National Institute for Public Health
and the Environment
Ministry of Health, Welfare and Sport

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Assessment of exposure levels and immune effects

RIVM Letter Report 340301005/2012

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This investigation has been performed by order and for the account of Netherlands Food and Consumer Product Safety Authority (NVWA), within the framework of kennisvraag 9.1.2. Allergene stoffen in geurproducten voor de consument

Abstract

Fragrance allergens in scented consumer products: assessment of exposure levels and immune effects

The National Institute for Public Health and the Environment (RIVM) has been asked to investigate if consumers who use scented products, such as air fresheners are at risk for respiratory allergies. There are currently no validated methods available to assess these risks. In order to gain an indication of the possible risks, the fragrance exposure levels were calculated for consumers using air fresheners. Subsequently, possible effects on immune system of mice were assessed. This research has been conducted by order and for the account of the Netherlands Food and Consumer Product Safety Authority (NVWA).

Scented products often contain fragrance allergens
Twenty-six fragrances are known to be a cause of skin allergy, but it is not known whether or not they can cause respiratory allergy. For this reason, the NVWA sampled 109 scented products to determine which fragrance allergens they contained. Twenty of the 26 fragrance allergens were found in these products, especially the substances limonene and linalool. Subsequently, the RIVM calculated exposure levels for these fragrances when scented products are used. It was shown that trigger sprays and evaporators produce higher levels of exposure than air fresheners and scented blocks. In inhalation studies in mice, it was demonstrated that short-term inhalation of limonene and linalool did not activate the immune system; the fragrance allergen isoeugenol was, however, shown to do so.

The risk for respiratory allergy is small due to low exposure
Exposure to isoeugenol is considerably lower compared to limonene and linalool. This exposure is also lower than exposure to chemicals known to cause respiratory allergies, for example, the diisocyanates that can cause occupational asthma. Based on this comparison, it is not likely that limonene, linalool and isoeugenol will cause respiratory allergies, but due to the lack of a valid test method, this conclusion has been made with reservations. Furthermore, it cannot be excluded that long-term exposure to fragrance allergens in occupational settings might cause respiratory allergy.

Keywords:
fragrance allergens, inhalation, air fresheners, consumer exposure, immune effects

Rapport in het kort

Allergene geurstoffen in geurproducten voor de consument: consumentenblootstelling en immuun effecten

Het RIVM is gevraagd te onderzoeken of consumenten die geurproducten als luchtverfrissers en kamerparfums gebruiken het risico lopen op luchtwegallergieën, zoals astma. Momenteel zijn er echter geen valide methoden beschikbaar om dit gezondheidsrisico in te schatten. Om toch iets over risico's te kunnen zeggen, is berekend in welke mate mensen blootstaan aan allergene geurstoffen bij het gebruik van geurproducten. Vervolgens zijn eventuele reacties op het immuunsysteem in kaart gebracht. Het onderzoek is uitgevoerd in opdracht van de Nederlandse Voedsel en Warenautoriteit (NVWA).

Geurproducten bevatten vaak allergene geurstoffen
Van 26 geurstoffen is bekend dat ze huidallergie kunnen veroorzaken, maar niet of ze luchtwegallergie veroorzaken. De NVWA heeft daarom 109 geurproducten gemeten of ze bekende allergene geurstoffen bevatten. Twintig van de 26 bekende allergene geurstoffen zijn in deze producten aangetroffen, vooral de stoffen limoneen en linalool. Vervolgens heeft het RIVM onder andere de blootstelling berekend voor deze twee stoffen bij het gebruik van geurproducten. Uit deze studie blijkt dat verstuivers en verdampers hogere blootstellingen aan deze geurstoffen veroorzaken dan spuitbussen en geurblokjes. Met behulp van inhalatiestudies in muizen is aangetoond dat een kortdurende inhalatie van limoneen en linalool het immuunsysteem niet activeert. De allergene geurstof isoeugenol doet dat in deze studies wel.

Door lage blootstelling geringe kans op luchtwegallergie
De blootstelling aan isoeugenol is echter aanzienlijk lager dan die aan limoneen en linalool. Ook is deze blootstelling lager dan de blootstelling aan stoffen waarvan luchtwegallergische reacties bekend zijn, de diisocyanaten die beroepsastma kunnen veroorzaken. Op basis van deze vergelijking lijkt het onwaarschijnlijk dat limoneen, linalool en isoeugenol een verhoogd risico op luchtwegallergie geven. Vanwege het gebrek aan valide meetmethoden moet hierbij een slag om de arm worden gehouden. Ook is niet uitgesloten dat een langdurige blootstelling aan allergene geurstoffen in de beroepssfeer wellicht toch luchtwegallergie kan veroorzaken

Trefwoorden:
allergene geurstoffen, inhalatie, geurproducten, consumentenblootstelling, immuuneffecten

Contents

Summary

The use of scented consumer products, such as air fresheners, will lead to inhalation exposure to the emitted ingredients. Important ingredients in these products are fragrance chemicals and 26 such fragrances are potential skin sensitizers that can cause skin allergy. It is unknown if these fragrance allergens can sensitize via this route of exposure as well. The Netherlands Food and Consumer Product Safety Authority (NVWA) initiated a project to evaluate the risk for consumers using these products, with a focus consumer exposure and risk on induction of respiratory sensitization and allergy. Exposure to the fragrance allergens will occur, since the majority are present in scented products. The extent of consumer exposure is unknown since information on product concentrations was lacking.

Recently, the NVWA has performed a market survey and measured concentration levels of 24 fragrance allergens in 109 air fresheners purchased in the Netherlands. The data of this market survey was used to estimate consumer exposure using the computer program Consexpo for four product categories: trigger sprays, spray cans, evaporators and scented blocks. Adverse immune effects were assessed in the respiratory local lymph node assay (LLNA). The fragrances linalool and limonene were selected both for assessment of exposure and adverse immune effects, since these fragrances were most frequently used as ingredients in scented products and average product levels were higher compared to the other fragrances. Isoeugenol was also included in the exposure assessment, because isoeugenol was the only fragrance that induced a positive result in the respiratory LLNA, indicative for a possible adverse immune effect. According to the market survey of the NVWA, isoeugenol is not a common ingredient in scented products, it was detected in 10% of the products and the average product levels were much lower compared to limonene and linalool.

In the exposure assessment, peak and daily air concentrations were calculated for trigger sprays and spray cans and daily air concentrations for evaporators and scented blocks. The use of trigger sprays will result in the highest peak exposure to limonene and linalool. Peak exposure to isoeugenol can only result from the use of trigger sprays, since isoeugenol was not detected in spray cans. Peak exposure to isoeugenol is orders of magnitude lower compared to limonene and linalool. The use of evaporators will give a higher daily exposure than scented blocks for limonene and linalool. Again, calculated exposure levels for isoeugenol are much lower and scented blocks will give a slightly higher exposure than evaporators. In the respiratory LLNA, both limonene and linalool were negative, suggesting that these fragrances chemicals are not able to induce respiratory sensitization after short-term inhalation exposure.

The exposure assessment based on the market survey of the NVWA has shown that the use of scented products will lead to a higher consumer exposure to limonene and linalool than to isoeugenol. The risk on sensitization depends both on exposure and sensitizing potency of a compound. According to the respiratory LLNA, limonene and linalool, both classified as weak skin sensitizers, are probably not capable of inducing respiratory sensitization. The positive result of isoeugenol in the respiratory LLNA might indicate that inhalation exposure is a hazard for respiratory sensitization. The interpretation of this result in relation to the exposure data was complicated since the respiratory LLNA is not a validated animal test and a toxicological reference threshold value for respiratory sensitization is unknown. To at least get a feeling of the magnitude of exposure

in terms of risk a comparison was made with daily occupational diisocyanate exposure levels that were associated with an increased risk on occupational asthma. It was shown that consumer exposure to limonene and linalool caused by the use of evaporators is in the same range or slightly higher daily exposures to diisocyanates. The daily consumer exposure to isoeugenol was considerably lower. Additionally, diisocyanates are stronger potent sensitizers both after dermal and inhalation exposure than limonene, linalool and isoeugenol. Based on exposure levels and sensitizing potencies it was concluded that it is unlikely that consumer exposure to limonene, linalool and isoeugenol could induce sensitization of the respiratory tract after inhalation exposure. It cannot be excluded that in occupational settings or under specific circumstances chronic exposure to fragrance allergens might lead to respiratory sensitization, which has been shown sporadically for other fragrances in occupational settings.

Samenvatting

Consumenten die gebruik maken van geurproducten, zoals luchtverfrissers, zullen via de luchtwegen worden blootgesteld aan de ingrediënten die hieruit vrijkomen. Geurstoffen zijn belangrijke ingrediënten in deze producten en 26 geurstoffen zijn geïdentificeerd als huid sensibiliserende stoffen, die huid allergie kunnen veroorzaken. Het is onbekend of inademing van deze allergene geurstoffen kan leiden tot sensibilisatie van de luchtwegen. In opdracht van de Nederlandse Voedsel en Warenautoriteit (NVWA) heeft het RIVM onderzocht of consumentenblootstelling aan allergene geurstoffen een verhoogd risico geeft op sensibilisatie en allergie van de luchtwegen. Voorgaand onderzoek heeft aangetoond dat het gebruik van geurproducten leidt tot blootstelling, aangezien de meerderheid van de allergene geurstoffen aanwezig is in deze producten. De mate van blootstelling is onbekend, omdat er onvoldoende informatie beschikbaar was over product concentraties.

De NVWA heeft recent een studie uitgevoerd waarin de concentraties van 24 allergene geurstoffen gemeten zijn in 109 luchtverfrissers verkregen via Nederlandse winkels. De gegevens uit het NVWA meetrapport zijn gebruikt om consumentenblootstelling te berekenen met behulp van het Consexpo-computerprogramma voor vier product categorieën: spuitbussen, verstuivers, verdampers en geurblokjes. Ongewenste effecten op het immuunsysteem zijn bepaald in de respiratory local lymph node assay (LLNA). De geurstoffen linalool en limoneen werden het meest frequent en in de hoogste concentraties gedetecteerd in de bemonsterde luchtverfrissers. Deze allergenen geurstoffen zijn daarom meegenomen in de berekening van consumentenblootstelling en in de respiratory LLNA. Ook voor isoeugenol is de consumentenblootstelling bepaald, omdat deze geurstof als enige een positief effect veroorzaakte in de respiratory LLNA, wat kan duiden op een mogelijk risico op een ongewenste immuunstimulatie na inhalatie. Volgens het meetrapport van de NVWA wordt isoeugenol weinig gebruikt in luchtverfrissers en in lagere concentraties dan limoneen en linalool.

In het bepalen van de consumentenblootstelling zijn piek en dagelijkse luchtconcentraties berekend voor de spuitbussen en verstuivers en dagelijkse luchtconcentraties voor verdampers en geurblokjes. Het gebruik van verstuivers leidt tot de hoogste piek bloostelling voor limoneen en linalool. Piek bloostelling aan isoeugenol kan alleen veroorzaakt worden door het gebruik van verstuivers, aangezien isoeugenol niet gedetecteerd is in spuitbussen. Piek blootstelling aan isoeugenol is aanzienlijk lager dan piekblootstelling aan limoneen en linalool. De dagelijkse blootstelling aan limoneen en linalool is hoger voor verdampers dan voor geurblokjes. Voor isoeugenol geldt dat geurblokjes een iets hogere dagelijkse blootstelling veroorzaken dan verdampers. De berekende luchtconcentraties liggen wederom een stuk lager voor isoeugenol. Limoneen en linalool waren beide negatief in de respiratory LLNA, wat er op kan duiden dat deze allergene geurstoffen geen sensibilisatie induceren na kortdurende inhalatie blootstelling.

De consumentenblootstelling die is berekend op basis van de meetgegevens van de NVWA toont aan dat het gebruik van geurproducten leidt tot een hogere blootstelling aan limoneen en linalool dan aan isoeugenol. Het risico op sensibilisatie hangt af van zowel de blootstelling als de sensibiliserende potentie van een stof. Op basis van de uitkomsten van de respiratory LLNA, lijken limoneen en linalool niet in staat om respiratoire sensibilisatie te veroorzaken.

Het zijn ook zwak potente huid sensibiliserende stoffen. Het effect van isoeugenol in de respiratory LLNA geeft aan dat na inhalatie er een mogelijk risico is op sensibilisatie. De interpretatie van deze resultaten in relatie tot de blootstellingsgegevens is lastig, omdat de respiratory LLNA geen gevalideerde test is en er geen toxicologische drempelwaarde bekend is voor respiratoire sensibilisatie. Om een gevoel te krijgen van de mate van blootstelling in relatie tot het risico op sensibilisatie is een vergelijking gemaakt met dagelijkse blootstelling aan diisocyanaten op de werkvloer die geassocieerd was met een verhoogd risico op astma. De berekende dagelijkse blootstelling aan isoeugenol veroorzaakt door gebruik van verdampers was aanzienlijk lager dan de blootstelling aan diisocyanaten. Tevens is de sensibiliserende potentie van isoeugenol veel lager dan die van de diisocyanaten. Het is onwaarschijnlijk dat consumentenblootstelling aan isoeugenol zal leiden tot sensibilisatie van de luchtwegen. Het kan echter niet worden uitgesloten dat langdurige blootstelling in de beroepssfeer of onder bijzondere omstandigheden wellicht toch tot respiratoire allergie kan leiden, zoals sporadisch is aangetoond na beroepsblootstelling aan allergene geurstoffen.

1 Background

In the past years, the Netherlands Food and Consumer Product Safety Authority (NVWA) observed an increased number of scented consumer products on the market. Important ingredients in these consumer products are fragrance chemicals and twenty-six such chemicals are potential causes of allergic contact dermatitis, i.e. skin allergy. The majority of these 26 fragrance allergens is present in scented products as well (Ezendam *et al*., 2009b). Consumers that use these products will be exposed via the airways to these fragrance allergens. It is unknown if inhalation of fragrance allergens can induce respiratory allergies as well. The NVWA has initiated a project to evaluate the risks for consumers using these scented products. The outcomes of this research have been published in a RIVM report recently (Ezendam *et al*., 2011).

The main conclusion of this RIVM report was that it is currently not possible to estimate this risk, due to numerous uncertainties and knowledge gaps in the field of chemical respiratory sensitization. The most important issues were the absence of a well validated or widely accepted test method for prospective identification of chemicals with the potential to induce sensitization of the respiratory tract. Additionallly, the knowledge on exposure parameters that determine the risk on sensitization is limited. To study effects of inhalation exposure to fragrance allergens, the respiratory local lymph node assay (LLNA) was used. This assay is not validated but can be used to evaluate immune effects of short-term inhalation exposure. A positive result might indicate a possible hazard on respiratory sensitization (Arts *et al*., 2006). In this assay isoeugenol induced a positive response, whereas cinnamal, benzyl salicylate, methyl heptine carbonate and citral were negative (Ezendam *et al*., 2009a).

If consumers are at risk depends not only on the potential of chemicals to induce respiratory sensitization but also on the level of exposure. A previous literature survey conducted within this project has shown that the majority of the known fragrance allergens were present in scented products. Hence, the use of scented products leads to exposure to these fragrance chemicals. The exact level of exposure could not be estimated due to the limited availability of concentration levels in scented products (Ezendam *et al.*, 2009b). A recent market survey conducted by the NVWA offered the opportunity to estimate consumer exposure to scented products. The NVWA sampled 109 air fresheners from Dutch stores and measured concentrations of 24 fragrance allergens. The fragrance allergen mixtures oak moss and tree moss were not included in this survey. The information of this market survey has been used in the current report to estimate consumer exposure to isoeugenol, limonene and linalool in four categories of scented products. These fragrances were selected since limonene and linalool were the most frequently used fragrance allergens in scented products. Isoeugenol was the only positive chemical in the respiratory LLNA. Additionally, the effects on the immune system of limonene and linalool were evaluated in the respiratory LLNA.

In this report the outcomes of the exposure assessment and respiratory LLNA are described. To at least get a feeling of the magnitude of exposure, calculated air concentrations of the fragrances were compared to exposure concentrations of diisocyanates that were associated with an increased risk on occupational asthma (Pronk *et al.*, 2007).

2 Approach

2.1 Market survey NVWA

The NVWA has measured the levels of 24 fragrance allergens in 109 scented products. The products were categorized in four main categories:

- spray cans (aerosols) (n = 37);
- trigger sprays (pump or trigger mechanism) (n = 13);
- evaporators (n = 38);
- scented blocks (n = 18).

Three remaining products could not be placed in either category and were excluded from further analyses. Of the 24 fragrance allergens, 20 were indeed detected in the scented products tested. The fragrances methyl eugenol, anisyl alcohol, farnesol and amyl cinnamyl alcohol were not detected. The percentages of products that contain a fragrance allergen together with the average and maximum concentration per product category are summarized in Appendix 1. It was shown that the most frequently used fragrances were linalool (in 87% of the scented products), limonene (69%), and geraniol (50%).

2.2 Selection of fragrance allergens

Of the 20 measured fragrance allergens three fragrance allergens were selected for exposure assessment. The fragrances linalool and limonene were selected, since these substances were most frequently used as ingredients in scented products and average product levels were higher compared to the other fragrances. Next to limonene and linalool, isoeugenol was also included in the exposure assessment, because isoeugenol tested positive in the respiratory LLNA (Ezendam *et al.*, 2007; Ezendam *et al.*, 2009a).

2.3 Exposure assessment of fragrance allergens in scented products

The NVWA has measured concentrations of fragrance allergens in spray cans, trigger sprays, evaporators and scented blocks. Each type of scented product is characterized by its release pattern, where spray applications (spray cans and trigger[1] sprays) have high initial release to the air that diminishes over time whereas room perfumes (evaporators and scented blocks) have slow long lasting releases (Table 1). The chemical characteristics for the three substances are listed in Table 2.

Table 1 Applications, scent release patterns and relevant exposure scenario

Product type	Product category	Scent release pattern	Relevant exposure
Air freshener	Spray can	Peak	event concentration
Air freshener	Trigger spray	Peak	event concentration
Room perfumes	Evaporator gel, liquid	Constant	daily concentration
Room perfumes	Scented block	Constant	daily concentration

[1] A trigger spray is a spray application that requires the user to activate the spraying by pulling the trigger or by using a spray pump. Pump sprays, such as a typical eau de toilette, is also covered by trigger sprays in this report.

Table 2 Chemical properties and skin sensitizing potency of limonene, linalool and isoeugenol

	Limonene	Linalool	Isoeugenol
Chemical properties			
Mol weight (g/mol)	136.23	154.2	164.2
Log Kow	4.23	2.97	3.04
Vapour pressure (Pa)	190	21	0.7
Skin sensitizing potency			
EC3 (%, LLNA)*	10-69%	30-46%	1.5%
Human Category	weak	extremely weak	moderate

Sources: Limonene: CICADS; Linalool: IPCS; Isoeugenol: chembook.com and chemspider.com (visited July 28th 2011).
* Skin sensitizing potency is expressed as the EC3 value, which is the concentration needed to induce a stimulation index of 3 (Skold et al, 2004, RIFM, 2012, Wijnhoven et al. 2008).

The concentration of fragrances in products does not provide information on the actual exposure via inhalation of the consumer. Therefore a number of exposure calculations have been performed. The exposure assessment was performed using ConsExpo 4.1 (www.consexpo.nl) for the spray applications and evaporator. As ConsExpo is not suitable for estimating release of substances from solid matrices, such as scented blocks, the exposure assessment was performed with an emission model (downloadable at www.consexpo.nl - emission model).

It is currently unknown which determinants are the most important in the risk of becoming sensitized by respiratory sensitizers. For example, the impact of prolonged exposure to low concentrations compared to a single peak exposure is unknown. For this reason exposure assessments were performed for the following:

- Per product category an exposure assessment was carried out for the three selected substances, including estimates for the air concentration per event (not for scented products as the emission model does not provide this output), and the air concentration per day. It is assumed that the product always contains the fragrance allergen of interest; zero measurements are therefore not included.
- In case of spray products, i.e. spray cans and trigger sprays, two different exposure models have been considered, i.e. the spray model and the exposure to vapour - instantaneous release model of ConsExpo 4.1. The 'exposure to spray' model describes the exposure to non-volatiles, wherein the model assumes that volatiles are evaporated immediately, leaving only aerosols. The instantaneous release model assumes that all substance is released at once, which is a reasonable worst case assumption considering the very fast evaporation of volatiles from aerosols during the spray process. The decision on which of the two models to use is based on the volatility of the substance, hence the vapour pressure is shown in Table 2. Although there is no set rule to decide whether or not the spray model should be used (all substances are in a somewhat grey area), with careful consideration it is thought that only isoeugenol would 'act' as an aerosol particle due to its relatively low vapour pressure, hence the spray model would apply. Whereas the two other substances limonene and linalool are considered volatile thus more likely available in vapour form, which is then best described by the instantaneous release model.

Exposure scenarios have been described previously (Park et al. 2006), which partly are adopted in this report. Park et al. described two ways of exposure, i.e. by exposure to sprays and to passive room perfumes. In principle, the exposure to sprays scenario can be used for spray cans and trigger sprays, which was complemented by the exposure to vapour model as discussed below. The scenario for passive room perfumes can be used for evaporators and scented blocks. The scenarios need some refinement because of the more specific categorisation of products used in this assessment. The exposure scenarios and input parameters are described in sections 3.1. to 3.4.

2.4 Respiratory LLNA

In the respiratry LLNA, effects of inhalation of limonene and linalool were assessed. These fragrances are weak skin sensitizers, based on their potency determined in the LLNA and on human data (Table 2). Importantly, experimental studies have shown that the sensitizing potency of both limonene and linalool can increase considerably when these chemicals auto-oxidize in more reactive chemicals (Christensson et al., 2008, Karlberg et al., 1994, Skold et al., 2004).
The test was performed as described previously (Arts *et al.*, 2008). In short, groups of male BALB/c mice (six animals per group) were exposed nose-only to limonene or linalool on three consecutive days for 45, 90, 180, or 360 min/day. Control mice were exposed to the vehicle (acetone) for 360 min/day. The fragrances were nebulized in acetone. Both for limonene and linalool the partial vapour pressure was high enough and both fragrances were present as vapour and not as aerosols. An exposure level of 75 mg/m^3 was selected similar to previous experiments with fragrance allergens (Ezendam *et al.*, 2011). During the experiments, the actual exposure was 80 mg/m^3 for limonene and 81 mg/m^3 for linalool. The animals were sacrificed three days after the last exposure and the mandibular lymph nodes were excised, pooled for each animal, and single cell suspensions were prepared. Cell proliferation was measured using [^{3}H]-Thymidine incorporation and is expressed per animal. The mean [^{3}H]-thymidine incorporation per experimental group ± SEM was calculated. Stimulation indices (SI) were calculated by dividing the [^{3}H]-thymidine incorporation of the experimental group with the mean [^{3}H]-thymidine incorporation of the vehicle group.

3 Exposure assessment

3.1 Exposure to spray cans

Sprays can be used throughout the house, such as in the bedroom and bathroom. Their use is to mask unpleasant odours. The spray perfumes can be used as an application in the air or on furniture, resulting in different exposure scenarios. The focus lies on application as air space use, because inhalation exposure is more relevant for that specific use. As a reasonable worst case scenario the use of an air spray in a small bathroom is considered.

The exposure is calculated using the ConsExpo 4.1 'exposure to vapour-instantaneous release' model for limonene and linalool (see section 2.3). Isoeugenol was not detected in spray cans in the measurements performed by the NVWA. The model requires input values on environmental settings and product characteristics. The environmental setting is the bathroom with a room volume of 10 m^3 and a room ventilation of 2 h^{-1}. The product characteristics are derived from NVWA measurements, i.e. concentrations for each substance separately are inserted as lognormal distribution (geometric means and standard deviation. The amount used is estimated by multiplying the spray duration (1 second) with the mass generation rate, i.e. 1.5 g. Experimental results of a study on spray cans and trigger sprays demonstrated that the mass generation rate for air refresher spray cans ranged from 1 – 2 g/sec (Delmaar and Bremmer, 2009). A mass generation rate of 1.5 g/s was taken as default value.

Table 3 Input parameters for spray cans for the exposure to vapour

Input parameter	Vapour model
amount used (g)	1.5
room volume (m^3)	10
room ventilation (1/h)	2
Use frequency (1/d)	5
Exposure duration (min)	10

Based on the spray can scenario the following air concentrations were obtained for limonene and linalool based on exposure to vapour (Table 4).

Table 4 Calculated air concentrations (mg/m^3) for use of spray cans (instantaneous release model)

		Limonene	Linalool
weight fraction in product	median	0.01	0.007
	C.V.	2.14	2.1
Average (event)		1.28	0.893
st. dev. (event)		0.168	0.153
90th percentile		7.18	4.56
Average (day of exposure)		0.0443	0.031
st. dev. (day of exposure)		0.0060	0.00373
90th percentile		0.241	0.159

The event air concentrations represent the average or 90th percentile values during an event, in this particular case 10 mins (= exposure duration). These event concentrations represent an approximation of the peak concentration.
The 'day of exposure' air concentration represent the average or 90th percentile air concentration during the day (24hours) taking into account the frequency of use. In this case the product is used 5 times and thus 5 events will occur. The total substance release from 5 events is spread out over the day giving the average (or 90th percentile) air concentration over 24 hours.

3.2 Exposure to trigger sprays

Trigger sprays are often used to mask unpleasant odours and are almost exclusively used in bathrooms and toilets. The trigger sprays differ from spray cans in a sense that in general they contain slightly higher concentrations of fragrance allergens, are used in smaller packages (typically 10 mL), and generate larger droplets. The same scenario is considered for trigger sprays as is considered for exposure to spray cans, where only the product characteristics and use will be adjusted. The mass generation rate for trigger sprays is assumed to be the same as for spray cans, i.e. 1.5 g/s. The exposure to limonene and linalool is calculated with the Exposure to vapour: instantenous release model (see section 2.3). The exposure to isoeugenol, which is less volatile, is calculated using the Exposure to spray: spray model (see section 2.3). Additional parameters such as the particle size distribution and airborne fraction are needed. The particle size distribution and airborne fractions are different for trigger sprays compared to spray cans, which generally release larger aerosols and thus lower fractions are available for inhalation. However, as no recent measurement data are available for trigger spray air refresheners the same particle distribution was assumed as for spray cans, i.e. a median of 3.9 μm and a coefficient of variation (C.V.) of 0.65 (Delmaar and Bremmer, 2009). This choice seems worst case, but is supported by a similar particle distribution found for eau de toilette (median 2.7, C.V. 0.73). The airborne fraction of an eau de toilette was assumed to be applicable and an airborne fraction of 0.02 was used for the calculation (Delmaar and Bremmer, 2009).

Table 5 Input parameters for trigger sprays for the spray model and exposure to vapour model

Input parameter	Spray model	Vapour model
amount used (g)	1.5	1.5
room volume (m^3)	10	10
room ventilation (1/h)	2	2
Use frequency (1/d)	5	5
Exposure duration (min)	10	10
Airborne fraction	0.02	-
inhalation cut-off (µm)	15	-
spray duration (s)	1	-
median particle size distribution (C.V.) (in µm)	3.9 (0.65)	-

Table 6 Calculated air concentrations (mg/m3) for use of trigger sprays

		Limonene[a]	Linalool[a]	Isoeugenol[a]
Weight fraction in product	median	0.064	0.395	0.002
	C.V.	1.66	0.725	(one sample)
Average (event)		2.72	16.8	0.00152
st. dev. (event)		0.187	0.453	-
90^{th} percentile		11.3	39.3	-
Average (day of exposure)		0.0945	0.583	0.0000526
st. dev. (day of exposure)		0.0077	0.0155	-
90^{th} percentile		0.435	1.32	-

[a]Instantaneous release model: limonene and linalool; spray model: isoeugenol

3.3 Exposure to evaporators

Evaporators are generally used as room perfumes, which can be used throughout the house (including the bedroom) or in cars. Evaporators are developed so that slow release and long-lasting pleasant odours are ensured. The amount of product in a passive room perfume in the form of a gel or liquid ranges from 6 – 375 mL. The product is released over a several weeks, ranging from 4 – 8 weeks. The product amount released in a day can therefore range from 0.1 - 5 grams per day, assuming a specific weight of approximately 1 g/cm^3. The ConsExpo model 'exposure to vapour - evaporation' can be used as it includes evaporation from liquid surfaces.

Two examples of realistic worst case exposure scenarios are:

1) A person spends all day in a living room with a passive room perfume.
2) A person spends part of the day in a car with a passive room perfume. This scenario will not be calculated because of lacking information about environmental settings and the likely influence of active release of substance by using the car's ventilation.

The use of a room perfume in the living room is thus considered. The environmental settings of the living room are 58 m^3 and 0.5 h^{-1}. Product use is the wearing out of an entire product, i.e. 375 mL or g assume a density of 1 g/cm^3. The exposure duration is set at four weeks (worst case), which is equal to an application duration of 672 hours. The release area is estimated at 30 cm^2. The evaporation model further requests data on the mass transfer rate (measure for release from matrix) and the molecular weight of the matrix. By default the Langmuir method is used to determine the mass transfer rate (worst case) and 3000 g/mol was taken forward as molecular weight matrix (default for liquids and gels).

Table 7 Calculated air concentrations (mg/m^3) for use of evaporators

		Limonene	Linalool	Isoeugenol
Weight fraction in product	median	0.044	0.097	0.013
	C.V.	2.09	1.899	1.579
Average (day of exposure)		0.846	1.15	0.0132
st. dev. (day of exposure)		0.0869	0.00184	0.0004
90th percentile		4.72	1.9	0.0362

The 'day of exposure' air concentration describes the average or 90th percentile of the air concentration during the day (24hours) taking into account the frequency of use.

As a person will normally not stay in a living room for 24 hours per day the resulting air concentrations should not be viewed as a direct surrogate for exposure as no correction for exposure duration has taken place.

3.4 Exposure to scented blocks

Scented blocks are generally used as room perfumes, which can be used throughout the house (including the bedroom) or as toilet perfumes. Scented blocks are developed so that slow release and long-lasting pleasant odour are ensured. They are very similar to liquid or gel evaporators and may be used interchangeably for the same purpose. The product sizes reported in the measurements were all 150 g. Release area and environmental settings were set the same as for evaporators.

To describe emission from solid materials an emission model was used to determine the air concentrations of the fragrance allergens. The emission model as described in Zhao et al. 1999 was used. Emission of a substance from solid materials is dependent on the diffusion of the substance through the material and the mass transfer rate from the material to the air (often described by a partition coefficient). Such parameter values are not commonly available thus the data and methods described in Delmaar (2011) were used for this purpose. The diffusion coefficient for substances in a similar range of molecular weights that are used in similar matrices were considered. They ranged from 1×10^{-14} to 1×10^{-10} m^2/s. As a worst case the upper value was used. The partition coefficient was calculated using either Raoult's law or an equation based on empirical data (Delmaar, 2011). The results proved to be rather insensitive to changes in the partition coefficient and therefore the results from the equation were used.

The model only allowed inserting deterministic data and therefore the median weight fraction was used in the calculations.

Table 8 Calculated air concentrations for use of scented blocks

		Limonene	Linalool	Iso-eugenol
Weight fraction in product	median	0.012	0.022	0.0039
	C.V.	1.041	1.732	0.116
Diffusion coefficient (m^2/s)		1×10^{-10}	1×10^{-10}	1×10^{-10}
Partition coefficient (air-material)		88	796	23886
Average (day of exposure/entire duration) (mg/m^3		0.055	0.11	0.019

The average air concentration describes the more-or-less steady state release of substances from the scented blocks during its entire use. This equals the average air concentration per day as the equilibrium is reached relatively fast.

3.5 Summary

Table 9 summarizes the exposure in terms of air concentrations over the event (peak exposure) or during the day for the different product categories.

Table 9 Summary of the average (realistic worst case) air concentrations (mg/m^3) for the different substances and uses

	Limonene	**Linalool**	**Isoeugenol**
Spray cans			
- event	1.28	0.893	-
- day exposure	0.0443	0.031	-
Trigger spray			
- event	**2.72**	**16.8**	0.00152
- day exposure	0.0945	0.583	0.00005
Evaporator			
- day exposure	**0.846**	**1.15**	0.0132
Scented block			
- day exposure	0.055	0.11	**0.019**

Highest values derived per substance are given in bold. Note that for limonene and linalool two values are bold, dependent on the peak (event) or constant (day exposure) exposure.

- The highest air concentrations for peak exposure were found for limonene and linalool in trigger sprays (top bold values in Table 9). This can be explained by the fact that the weight fractions of the substances (limonene and linalool) are higher in trigger sprays than in spray cans.
- For isoeugenol, peak exposures can only occur for trigger sprays, since isoeugenol was not detected in spray cans. The peak exposure is very low compared to the other two fragrances.
- It was expected that evaporators and scented blocks would lead to relatively high daily air concentrations, since the release of fragrances is continuous and prolonged. This was confirmed by the exposure assessment in which it was shown that evaporators give rise to the highest daily air concentrations for limonene and linalool. For isoeugenol a slightly higher air concentrations was calculated for scented blocks compared to evaporators. On the contrary, for limonene and linalool this conclusion does not hold true for scented blocks, the daily air concentration was lower than that of trigger sprays. This might be explained by the higher weight fractions in trigger sprays and the assumption of instantaneous release (factor 10 higher) in contrast to the probably slow release of limonene and linalool from scented blocks.

- For isoeugenol, use of scented blocks leads to a higher daily air concentration compared to trigger sprays, despite higher weight fraction in the trigger spray. The calculations are based on the spray model and in this model not all released substance becomes available for inhalation (see below).

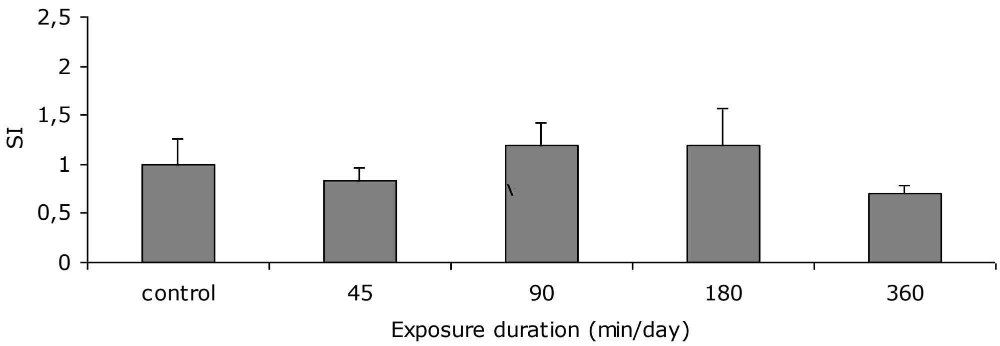
It should be noted that the results for the spray applications are subject to model uncertainties, where it has been assumed that the more volatile substances were described best with the instantaneous release model. The instantaneous release model assumes that all substance is released immediately and is available for inhalation. Therefore, the air concentrations are based solely on the amount sprayed and the weight fractions (considering that environmental settings were kept the same). Much lower event concentrations would have been obtained when the spray model was used for limonene and linalool as well. In that case removal of substance from the air is also dependent on gravitational movement by the aerosols besides removal by ventilation. Vice versa, if isoeugenol air concentrations were simulated using the instantaneous release model, then a much higher concentration would have been found. A difference in the air concentrations derived with the instantaneous release model compared to those obtained with the spray model could amount up to a factor of 56 (data not shown).

Also parameter input is subject to uncertainties, although the influence thereof on the comparison of the results has been reduced as much as possible by consistently using realistic worst case estimations for the input. The input data for the spray applications are predominantly based on spray experiments and are therefore relatively robust, except for the product specific particle size distribution (only used for isoeugenol). Using the information from a comparable product as input for the particle size distribution is an acceptable approach, however provides no input on the amount of uncertainty. Information on product amounts, use durations and release areas of evaporators and scented blocks had to be estimated. Especially, the product amount and use duration are of major influence and were kept the same as much as possible for comparison purposes. Unfortunately, information is lacking on for instance the mass transfer rate (evaporation model) air-material partition coefficients and diffusion coefficients (emission model). The air-material partition coefficient proved to be rather insensitive to changes, however, the diffusion coefficients found in literature range several orders of magnitude and can have signicifant influence on the outcome. The results for scented blocks are therefore considered to be more uncertain than the other results.

4 Immune effects after inhalation: respiratory LLNA

Limonene and linalool were tested in the respiratory LLNA to assess effects of inhalation exposure on the immune system. Cell proliferation in the mandibular lymph nodes was assessed as a read-out for immunostimulation. Exposure to linalool did not increase cell proliferation in the mandibular lymph nodes at any of the exposure times (Figure 1A). Similarly, limonene did not increase cell proliferation, although a slight increase in cell proliferation is observed for 45 minutes exposure per day (Figure 1B). This increase was not statistically significantly different compared to the control group.

A



B

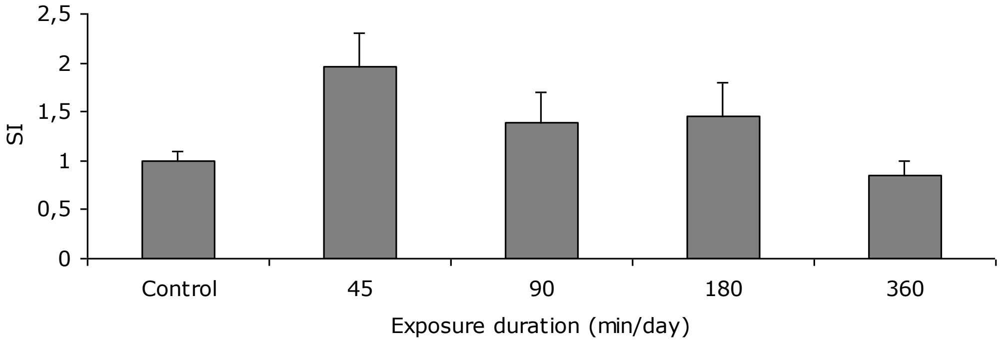


Figure 1.Stimulation indices in the mandibular lymph nodes in the respiratory LLNA.
Mice were exposed to 75 mg/m^3 Linalool (A) or limonene (B) on three consecutive days. Exposure duration increased from 45 to 360 minutes per day (min/day). SI values were calculated by dividing the [^{3}H]-thymidine incorporation (cpm) of the experimental group with the mean [^{3}H]-thymidine incorporation of the control group.

5 Discussion

This study has demonstrated that consumers who use scented products will more likely be exposed to limonene and linalool than to isoeugenol, since these fragrances are used more frequently and in higher concentrations than isoeugenol. Air concentrations were calculated for different types of scented products and it was shown that the use of trigger sprays will lead to the highest peak exposure to limonene and linalool compared to spray cans. Peak exposure to isoeugenol, which is being used as an ingredient in spray cans and not in trigger sprays, is much lower compared to linalool and limonene. The use of evaporators will give the highest daily exposure for limonene and linalool. For isoeugenol scented blocks will result in a slightly higher daily exposure than the use of evaporators. Again, compared to limonene and linalool, air concentrations are low. Furthermore, the use of evaporators will give rise to a high exposure during the day that approximates the peak exposures of spray cans.

The outcomes of the market survey of the NVWA are in line with previous studies, showing that limonene and linalool were the most frequently used fragrances in scented products (Ezendam *et al.*, 2009b, Pors J & Fuhlendorff R, 2003). Until now, information on emission of fragrance allergens from scented products was limited. In a study performed by the BEUC (Bureau Européen des Consommateurs) actual indoor air concentrations of fragrances were measured after spraying air fresheners in an empty closed room. Similar to our results, the highest concentrations were measured for limonene followed by linalool and isoeugenol was not detected. For limonene indoor air concentrations up to 2.0 mg/m^3 were measured, which is in line with the calculated event concentrations in spray cans and trigger sprays (1.3 and 2.7 mg/m^3 respectively). For linalool the indoor air concentration of the BEUC study was 0.13 mg/m^3 which is in line with the peak concentrations of spray cans (0.89 mg/m^3), but much lower than the peak concentration of trigger sprays (16.8 mg/m^3). It is unknown which types of air fresheners were used in the BEUC study, which impairs the comparison with our study. Additionally, the ventilation rate of the room was unknown, but likely to be low since the room was closed (BEUC, 2005; SCHER, 2006). Despite the differences between the studies, the calculated air concentrations which are based on worst-case-scenarios are for limonene in the same order of magnitude as the measured indoor air concentrations.

The absence of a toxicological reference threshold value for respiratory sensitization makes it impossible to determine if the air concentrations of limonene, linalool and isoeugenol should be considered as high in terms of sensitization risk. To at least get a feeling of the magnitude of exposure in relation to the risk a comparison was made with exposure levels of diisocyanates, well-known respiratory sensitizers, which are associated with an increased risk on occupational asthma. Pronk et al. (2007) measured air concentrations of 23 diisocyanates and compared the total exposure level of this mixture with the occurrence of asthma and other respiratory complaints in spray painting industry. Workers were exposed to levels ranging from 0.004 to 66.4 mg/m^3 x hour (concentration-time product) per month. The median value of 3.682 mg/m^3 x hour per month is considered to be the cumulative dose in the period of a month. Exposure to diisocyanates was associated with a 1.2-fold increased risk on asthma and the risk increased dose-dependently. The authors stated that due to variation in tasks a reliable average daily concentration cannot be derived and would be driven predominantly by peak concentrations for certain tasks. For comparison purposes only, an estimate of the median daily concentration (over 24 hours) was derived by taking the median value of 3.682 mg/m^3 x hour per month divided by the 82 working-hours[2] equals a daily exposure of 0.045 mg/m^3. In a worst case scenario the maximum level should be taken into account leading to an upper level of the average daily concentration of 0.81 mg/m^3. It was not possible to derive peak exposures from the study of Pronk et al. (2007) and therefore only the calculated daily exposures to evaporators and scented blocks were compared to diisocyanaten exposure. To simplify the comparison to exposure to fragrance allergens from consumer products, we assume that exposure to the median daily air concentrations of 0.045 mg/m^3 and 0.81 mg/m^3 for diisocyanates increase the risk on asthma-like symptoms. The comparison is made with calculated air concentrations for evaporators, since these products give rise to the highest daily exposure. For limonene and linalool, daily air concentrations, which are based on a worst case scenario, exceed the maximum level of diisocyanates, whereas for isoeugenol the daily exposure is considerably lower.

In order to state whether or not air concentrations of fragrances are high or low, information on their respective sensitizing potencies is required. The potency of sensitizers is important in the risk of respiratory sensitization since it is expected that strong sensitizers will induce sensitization at lower concentrations than weak sensitizers. Based on LLNA and human data limonene and linalool are categorized as weak skin sensitizers and isoeugenol as a moderate sensitizer (Table 2). Auto-oxidation due to air exposure can increase the sensitizing potency of limonene and linalool as has been shown in experimental studies (Christensson et al., 2008, Karlberg et al., 1994, Skold et al., 2004). To what extent this actually occurs in cosmetic or scented products is unknown, making it difficult to estimate the relevance of auto-oxidation for consumer exposure (SCCS, 2012). Thus in absolute sense the air concentrations of limonene and linalool appear to be high, in terms of risk for respiratory sensitization they are probably not, since these weak skin sensitizers were negative in the respiratory LLNA. Exposure to isoeugenol is much lower, but isoeugenol induced a positive response in the respiratory LLNA, but the sensitizing potency compared to diisocyanates is much lower. The EC3 value of isoeugenol is about 15-fold lower compared to diisocyanates, with reported EC3 values of 0.1 and 0.3% for toluene diiocyanate and diphenylmethane diisocyanate respectively) (Van Och et al., 2000, Corsini et al., 2009). Similarly, in the respiratory LLNA the ED3 value of isoeugenol was about 32-fold lower than the tested diisocyanates (Arts et al., 2006). The ED3 value is the respiratory exposure dose that induced a three-fold increase of cell proliferation compared to control value). If this value can be used as a measure for respiratory sensitizing potency is unknown, since human potency data are lacking (Van Amsterdam et al., 2011). The potency does, however, give an indication that the amount of diisocyanates required to induce an immune response after inhalation exposure is much lower compared to isoeugenol.

In conclusion, limonene and linalool are frequently used as ingredients in scented consumer products but are probably not able to induce respiratory

[2] The reported concentration-time products reported by Pronk et al. (2007) are given over the period of one month, which includes an average of 82 hours.

sensitization. Similarly, linalool and limonene are the most frequently used fragrances in cosmetics, but they rarely cause allergic contact dermatitis. This has been explained by the fact that although skin exposure to these fragrances is common, they are weak skin sensitizers (Schnuch *et al.*, 2007; Wijnhoven *et al.*, 2008). The respiratory LLNA has identified isoeugenol as a potential sensitizer. In comparison to diisocyanates, exposure levels and sensitizing potency of isoeugenol are lower. It therefore not likely that isoeugenol will induce respiratory allergies in consumers using scented products that contain this fragrance. It should be noted that although the risk for consumers is probably low, the way consumers use these products might have an impact on actual exposure, i.e. do they use scented products on a daily base, how long are they exposed, in which rooms do they use the scented products, and do consumers use multiple products at the same time. In occupational settings or under specific circumstances, it cannot be excluded that chronic exposure might lead to respiratory sensitization, which has been shown sporadically for other fragrances in occupational settings as well (Baur *et al.*, 1999; Guarneri *et al.*, 2008; Quirce *et al.*, 2008).

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References

1. Arts JHE, De Jong WH, De Klerk A, van Loveren H, Woutersen RA & Kuper CF (2006) The respiratory local lymph node assay (LLNA) as a tool to study respiratory sensitisers. Toxicol. Letters 164S, S109-110.
2. Arts JHE, de Jong WH, van Triel JJ, Schijf MA, de Klerk A, van Loveren H & Kuper CF (2008) The Respiratory Local Lymph Node Assay as a Tool to Study Respiratory Sensitizers. Toxicol. Sci. 106, 423-434.
3. Baur X, Schneider EM, Wieners D & Czuppon AB (1999) Occupational asthma to perfume. Allergy 54, 1334-1335.
4. BEUC (2005) The European Consumers Organisation. Emission of chemicals by air fresheners - Tests on 74 consumer products sold in Europe.
5. Christensson J B, Johansson S, Hagvall L, Jonsson C, Borje A, Karlberg A T. (2008). Limonene hydroperoxide analogues differ in allergenic activity. Contact Dermatitis 59: 344-52.
6. Corsini, E., Mitjans, M., Galbiati, V., Lucchi, L., Galli, C.L., Marinovich, M., 2009. Use of IL-18 production in a human keratinocyte cell line to discriminate contact sensitizers from irritants and low molecular weight respiratory allergens. Toxicol In Vitro 23, 789-796.
7. Ezendam J, de Klerk A, R. CF, Fokkens PHB, Park MVDZ, Van Loveren H & De Jong WH (2007) Immune effects of respiratory exposure to fragrance chemicals. Pilot studies with isoeugenol and cinnamal. RIVM report 340301001.
8. Ezendam J, De Klerk A, Vermeulen J, Fokkens PHB & Van Loveren H (2009a) Immune effects of inhalation exposure to fragrance allergens. RIVM letter report 340301003.
9. Ezendam J, Te Biesebeek JD & Wijnhoven SWP (2009b) The presence of fragrance allergens in scented consumer products. RIVM letter report 340301002.
10. Ezendam J, Ter Burg W & Wijnhoven SWP (2011) Inhalation exposure to fragrance allergens. Are consumers at risk for respiratory allergies? RIVM report 340300004.
11. Guarneri F, Barbuzza O, Vaccaro M & Galtieri G (2008) Allergic contact dermatitis and asthma caused by limonene in a labourer handling citrus fruits. Contact Dermatitis 58, 315-316.
12. Karlberg A T, Shao L P, Nilsson U, Gafvert E, Nilsson J L (1994). Hydroperoxides in oxidized d-limonene identified as potent contact allergens. Arch Dermatol Res 286, 97-103.
13. Pors J & Fuhlendorff R (2003) Mapping of chemical substances in air fresheners and other fragrance liberating products. Survey of chemical substances in consumer products. Danish Environmental Protection Agency Survey no. 30.
14. Pronk A, Preller L, Raulf-Heimsoth M, Jonkers IC, Lammers JW, Wouters IM, Doekes G, Wisnewski AV & Heederik D (2007) Respiratory symptoms, sensitization, and exposure response relationships in spray painters exposed to isocyanates. Am J Respir Crit Care Med 176, 1090-1097.
15. Quirce S, Fernández-Nieto M, Pozo Vd, Sastre B & Sastre J (2008) Occupational asthma and rhinitis caused by eugenol in a hairdresser. Allergy 63, 137-138.
16. SCHER (2006) Scientifc Committee on health and environmental risks (SCHER) - Opinion on the report 'Emission of chemicals by air fresheners. Tests on 74 consumer products sold in Europe'. BEUC report January 2005.

17. Schnuch A, Uter W, Geier J, Lessmann H & Frosch PJ (2007) Sensitization to 26 fragrances to be labelled according to current European regulation. Results of the IVDK and review of the literature. Contact Dermatitis 57, 1-10.
18. Scientific Committee on Consumer Safety (SCCS) Opinion on fragrance allergens in cosmetic products. SCCS 1459/11 (January 2012: http://ec.europa.eu/health/scientific_committees/consultations/public_consultations/sccs_consultation_04_en.htm
19. Skold, M., Borje, A., Harambasic, E., Karlberg, A. T. (2004). Contact Allergens Formed on Air Exposure of Linalool. Identification and Quantification of Primary and Secondary Oxidation Products and the Effect on Skin Sensitization. Chem. Res. Toxicol. 17, 1697-1705
20. Van Och, F.M., Slob, W., de Jong, W.H., Vandebriel, R.J., Van Loveren H., 2000. A quantitative method for assessing the sensitizing potency of low molecular weight chemicals using a local lymph node assay: employment of a regression method that includes determination of the uncertainty margins. Toxicology 146, 49-59.
21. Van Amsterdam J., Van Loveren & Ezendam J. (2011). Sensitizing potency of chemical respiratory allergens in humans. Can animal data be used to estimate human potency? RIVM letter report 340300004.
22. Wijnhoven SWP, Ezendam J, Schuur AG, Van Loveren H & Van Engelen JGM (2008) Allergens in consumer products. RIVM report 320025001

Appendix 1: Summary of the presence and concentration levels of fragrance allergens in scented products

	limoneen	Linalool	citral	citronellol	geraniol	methylionon-gamma	benzyl alcohol	hydroxycitronellal	cinnamal	lillial	eugenol	Amylcinnamal	cinnamylalcohol	iso eugenol	hexylcinnamal	coumarine	lyral	benzylbenzoaat	benzylsallicylaat	benzyl cinnamate
overall (n=109)																				
presence* (%)	69	87	26	46	50	30	44	14	6	50	28	17	11	6	42	32	14	20	28	2
mean	0,342	0,827	0,158	0,129	0,043	0,210	0,104	0,010	0,080	0,053	0,072	0,084	0,115	0,027	0,078	0,099	0,038	0,052	0,022	0,027
maximum	6,340	15,033	1,156	3,058	0,272	2,837	2,944	0,045	0,492	0,732	0,876	0,914	0,855	0,150	0,927	0,994	0,249	0,231	0,130	0,053
spray cans (n=37)																				
presence (%)	59	89	19	35	46	22	27	3	3	46	14	5	8	0	22	32	8	8	30	3
mean	0,098	0,100	0,049	0,016	0,010	0,008	0,046	0,001	0,002	0,023	0,017	0,004	0,011		0,032	0,005	0,003	0,128	0,006	0,001
maximum	0,831	0,769	0,304	0,086	0,063	0,049	0,190	0,001	0,002	0,116	0,067	0,006	0,027		0,105	0,018	0,005	0,201	0,020	0,001
trigger sprays (n=18)																				
presence (%)	100	92	23	46	62	46	77	38	8	62	23	23	8	8	46	23	38	23	38	8
mean	0,131	0,383	0,162	0,121	0,141	0,067	0,111	0,010	0,012	0,076	0,032	0,070	0,059	0,002	0,160	0,006	0,071	0,009	0,021	0,053
maximum	0,742	0,778	0,460	0,222	0,272	0,190	0,232	0,029	0,012	0,283	0,084	0,104	0,059	0,002	0,536	0,010	0,249	0,016	0,051	0,053
evaporators (n=38)																				
presence (%)	74	82	29	42	39	37	39	16	8	45	47	18	16	11	53	34	13	32	24	0
mean	0,772	2,254	0,321	0,324	0,051	0,460	0,222	0,013	0,182	0,090	0,107	0,168	0,210	0,045	0,102	0,255	0,037	0,037	0,037	
maximum	6,340	15,033	1,156	3,058	0,139	2,837	2,944	0,045	0,492	0,732	0,876	0,914	0,855	0,150	0,927	0,994	0,091	0,231	0,130	
scented blocks (n=18)																				
presence (%)	56	89	28	78	72	28	72	17	11	61	22	39	11	11	61	39	11	17	33	0
mean	0,016	0,043	0,007	0,024	0,021	0,005	0,007	0,006	0,001	0,014	0,013	0,028	0,015	0,004	0,028	0,008	0,012	0,036	0,032	
maximum	0,056	0,297	0,012	0,112	0,081	0,009	0,038	0,015	0,002	0,030	0,025	0,058	0,028	0,004	0,077	0,019	0,022	0,054	0,085	

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