrus paradisi §	8016-20-4	none	R43	n.a.
CUMINALDEHYDE	122-03-2	limited	none	+
CYCLOPENTADECANONE	502-72-7	limited	none	+
trans-trans-delta-DAMASCONE	71048-82-3	limited	none	+
2,4-dimethyl-3-cyclohexen-1-carboxaldehyde §	68039-49-6	none	R43	+
DIMETHYLTETRAHYDRO BENZALDEHYDE	68737-61-1	limited	none	+
ETHYL VANILLIN	121-32-4	limited	none	+
HELIOTROPINE	120-57-0	limited	none	+
ISOAMYL SALICYLATE	87-20-7	limited	none	++
ISOLONGIFOLENEKETONE	33407-62-4	limited	none	+
Longifolene §	475-20-7	none	R43	+
Mentha arvensis §	68917-18-0	none	R43	n.a.
METHOXYCITRONELLAL	3613-30-7	limited	none	+
METHYL CINNAMATE	103-26-4	limited	none	++
METHYLIONANTHEME	55599-63-8	limited	none	+
5-METHYL-alpha-IONONE	79-69-6	limited	none	+
MYRCENE	123-35-3	limited	none	++
MYRTENOL	515-00-4	limited	none	+
NEROL	106-25-2	limited	none	++
Nerolidol (isomer not specified)	7212-44-4	limited	none	++
NOPYL ACETATE	128-51-8	limited	none	+
PHYTOL	150-86-7	limited	none	+
RHODINOL	6812-78-8	limited	none	+
trans-ROSE KETONE-5	39872-57-6	limited !	none	++
§ Substances/natural mixtures were classified as R43, according to the submission by IFRA. The evidence on which this classification was based was not available to the SCCS, so the validity of classification cannot be assessed. Nevertheless, the four substances/substance mixtures should be treated as likely contact allergens. n.a.: not applicable (natural mixture)				

Source: SCCS, Opinion on Fragrance allergens in cosmetic products [see http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_o_102.pdf], pages 110-111