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Risk assessment for scented products: a pre-study

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Rapport in het kort

Risico-evaluatie voor geurproducten: een voorstudie

Er is weinig bekend over de risico's als gevolg van de blootstelling van consumenten aan geurstoffen uit consumentenproducten. Toevoeging van deze stoffen vindt plaats aan tal van consumentenproducten, variërend van wasmiddelen tot speelgoed. Passieve huiskamerparfums en spuitbusparfums zijn twee groepen producten die populair zijn in gebruik en die voor langdurige dan wel hoge blootstelling van de consument aan chemische stoffen kunnen zorgen. Voor het schatten van de mate van deze blootstelling is het softwareprogramma ConsExpo beschikbaar. Bijzondere aandacht gaat in deze studie uit naar het risico van het inademen van geurstoffen waarvan bekend is dat ze bij contact met de huid een allergische reactie kunnen veroorzaken. Door een gebrek aan een geaccepteerde methode echter, is het op dit moment niet mogelijk om te bepalen of dergelijke allergische reacties ook kunnen optreden bij inademing van deze geurstoffen. Dit onderwerp van de relatie tussen dermale en inhalatoire chemische allergie zal in de komende periode nader onderzocht worden in een pilot dierexperiment met twee geurstoffen.
De groep 'geurproducten' zoals besproken in dit rapport omvat alle consumentenproducten die specifiek en alleen bedoeld zijn om een aangename geur te verspreiden in leefruimtes. Bijvoorbeeld ook geurkaarsen en wierook vallen hieronder. Uit een eerste inventarisatie is een enorme variëteit in het commerciële aanbod van geurproducten gebleken. De chemische samenstelling van deze producten is complex en nadere kwantitatieve informatie over die samenstelling is vaak moeilijk te achterhalen. Ook door deze beperking is het volledig in kaart brengen van de risico's van alle stoffen in alle soorten geurproducten op dit moment niet mogelijk. Op basis van de beschikbare kennis wordt volstaan met enkele algemene aanbevelingen over waar men in de risico-evaluatie van een bepaald geurproduct op dient te letten.

Trefwoorden: Geurproducten, luchtverfrissers, geurstoffen, blootstellingsschatting, respiratoire allergie

Abstract

Risk assessment for scented products: a pre-study

Little is known about the possible risks when consumers are exposed to fragrances. Fragrances are added to many consumer products, from detergents to toys. Passive room perfumes and spray perfumes represent two groups of products that are popular in use and may lead to high and long-lasting exposures for consumers. The degree of exposure can be estimated using the computer programme ConsExpo. Special attention is given in this study to the risk of inhaling fragrances known to produce allergic reactions upon dermal contact. Due to lack of an accepted method, however, it is not possible at this stage to determine if allergy will result when these fragrances are inhaled. Further research in this area is recommended.
‘Scented products’ as dealt with in the present report stands for all consumer products specifically intended for providing a pleasant odour in private and public living-spaces. This includes for instance scented candles and incense. An initial inventarisation shows an enormous variety of scented products available on the market. The chemical composition of scented products is complex; further quantitative information on that composition is difficult to obtain. Thus a complete inventarisation of the risks these products may pose is not possible at the present stage. Based on available knowlegde general recommendations are given as to points that require attention when evaluating the risk of a particular scented product.

Keywords: Scented products, air fresheners, fragrances, exposure assessment, respiratory allergy

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Samenvatting

Deze voorstudie is uitgevoerd om de mogelijke risico's van blootstelling aan stoffen uit geurproducten in kaart te brengen. Geurstoffen worden tegenwoordig aan veel consumentenproducten toegevoegd, variërend van wasmiddelen tot speelgoed. Er is echter weinig bekend over de mogelijke risico's van blootstelling aan deze geurstoffen.
'Geurproducten' zoals besproken in dit rapport zijn consumentenproducten die als enig doel hebben een aangename geur te verspreiden. Het assortiment aan geurproducten blijkt zeer omvangrijk terwijl hun individuele samenstelling moeilijk te achterhalen is. Het rapport geeft een overzicht van beschikbare geurproducten en hun mogelijke indeling in categorieën gebaseerd op producttype, geurstofafgifte, gebruikslocatie, toepassing en blootstellingsscenario. Vooral passieve kamerparfums en spuitparfums worden veel gebruikt en gaan waarschijnlijk gepaard met langdurige, respectievelijk hoge blootstelling. Om deze reden wordt aan deze beide categorieën geurproducten meer aandacht besteed in dit rapport.
Er wordt een leidraad gegeven om de blootstellingsniveaus aan stoffen in huisparfums en sprayparfums in te schatten met behulp van het computerprogramma ConsExpo 4.0. De blootstellingsschatting zou verbeterd kunnen worden met behulp van nadere informatie op het gebied van eigenschappen en wijze van gebruik van deze geurproducten.
In geurproducten zijn naast geurstoffen tal van andere stoffen aanwezig, zoals oplosmiddelen en conserveermiddelen. Bovendien worden bij gebruik van bepaalde geurproducten nieuwe stoffen gevormd, zoals verbrandingsproducten bij het branden van geurkaarsen. Er worden in dit rapport enkele aanbevelingen gedaan voor de risico-evaluatie van verschillende typen geurproducten.
Speciale aandacht wordt besteed aan de risicoschatting van geurstoffen waarvan bekend is dat ze allergene reacties bij consumenten voortbrengen bij dermaal contact. Op basis van beperkte informatie wordt de aanwezigheid van allergene geurstoffen in huisparfums en sprayparfums in kaart gebracht. Als gevolg van het ontbreken van geschikte methoden is het op dit moment niet mogelijk om de risico's van inademing van allergene geurstoffen te kwantificeren. Verder onderzoek op dit gebied wordt aanbevolen. Ook worden verdere aanbevelingen gedaan om de risicoschatting en de blootstelling aan stoffen in geurproducten beter in kaart te brengen.

Summary

The current pilot study was conducted to investigate possible risks from the application of scented products. Nowadays fragrance chemicals are added to many consumer products, varying from laundry detergents to toys. However, little is known about the possible risks for consumers associated with the exposure to these fragrance chemicals.

'Scented products' as discused in the present report are consumer products the sole purpose of which is to spread a pleasant scent in living-spaces. There is a large variation in types of commercially available scented products and, in addition, information on their chemical composition is difficult to obtain. An overview is given of the scented products available on the market and on their possible categorizations according to product type, fragrance release pattern, location of use, application and exposure scenario. Passive room perfumes and spray perfumes are especially popular and are probably associated with long-term and high exposure levels, respectively. Therefore the present study gives extra attention to these specific categories of scented products. Guidance is provided as to how exposure levels to chemicals in passive room perfumes and spray perfumes can be assessed using the computer program ConsExpo 4.0. At the present stage information is limited and the first step in improving the exposure assessment is more information on the characteristics and use of these scented products.

Apart from fragrance chemicals, many other chemicals are present in scented products, such as solvents and preservatives. Further, new chemicals may be formed during the use of scented products, such as combustion by-products from burning candles. Some considerations are given for the risk evaluation of different types of scented products.

Special attention is given to the risk evaluation of fragrance chemicals known to be able to produce allergic reactions upon dermal contact. Based on limited information, an overview is given of the presence of allergenic fragrance chemicals in passive room perfumes and spray perfumes. Due to lack of adequate methods it is currently not possible to quantify the risks of inhaling these fragrances. Further research in this area is recommended. In addition, further recommendations are provided to improve of the risk evaluation of scented products.

1 Introduction

Fragrance chemicals have long been part of consumer products such as cosmetics and cleaning products. In recent years, it has become a trend to add fragrance chemicals to many other types of consumer products, such as childrens' toys, toilet paper and nappies. In addition, an increasing number of consumer products specifically intended for spreading a pleasant smell, is nowadays available on the market and their use is growing. These products are the focus of this pilot study and will be referred to in this report as 'scented products'.

Scented products are available in many different applications, varying from bathroom spray cans to perfumes for use in vacuum cleaners. The wide variation in scented products and other consumer products containing fragrance chemicals has led to a situation in which consumers may be exposed to fragrance chemicals almost continuously, i.e. while residing in different rooms at home, in the car, office and stores. In addition to fragrance chemicals, scented products often contain other chemicals to which exposure may occur, such as solvents and propellants in sprays. In the face of the increasing use of scented products there appears to be a paucity of information regarding exposure levels to fragrance chemicals and other chemicals in such consumer products and the possible risks for the users.

It has been suggested that as a general rule the flavour or fragrance levels needed for the desired effect (a pleasant smell or taste) are sufficiently low for the risk to be negligible (Smith et al., 2005). This assumption is partly based on the principle that flavours and fragrances act directly on the gustatory and olfactory receptors in the nose, which are saturated at very low levels. However, at present, little is known about the exposure to fragrance chemicals in scented products via inhalation. Although in principle only low levels may be required to obtain the intended effect of a pleasant smell, the actual exposure levels to fragrances via inhalation are unknown. At the same time, the barrier for absorption of the fragrance chemicals via the lungs may be relatively small compared to uptake via the skin or the digestive tract, such as occurs with cosmetic products. It was suggested that toxic effects of a number of volatile organic chemicals present in air fresheners, including carcinogenic and teratogenic effects, were not expected at maximum concentrations of air fresheners (Cooper et al., 1995). Some fragrances used in scented products are well-recognized skin contact allergens and very low levels of allergenic chemicals may already elicit a dermal allergic response in sensitized individuals. However, the allergenic potential of fragrance chemicals via inhalation has not been well addressed in safety evaluations, as this route of exposure is usually considered of no great importance (Ford et al., 2000; Cadby et al., 2002).

Within the EU, the use of fragrance chemicals is regulated separately for food, cosmetics and consumer products. The application of fragrances in foods is regulated in EU Community Legislation related for all substances used to give taste and/or smell to food. The legislation sets out the definition of flavorings, general rules for their use, and requirements for labeling and maximum levels for substances which raise concern for human health. It furthermore lays down a procedure for the establishment of an EU-wide positive list of flavoring substances. After its establishment, only those flavoring substances listed may be added to foods.

In contrast with the situation for food, the presence of fragrance ingredients in cosmetics and consumer products is largely self-regulated by industry through the Code of Practice of the International Fragrance Association (IFRA). IFRA issues recommendations for the safe use of fragrance chemicals, which are published in the IFRA Code of Practice and its guidelines. Furthermore, the IFRA provides a list of restricted materials which may not be used in products except when subject to the restrictions and conditions laid down.

Specifically for cosmetics, in 1999 the European Union Scientific Committee on Consumer and Non Food Products (SCCNFP) has drawn up a list of fragrance chemicals which have been identified as an important cause of contact-allergy reactions in fragrance-sensitive consumers. This has led the European Parliament and the Council of the European Union to produce a list of fragrance chemicals that need to be mentioned in the list of ingredients on labels of cosmetic products. No such specific EU regulations currently exist for fragrance chemicals in other consumer products, unless the fragrance chemical has been classified by the EU as a dangerous substance, (e.g. sensitizing), in which case products containing more than 1% of the fragrance chemical needs to be labeled.

Within its responsibility to protect the safety of consumer products, the Dutch Food and Consumer Product Safety Authority (VWA) is in need of more information regarding the exposure and potential risk associated with the use of scented products. The current study represents an initial orientation on the field. Its aim is to gather information needed for assessing the use of scented products and the associated potential risks due to inhalation of chemicals released from these products. The study initially focuses on two main categories of scented products for which the highest or most chronic levels of exposure to chemicals are anticipated: air freshener sprays and passive room perfumes. Chemicals of particular interest in this pilot study were the fragrance chemicals listed by the SCCNFP as contact allergens (SCCNFP, 1999).

2 Inventory of scented products

The first step in assessing the risks of using scented products was to make an inventory of the available products. The paragraphs below present an overview of the product types available. To enable making an assessment of the exposure levels to chemicals in the different types of products, they have been categorized according to location of use and application types.

2.1 Type of products

There is a number of different types of products available on the market:

- *Room perfume in holders* This is a large group of scented products, comprised of perfumes enclosed by a container, such as a glass disc or plastic flask, from which the scent is released slowly over time. The perfume can be in the form of a water-based or solvent-based liquid, a gel, or a solid soap-like substance.
- *Fragrant candles + wax* Candles made of a fragrant wax, or sole wax. The scent is released by burning the candle or heating the wax.
- *Ethereal oils* Fragrant oils that generally need heating before the scent is released fully. Candles or other warm objects such as lamps can heat the oils.
- *Fragrant sachets* Bags of textile such as lace or cotton filled with synthetic or natural scented products, such as lavender bags. The sachets can be placed in a room, but usually are placed between clothes and linen.
- *Sprays* Many scented products are available in the form of aerosol spray cans or bottles. The product is often dissolved in volatile solvents, although some sprays may be water-based.
- *Potpourri* Mix of (dried) flowers, fruits or other material, with natural scent or impregnated with perfume. The mix is placed in an open container.
- *Fragrant cardboards* Pieces of cardboard, usually in the form of a leaf or other decorative figure, impregnated with perfume. They are commonly suspended from rear view mirrors in cars.
- *Toilet bowl rim hangers* Container with grid, enclosing a fragrant solid, gel or liquid specifically designed to suspend from the toilet bowl rim. The scent is released by flushing the toilet, so that water flows through the container.
- *Incense* Cones or sticks of resin-like material that release the scent when burnt.
- *Ironing-perfumes* A liquid perfume to be added to the water container in a steam iron. The scent is released when the appliance is switched on.
- *Vacuum perfumes* A ball of material to be placed in the vacuum cleaner. The scent is released when the appliance is switched on.

2.2 Product categories

The product types described in section 2.1 can be categorized based on different characteristics, such as scent type and market share. For exposure assessment for chemicals contained in scented products it is useful to make categories based on factors that are important in the definition of exposure scenarios. The latter categories are discussed below.

2.2.1 Location of use

An important factor in determining the exposure to a product is the location where it is used. The different locations where scented products may be used will have different volumes and ventilation rates resulting in different exposure levels. For example, the use of a product in a small, poorly ventilated room tends to lead to much higher exposure levels than use in large, open spaces. In addition, multiple sources of chemicals in scented products can be present in one room. In the table below, products are grouped according to their most relevant locations of use.

Table 1 Locations of use for different scented product types

Product type	Location of use
Room perfume in holders	Living-room, bedroom, kitchen, toilet, garage, car, office, stores
Fragrant candles + wax	Living-room, bedroom, stores
Ethereal oils	Living-room, bedroom, sauna, office, stores
Fragrant sachets	Living-room, bedroom, kitchen, toilet, garage, car, office, stores
Sprays	Living-room, bedroom, kitchen, toilet, garage, car, sauna, office, stores
Potpourri	Living-room, bedroom, kitchen, toilet, garage, car, office, stores
Fragrant cardboards	Living-room, bedroom, kitchen, toilet, garage, car, office, stores
Toilet bowl rim hangers	Toilet (home and office)
Incense	Living-room, bedroom, stores
Iron perfumes	Living-room, bedroom, kitchen, toilet, garage, car
Vacuum perfumes	Living-room, bedroom, kitchen, toilet, garage, car

2.2.2 Application types

For many products, no specific action is needed to release the scent, such as for fragrant bags, potpourri and room perfumes in holders. Other products may require a specific application, such as use of a spray on textiles. The different application types result in different exposure levels, with regard to duration and amount of immediate release. The purpose of some

products is to spread a *constant* pleasant scent in a room (‘constant release pattern’). For example, potpourri releases a relatively low level of scent slowly over a longer period of time and is in use constantly until the source is exhausted. Other products are used only once or at intervals, releasing relatively high levels of fragrance chemicals with the source of the scent often possibly being switched on and off in-between . It is inherent to sprays that the products are released during a relatively short period of time. Other examples of products in this category are scented candles and incense cones. The purpose of these products is to *temporarily* spread a pleasant scent, the aim sometimes being that of masking an unpleasant smell (‘peak release pattern’).
Application types with their scent release patterns for each product type can be found below:

Table 2 Applications of scented products

Product type	Application types	Scent release pattern
Room perfume in holders	Electric plug, ventilation, no specific action	Constant
Fragrant candles + wax	Heating, Burning	Peak
Ethereal oils	Heating	Peak
Fragrant sachets	No specific action	Constant
Sprays	Spray on targeted spot, general surfaces, or in air space	Peak
Potpourri	No specific action	Constant
Fragrant cardboard	No specific action	Constant
Toilet bowl rim hangers	Flushing	Peak
Incense	Burning	Peak
Iron perfumes	Ironing	Peak
Vacuum perfumes	Vacuuming	Peak

2.3 Exposure scenario categories of different product types

To assess the risks of the use of scented products it is important to gain insight into the extent of exposure to chemicals in the different product types and important factors influencing this exposure. Based on combining the categories described above, the following exposure scenario categories have been identified.

2.3.1 Passive room perfumes

This group includes products that do not need any action to release their scent and are used constantly until the source of the scent is exhausted. An important type of product in this group is the room perfume in holders, but also fragrant sachets, potpourri and fragrant cardboard. Exposure time of these products generally depends on the time it takes to exhaust the source of the scent. Exposure is therefore commonly long-term. The products in this group are commonly used in many locations, in any room inside the home but also in offices, cars and stores.

2.3.2 Mechanical room perfumes

The products in this group need some form of mechanism involving electricity or ventilation before the scent is released. The fragrance is released constantly and levels may be higher than passive perfumes that do not need electricity or ventilation. The major type of products in this group is room perfume in a holder that needs to be plugged into an electric socket and perfume in holders that can be attached to the ventilation system in a car. Exposure to the product and its possible by-products takes place constantly as long as the product is plugged in. Long-term exposures are common in this group. The mechanism of release of the product will influence the evaporation of the chemicals and is therefore an important factor in the exposure assessment to these products.

2.3.3 Heating or burning perfumes

This group comprises products that need heating or burning before the scent is released. The exposure time to these products is often no longer than a few hours. The group includes incense, candles, fragrant waxes, and ethereal oils. In addition to a risk assessment of the fragrance chemical itself, it is important to consider possible by-products that may be formed through heating or burning, such as poly-aromatic hydrocarbons or other particles. Increased temperature will influence the vapour pressure of the chemicals and is therefore an important factor in the exposure assessment to these products.

2.3.4 Spray perfumes

This group comprises a wide range of scented products that are contained in a spray can or spray bottle, and are often designed to mask unpleasant odours. The extent of exposure to these products depends largely on the target use of the spray (spot, general surfaces, or air). Another important factor in the exposure to chemicals in a spray is the nozzle of the spray, the propellant and the solvent used. The nozzle, the propellant and the solvent are the main contributing factors to the size of the droplet, which in turn determines to what extent the product is inhaled in the lungs. Inherent to sprays is that the duration of release of the product is short. The use of a spray may result in a high acute exposure to chemicals in the product.

2.3.5 Home appliance perfumes

This relatively small group of products releases the scent by use of a home appliance. The group includes toilet bowl rim hangers, vacuum cleaner perfumes and ironing-perfumes. Exposure scenarios are very different for each of these products. Exposure to chemicals in toilet bowl rim hangers depends on the amount of water flushed. Chemicals in iron perfumes are released with increased temperatures. Exposure to chemicals in vacuum cleaner perfumes depends on the ventilation rate. The exposure time of all the products in this category are directly correlated with the use of the home appliance.

3 Rationale for the focus on allergenic fragrance chemicals in passive room perfumes and spray perfumes

As shown in the previous chapter, there is a wide variation of types of scented products available on the market. For all of these products there is a paucity of information regarding potential exposure levels and associated risks of chemicals in the products. It was impossible within the scope of this pilot study to review all product types in order to determine which would potentially pose the highest risk for consumers. Therefore, a selection needed to be made.

It was decided that the focus would be on passive room perfumes and sprays. These groups of products are widely used by consumers, as judged by their wide availability in pharmacies and grocery stores. However, very little information is available in scientific literature on the possible risks of using passive room perfumes or sprays. Although the exposure to chemicals in room perfumes may be relatively low, the exposure is likely of a long term nature. On the other hand, although short-term exposure is inherent to sprays, the exposure levels may be high.

The exact composition of scented products is proprietary information. Based on informal enquiries made to manufacturers of scented products, however, they appear as complex products which may be composed of hundreds of different chemicals. It was decided that the current pilot study will focus on fragrance chemicals listed by the EU Scientific Committee on Consumer and Non Food Products (SCCNFP) in 1999 as being consumer allergens (Table 3 and Table 4). Currently, two of the fragrance chemicals on this list have officially been classified as contact sensitizers in the EU-classification scheme and are to be labeled as such: citral and d-limonene.

Inclusion of fragrance chemicals on SCCNFP's list of consumer allergens is mostly based on results from skin sensitization tests. However, it has been suggested that dermal contact allergens may also produce airway hypersensitivity (Arts et al., 1998). One study found a positive, independent and significant association between eye and airway symptoms elicited by fragrance products and positive patch tests to perfume-related haptens (Elberling et al., 2004). Other studies indicate that fragrance chemicals may be related to the increasing prevalence of asthma or asthma-like symptoms (Millqvist et al., 1999; Norback et al., 1995). For example, in an epidemiological survey on asthmatic symptoms and volatile organic chemicals (VOCs), bronchial hyper-responsiveness was found to be related to indoor concentration of limonene (Norback et al., 1995).

Some of these fragrance chemicals such as linalool and limonene show sensitizing effects mostly upon the formation of hydroperoxides by oxidation, for example when exposed to air (Skold et al., 2004). In cosmetic products, these fragrance chemicals are therefore often accompanied by anti-oxidants. However, it is unknown whether anti-oxidants are added in scented products and whether hydroperoxides can be formed from fragrance chemicals once they are airborne.

Table 3 Fragrance chemicals, which according to existing knowledge, are most frequently reported and well-recognized consumer allergens. Source: SCCNFP (1999)

Common name	**CAS no**
Amyl cinnamal	122-40-7
Amylcinnamyl alcohol	101-85-9
Benzyl alcohol	100-51-6
Benzyl salicylate	118-58-1
Cinnamyl alcohol	104-54-1
Cinnamal	104-55-2
Citral	5392-40-5
Coumarin	91-64-5
Eugenol	97-53-0
Geraniol	106-24-1
Hydroxycitronellal	107-75-5
Hydroxymethylpentyl -cyclohexenecarboxaldehyde	31906-04-4
Isoeugenol	97-54-1

Table 4 Fragrance chemicals, which are less frequently reported and thus less documented as consumer allergens. Source: SCCNFP (1999)

Common name	**CAS no**
Anisyl alcohol	105-13-5
Benzyl benzoate	120-51-4
Benzyl cinnamate	103-41-3
Citronellol	106-22-9
Farnesol	4602-84-0
Hexyl cinnamaldehyde	101-86-0
Lilial	80-54-6
d-Limonene	5989-27-5
Linalool	78-70-6
Methyl heptine carbonate	111-12-6
3-Methyl-4-(2,6,6-trimethyl-2-cyclohexen-1-yl)-3-buten-2-one	127-51-5

It has to be emphasized that the fragrance chemicals on this list are probably not the only fragrance chemicals that may elicit allergenic reactions. Other fragrance chemicals may also be allergenic, but may not be known as such due to a lack of data.

4 Fragrance chemicals in passive room perfumes and spray perfumes

As stated before, the composition of scented products is not publicly available. According to communications with manufacturers, fragrance mixes used in scented products may be composed of hundreds of different fragrance chemicals. Information on the presence of fragrance chemicals in room perfumes and sprays has been obtained from a limited number of different sources:

- *Product labels* Little information is available on the composition of scented products from the labels of the product. The information is often limited to a list of ingredients, without data on concentrations.
- *Reports* The Danish Environmental Protection Agency has conducted a number of surveys on chemical substances in consumer products. One survey in particular mapped chemical substances in air fresheners and other fragrance liberating products. The data from this survey have been used for this study (Pors and Fuhlendorff, 2003).
- *Manufacturers* Some information on the composition of scented products was provided by manufacturers.

It must be emphasized that because of the limited data sources, the concentrations of fragrance chemicals listed below should be considered as indicative only.

4.1 Composition of passive room perfumes

The table below is an overview of the concentration ranges of fragrance chemicals measured in different passive room perfumes (table 5), as reported in the different sources mentioned above. Since only limited information was available, these figures should be considered as indicative values.

Table 5 Fragrance chemicals in passive room perfumes

Common name	CAS no	Concentration range in products (mg/kg)	Allergenic list SCCNFP
1-carvone	99-49-0	Unknown	-
6,10-dimethylundecene-2-one	1322-58-3	Unknown	-
Amyl-cinnamal	122-40-7	640-16000	A
Amyl-cinnamyl alcohol	101-85-9	17-50	A
Benzyl alcohol	100-51-6	290 – 840	A
Benzyl benzoate	120-51-4	8 – 4600	B
Benzyl cinnamate	103-41-3	490-500	B
Benzyl salicylate	118-58-1	5000-16000	A
Bourgeonal	18127-01-0	Unknown	-
Cinnamal	104-55-2	10-35	A
Cinnamyl alcohol	104-54-1	19-320	A
Citral	5392-40-5	450-26000	A
Citronellol	106-22-9	190-13000	B
Coumarin	91-64-5	57-1400	A
Damascone delta	57378-68-4	Unknown	-
Eugenol	97-53-0	11-7500	A
Geraniol	106-24-1	410-3100	A
Hexyl cinnamaldehyde	101-86-0	39-22000	B
Hydroxycitronellal	107-75-5	450-460	A
Hydroxymethylpentyl-cyclohexenecarboxaldehyde	31906-04-4	36000-37000	A
Isoeugenol	97-54-1	110-120	A
Ligustral	27939-60-2	Unknown	-
Lilial	80-54-6	470-27000	B
d-Limonene	5989-27-5	140-8700	B
Linalool	78-70-6	970-37000	B
Methyl heptin carbonate	111-12-6	13-27	B
3-Methyl-4-(2,6,6-trimethyl-2-cyclohexen-1-yl)-3-buten-2-one	127-51-5	1800-2900	B
Phenylacetaldehyde	122-78-1	Unknown	-

The fragrance chemicals are present in the products in different combinations. Total weight% of fragrance chemicals in a passive room perfume may range from 0.2-14%.

4.2 Composition of spray perfumes

The table below is an overview of the concentration ranges of fragrance chemicals measured in different spray perfumes (Table 6) as reported in the different sources mentioned above. Since only limited information was available, these figures should be considered as indicative values.

Table 6 Fragrance chemicals in spray perfumes

Common name	CAS no	Concentration range in products (mg/kg)	Allergenic list SCCNFP
Amyl-cinnamal	122-40-7	unknown	A
Benzyl alcohol	100-51-6	11 - 12	A
Benzyl benzoate	120-51-4	450 - 470	B
Benzyl salicylate	118-58-1	4.1 - 4.2	A
Cinnamal	104-55-2	47 – 63	A
Citronellol	106-22-9	2700 - 8400	B
Eugenol	97-53-0	93 - 3400	A
Geraniol	106-24-1	6300 – 6400	A
Hexyl cinnamaldehyde	101-86-0	34 – 2900	B
Hydroxycitronellal	107-75-5	440 – 450	A
Hydroxymethylpentyl-cyclohexenecarboxaldehyde	31906-04-4	61000-62000	B
Isoeugenol	97-54-1	23 - 32	A
Lilial	80-54-6	2700 – 12000	B
d-Limonene	5989-27-5	41 - 7200	B
Linalool	78-70-6	1400 - 1500	B
Lyral	31906-04-4	unknown	-
3-Methyl-4-(2,6,6-trimethyl-2-cyclohexen-1-yl)-3-buten-2-one	127-51-5	220 - 5200	B

The fragrance chemicals are present in the products in different combinations. Total weight% of fragrance chemicals in a spray perfume may range from 0.0050-13%.

5 Exposure assessment for fragrance chemicals from passive room perfumes and spray perfumes

No public data are available on actual air concentrations for fragrance chemicals from using passive room perfumes or spray perfumes. Information on exposure levels of chemicals in consumer products form a core part of the risk assessment of consumer products (Van Veen et al., 2001). Even if some measured data on emission of chemicals from products or actual exposure concentrations are available, these data are rarely sufficient to base a risk assessment upon for all conditions under which a product can be used. This is because exposure levels are influenced by a great number of exposure factors, such as room ventilation and product use, which may vary greatly from case to case. Exposure assessors therefore often take recourse to estimating exposure levels using models. ConsExpo 4.0 is a computer software program with mathematical models to assist in the exposure assessment of chemicals in consumer products.

The following paragraphs provide guidance on how to assess ‘realistic worst case’ exposure levels to chemicals from passive room perfumes and spray perfumes using ConsExpo 4.0. For more guidance on the use of ConsExpo 4.0, the reader is referred to the manual (Delmaar et al., 2005).

5.1 Passive room perfumes

This paragraph provides some first guidance on the appropriate models for performing an exposure assessment for chemicals in passive room perfumes with ConsExpo 4.0. The guidance particularly focuses on exposure assessments of chemicals in passive room perfumes in the form of a gel or a liquid. Suggestions for parameter value ranges associated with these models are given in Appendix I. However, these values should only be used if no other more appropriate data are available.

5.1.1 Defining an exposure scenario

Passive room perfumes can be used throughout the house (including the bedroom), in the car, at the office and even at stores. Different room perfumes may be used in different locations and exposure assessments should therefore be performed for each separate product. 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

The exposed person may be of any age or gender, any population subgroup and perform any kind of activity while exposed. Parameters that need to be defined for the exposure scenario are body weight and use frequency.

5.1.2 Exposure routes

The main route of exposure to a chemical in passive room perfumes is via inhalation. ConsExpo 4.0 offers two models describing inhalation exposure: ‘exposure to vapour’ and ‘exposure to spray’. For passive room perfumes, the exposure to vapour model is appropriate. Within this model, three modes of release can be selected: instantaneous release, constant rate or evaporation. All three modes can be used to describe the release of the chemical from the room perfume. They can be used in a tiered approach: the instantaneous release mode being the most simple and the evaporation mode being the most detailed.

Instantaneous release

The instantaneous release mode will give a worst case exposure assessment and can be used for a first tier assessment, for quick screening or when limited information is available on the physicochemical properties of the chemical. It assumes that all of the chemical is released in the air at once.

Constant rate

The constant rate mode can be used if an estimate can be given of the time during which the chemical is emitted in the air (emission duration). In reality, the concentration of a chemical in the air is limited by its vapour pressure. If the physicochemical properties vapour pressure, molecular weight and temperature of the chemical of interest are known, the mode can assess the exposure level taking into account this limitation.

Evaporation

This last mode describes the actual evaporation process of the chemical in the air based on its physicochemical properties and more details about the product use. It estimates exposure levels more accurately than the other two modes and as such can be used for a higher tier assessment.

For all three modes, some general parameters need to be defined: exposure duration, product amount, weight fraction chemical, room volume and ventilation rate. In addition, the constant rate mode needs definition of the emission duration. For the evaporation mode, a number of additional parameters need to be filled out. Apart from some basic parameters such as release area, application duration and physicochemical properties of the chemical of interest, the following parameters need to be defined:

- mass transfer rate: the velocity by which a chemical is transferred between the product and the air. ConsExpo 4.0 offers two models to approximate this rate: Langmuir’s method and Thibodeaux’ method. Langmuir’s method generally gives a worst case estimate. If the chemical is contained in a product consisting mostly of water, Thibodeaux’method can be used. For mechanical room perfumes, these methods are not applicable. The mass transfer rate of chemicals in these product types is largely dependent on the mechanism by which the fragrance is released and this should be estimated based on measured emission data.

- molecular weight of the matrix: Usually, the chemical of interest is part of a matrix, such as a liquid or gel product containing many other chemicals. The molecular weight of this matrix needs to be defined.

ConsExpo 4.0 calculates the uptake of the chemical in the body via inhalation on the basis of an uptake fraction and the inhalation rate. The uptake fraction is chemical-specific and should be based on experimental data. A default inhalation rate can be calculated in ConsExpo 4.0 based on body weight and exercise level.

5.2 Spray perfumes

This paragraph provides guidance on the appropriate models for performing an exposure assessment of chemicals in spray perfumes with ConsExpo 4.0. The guidance focuses on exposure assessments to non-volatile chemicals in spray cans and trigger sprays. Suggestions for parameter value ranges associated with these models are given in Appendix II. However, these values should only be used when other more appropriate data are not available.

5.2.1 Exposure scenario

Spray perfumes can be used throughout the house, such as the bedroom and the bathroom and are often used to mask unpleasant odours. The spray perfumes can be used as an application in the air or on furniture, resulting in different exposure scenarios. Apart from exposure of the user of the product, secondary exposure of potentially more sensitive bystanders may also occur and should be included in the risk assessment with a separate exposure assessment. The (secondary) exposed person may be of any age or gender, any population subgroup and perform any kind of activity while exposed. Two examples of common scenarios in using spray perfumes are:

1) A user sprays an air spray in a small bathroom.
2) A perfume spray is used to mask unpleasant odors on a couch in a living room. After spraying, a young child crawls on the couch.

Parameters that need to be defined for the exposure scenario are body weight and use frequency.

5.2.2 Exposure routes

There are two relevant routes of exposure to a chemical in spray perfumes: via inhalation and via the skin.

For the air spray used in the bathroom, exposure via inhalation is likely highest for the user, during use. However, secondary inhalation exposure to potentially more sensitive persons entering the bathroom afterwards may also occur. Some dermal exposure to chemicals in air sprays could also occur on the hands while spraying. If dermal toxicity of the chemical of interest occurs at low exposure levels, this route also needs to be considered in the risk assessment of the air spray.

For sprays used to treat furniture or textiles, inhalation exposure for the user may occur, although it is likely to be lower than inhalation exposure to an air spray. This is because the product is aimed at a surface and less of it will be airborne. Dermal exposure may occur if the user or a potentially more sensitive bystander contacts the treated surface. Some fragrances in scented products, such as those listed by the SCCNFP, are contact allergens and secondary dermal exposure to these chemicals is therefore a relevant route to consider in the risk assessment for this type of spray perfumes.

5.2.2.1 Inhalation exposure

ConsExpo 4.0 offers two models describing inhalation exposure: ‘exposure to vapour’ and ‘exposure to spray’. The ‘exposure to spray’ model describes the indoor exposure to slowly evaporating or non-volatile chemicals in droplets that are released from a spray product. For volatile substances, sub-models of the ‘exposure to vapour’ model are more appropriate. Therefore, for the exposure assessments of volatile chemicals in spray perfumes, the ‘exposure to vapour’ model is most appropriate, whereas for exposure assessments of usually non-volatile and slowly evaporating fragrances, the ‘exposure to spray’ model is most appropriate. Exposure assessment using the ‘exposure to vapour’ model has been discussed in the section on passive room perfumes (section 5.1). The current section will cover the exposure assessment for non-volatile substances using the ‘exposure to spray’ model only. Some basic parameters that need to be defined in this model are spray duration, exposure duration, room volume, height and ventilation rate. Product composition data such as weight fractions of the chemical, propellant, non-volatile and solvent, and density of solvent and non-volatile components are also needed. Additional parameters are:

- Mass generation rate: the amount of spray generated per unit of time.
- Airborne fraction: the amount of spray staying in the air. Air spray perfumes are designed to provide a pleasant smell in the room for longer periods of time. To achieve this, the air spray system (nozzle, solvent) is usually designed to generate droplets as small as possible, which remain in the air longer. For sprays to treat furniture the droplets are aimed at a surface and the airborne fraction consists of the droplets bouncing off or missing this surface.
- Initial particle distribution: the normalized mass distribution of the particles immediately after they are ejected. The particle distribution greatly varies between spray perfumes, depending on the nozzle, solvent and other factors.
- Inhalation cut-off diameter: the diameter of a droplet that can be inhaled rather than deposited in the upper airways, resulting in oral uptake.

ConsExpo 4.0 calculates the uptake of the chemical in the body via inhalation of a spray on the basis of an uptake fraction, the inhalation rate and an oral uptake fraction. The fraction of chemical taken up by the lungs is chemical specific and should be based on experimental data. A default inhalation rate can be calculated in ConsExpo 4.0 based on bodyweight and exercise level. The oral uptake fraction is the fraction of the chemical that will be taken up by the gastrointestinal tract after swallowing droplets deposited in the upper airways. Similar to the inhalation uptake fraction, this value is chemical specific and should be based on experimental data.

5.2.2.2 Dermal exposure

As discussed before, secondary dermal exposure may be a relevant route of exposure for perfume sprays used to treat furniture or textiles, although in some cases, for example for strong contact allergens, it may be relevant to also assess the primary dermal exposure for air sprays.

ConsExpo 4.0 currently offers one dermal model: Direct dermal contact with product. This model consists of a number of dermal loading modes describing ways in which a product or chemical is loaded onto the skin.

Both exposure scenarios (an air spray user and a child crawling on a textile freshener treated surface) can be described by both the instant application and the constant rate modes. The scenario for the textile freshener can also be described by the rubbing off mode.

Instant application

The instant application mode will give a worst case exposure assessment and can be used for a first tier assessment, for quick screening or when limited information is available on the use of the product. It assumes that all of the chemical is applied to the skin at once. Parameters that need to be defined are weight fraction chemical and product amount. For an air spray, the amount of product available for dermal exposure depends on what is assumed to be the airborne fraction. For example, if the airborne fraction was assumed to be 90%, then the product amount remaining for dermal exposure would be 10% of the total amount of product sprayed. For a textile spray, it can be assumed that all of the product sprayed is available for dermal exposure.

Constant rate

The constant rate mode can be used if some estimate can be given of the amount of time during which the dermal exposure takes place. Dermal exposure to an air spray can be assumed to take place only during spraying. The release duration is in this case equal to the spray duration. On the other hand, release duration of a textile spray depends on the time spent in contact with the treated surface, which may be much longer than the actual spraying time. As for the amount of product available for dermal exposure, for air sprays this depends on the airborne fraction, as discussed under the instant application mode. For textile sprays, the product amount available for dermal exposure is the total amount sprayed on the treated surface.

Rubbing off

The rubbing off mode is the most accurate mode to describe the dermal exposure of a child on a couch treated with textile spray, but is not applicable for an air spray used in the bathroom. Parameters needed for this mode are:

- Transfer coefficient: the textile area treated with spray that is in contact with the skin of the child per unit of time. For example, for a couch, the area in contact with the skin of a child consists of the sitting surface area and the arm chairs. For curtains, the contacted area is likely much smaller, consisting only of the part of the curtains touched by the hands of the child.
- Dislodgeable amount: the amount of textile spray applied on the couch that may potentially be wiped off, per unit of surface area. When the child crawls on the couch, part of the spray perfume may be rubbed onto the skin of the child.
- Contact time: as described for the release duration in the constant rate mode, the contact time may be longer than the spray duration for a textile spray, depending on how long the child touches the treated surface of the couch.
- Rubbed surface: the area of the treated couch that is actually rubbed. This area may be smaller than the treated surface. For example, a child cannot crawl on the back of the couch.

5.3 ConsExpo 4.0 exposure assessment results

The results of the exposure assessment with ConsExpo 4.0 can be viewed in a number of different output options. Point values reporting the acute and chronic external and internal exposure levels give a quick overview of the results. It is however recommended to also view the results in graphs, for example to determine when maximum exposure takes place and what the maximum exposure level is. In addition, a sensitivity analysis can be performed to determine which parameters affect the exposure levels most. It is recommended that a distribution of values for at least these parameters is then defined. A distribution of exposure levels can then be calculated by means of a Monte Carlo calculation. It has to be realized that many of the exposure factors may be correlated, which will not be taken into account in the distribution calculations in ConsExpo 4.0. The range of the obtained distribution may therefore be wider than if these correlations would have been taken into account.

An important consideration is that exposure to chemicals in different scented products may occur up to 24 hours a day and the exposure to one chemical that is contained in more than one scented product may therefore be much higher than estimated based on the use of a single product.

Reliable input data for the models in ConsExpo 4.0 are difficult to obtain. At present, little information is available on consumer use patterns of scented products and many parameters will therefore need to be estimated.

A general idea of which parameters will mostly affect the exposure levels to chemicals in passive room perfumes and spray perfumes is difficult to give, since this strongly depends on the properties of the chemical of interest. However, parameters that are often important for exposure assessments in general are use frequencies, exposure duration, product amount and ventilation rates. In addition, for the spray model, the airborne fraction and initial particle distribution may be important parameters. For dermal exposure to textile sprays, the transfer coefficient and dislodgeable amount parameters are important, but difficult to estimate. Many of these parameter values are very product specific, but more research to obtain data for the more general parameters could also greatly improve the exposure assessment.

6 Current state of risk characterization for allergenic fragrance chemicals

As discussed before, some fragrance chemicals in scented products may be sensitizing agents. Sensitisation may be the most critical effect for these substances. Sensitization by these agents can occur via the airways or the skin. In sensitized individuals, exposure to relatively low concentrations may lead to allergic reactions. Contact via the skin leads to skin reactions; exposure via the airways leads to airway reactions.
The current safety research on sensitizing agents in general focuses on qualitatively identifying potentially sensitizing activity of chemicals. Results of this research are subsequently used for labeling; the chemical does or does not have sensitizing properties, a simple yes or no answer. According to EU legislation, consumer products containing sensitizing agents are required to be labeled as sensitizing if the sensitizing agent comprises more than 1% of the product.

The risk assessment of sensitizing agents is not carried out the same way as in general toxicology, with regard to the determination of no-effect levels and the application of safety factors to assess what levels are expected to be safe for humans. Quantitative risk assessment for sensitizing agents is not yet possible. There is however a great need for such assessments and some research is conducted to develop a quantitative method. For example, Griem et al. (2003) proposed a risk assessment methodology for skin sensitization and elicitation based on sensitization potency data from the local lymph node assay (LLNA). They suggest derivation of an ‘acceptable non-sensitizing area dose’ (ANSAD) from the LLNA EC3 data by applying an extrapolation factor of 300 to account for inter- (3) and intra- (10) species differences and for the fact that a chemical may have a higher sensitizing potency upon repeated exposure (10). They reported skin sensitization thresholds from both human and mouse studies for some fragrances on the list of SCCNFP (Table 7). Some elicitation threshold values from patch tests for these fragrances were also reported (Table 8). The authors found a relationship between the ratio of sensitization/elicitation threshold and the sensitization threshold:

$$\log(\text{ratio sensitization/elicitation threshold}) = 0.84 * \log(\text{sensitization threshold } [\mu\text{mol/cm}^2]) + 1.81$$

This relationship could potentially be used to predict the elicitation threshold values for chemicals based on their sensitization threshold values. The authors further propose to derive an acceptable non-eliciting area dose (ANEAD), by applying an extrapolation factor of 100 (10 for intra-species differences and 10 for repeated exposure) to the elicitation NOEL from a human one-time patch test. If the ANEAD is based on the sensitization potency in an LLNA, a variable sensitization-elicitation extrapolation factor of 10ˆ(0.84 * log(NOEL sensitization

threshold[μmol/cm^2]) + 1.81) as derived above and an interspecies factor of 3 have to be applied additionally. It has to be emphasized that these factors are quite arbitrary.
As the authors imply themselves, the proposed method by Griem et al. (2003) is only a first attempt to develop a quantitative risk assessment for sensitizing agents via skin exposure and is based on a very limited data set. It is by no means an accepted method and much development and validation will need to take place before it can be used as a reliable method. In addition, it has to be realized that LLNA data do not identify a sensitization threshold. The LLNA has been established for hazard identification with the EC3 value as cutoff point. Using the LLNA data it is possible to compare chemicals with each other and determine the relative sensitization potency of chemicals. Chemicals with a high EC3 value are considered weaker sensitizers than chemicals with a low EC3 value. How this relates to doses needed for sensitization is unknown. Finally, the EC3 values from the LLNA refer to a short exposure duration. It is known that for some chemicals a longer exposure duration will give a different EC3 value. A factor 10 is now included to account for this difference but, as indicated above, the size of this factor is arbitrary.

Additional efforts have been made by an expert group of the EU working on potency classification. In their recent EU report, it was concluded that by using a number of different endpoints in the current LLNA, it is possible to determine dose response relations and use these data to identify thresholds for sensitization (Ehling et al., 2005b; Ehling et al., 2005a). It was even proposed, based on analyzing literature, that the assay can be used for classification. It is therefore anticipated that, based on a similar approach and on up to date exposure level data, a quantitative risk assessment for sensitization through skin exposure is feasible.

It has to be noted that the proposed risk assessment methods are only related to skin sensitizers. Research on the potency evaluation of respiratory sensitizers is still in its infancy. In fact, research on the identification of potential respiratory sensitizers is far from completed. Respiratory models are very laborious and the determination of dose response relations may require the use of a great number of test animals. However, it may be worthwhile to examine any relationship between the potency of substances to induce respiratory sensitization and their potency to induce skin sensitization. If such a relation exists, this may provide a practical way forward in the risk assessment of respiratory sensitizing compounds.

In conclusion, despite ongoing developments in this area, it is at present not yet possible to define quantitative end-points for the risk characterization of allergenic fragrance chemicals used in scented products.

Table 7 Skin sensitization: NOEL/LOEL values in humans and murine LLNA EC3 values for some fragrances on the SCCNFP list. Source: Griem et al. (2003)

Fragrance	Human study			Mouse study	
	Study type; effect level	Concentration (solvent)	Area dose [µg/cm^2] (µmol/cm^2)	LLNA EC3 [%] (solvent)[a]	Area dose [µg/cm^2] (µmol/cm^2)
Amyl cinnamal	HRIPT; NOEL	20 (diethylphthalate)	23622 (177)	11 (AOO)	2750 (13.6)
Benzyl benzoate	HMT; NOEL	30 (petrolatum)	20690 (97.5)	17 (AOO)	4250 (20.0)
Cinnamyl alcohol	HMT; NOEL	4 (petrolatum)	4000 (29.8)	21 (unknown)	5250 (39.1)
	LOEL	10 (petrolatum)	10000 (74.6)		
Cinnamal	HRIPT; NOEL	0.5 (ethanol)	590 (4.46)	1.4 (AOO)	350 (2.65)
	LOEL	1.0 (ethanol)	1200 (9.08)	2.0 (AOO)	500 (3.78)
				3.1 (AOO)	780 (5.90)
Citral	HRIPT; NOEL	0.5 (ethanol)	500 (3.29)	6.6 (AOO)	1700 (11.2)
	LOEL	1.0 (ethanol)	1000 (6.57)		
Eugenol	HRIPT; NOEL	2.5 (ethanol)	1938 (11.8)	9.8 (AOO)	2500 (15.2)
	LOEL	8 (ethanol)	8000 (48.7)		
Geraniol	HRPT; NOEL	6 (petrolatum)	6000 (38.9)	57 (AOO)	14250 (92.4)
	LOEL	10 (ethanol)	10000 (64.8)		
Hexyl cinnamaldehyde	HRPT; NOEL	20 (diethylphthalate)	23662 (109)	14 (AOO)	3500 (16.2)
				9 (AOO)	550 (3.35)

Table 7 (continued) Skin sensitization: NOEL/LOEL values in humans and murine LLNA EC3 values for some fragrances on the SCCNFP list. Source: Griem et al. (2003)

Fragrance	Human study			Mouse study	
	Study type; effect level	Concentration (solvent)	Area dose [μg/cm^2] (μmol/cm^2)	LLNA EC3 [%] (solvent)[a]	Area dose [μg/cm^2] (μmol/cm^2)
Hydroxycitronellal	HMT; NOEL	5 (petrolatum)	5000 (29.0)	18 (AOO)	4500 (26.1)
	LOEL	12 (petrolatum)	12000 (69.6)	33 (AOO)	8250 (47.9)
	HRPT; LOEL	2.5 (ethanol + 25% diethylphthalate)	4200 (24.4)		
Isoeugenol	HRIPT; NOEL	0.5 (ethanol)	69 (0.42)	2.2 (AOO)	550 (3.35)
	LOEL	1.0 (ethanol)	775 (4.72)		
Lilial	HRIPT; NOEL	5 (diethylphthalate)	3750 (18.3)	19 (AOO)	4750 (23.3)
Linalool	HMT; NOEL	20 (petrolatum)	13.793 (89.4)	30 (AOO)	7500 (48.6)

[a] The EC3 is the effective concentration of a chemical (percent of chemical in vehicle) required to produce a 3-fold (i.e. threshold level) increase in the proliferation of lymph node cells compared to vehicle controls in the murine local lymphnode assay (LLNA).

AOO: acetone-olive oil; HMT: human maximization test; HRIPT: human repeat-insult patch test; LOEL: lowest observed effect level; NOEL: no observed effect level

Table 8 Elicitation values in humans from patch tests for some fragrances on the list of SCCNFP. Source: Griem et al. (2003)

Chemical	Elicitation threshold in patch test	
	Effect level test – concentration [%] (solvent)	Area dose [μg/cm^2] (μmol/cm^2)
Cinnamyl alcohol	LOEL 0.025 (petrolatum)	7.5 (0.056)
Cinnamal	NOEL 0.01 (petrolatum)	3 (0.023)
Isoeugenol	LOEL 0.01 (petrolatum	4 (0.024)
Hydroxycitronellal	LOEL 0.05[a] (hydroalcoholic)	1.83 (0.011)

[a] Repeated open use test with hydroalcoholic eau de cologne; for this type of cosmetic formulation, a use of 0.43 g on 235 cm2 of skin is assumed.

LOEL: Lowest observed effect level; NOEL: no observed effect level

7 Considerations for risk assessment of other scented product types and chemicals

The focus of this study on allergenic fragrance chemicals in passive room perfumes and spray perfumes does not imply that other product types and chemicals are automatically considered safe. Some factors that need to be considered in the risk assessment of other scented product types and chemicals are discussed below.

7.1 Risk assessment considerations for different product types

The potential risk of using scented products is determined in part by the frequency of use of the product, the exposure time and exposure levels of potentially harmful ingredients released from the product. Some considerations for the risk assessment of each product type are discussed below.

7.1.1 Mechanical room perfumes

Mechanical room perfumes appear to be very popular, considering their wide availability in grocery stores. Similar to passive room perfumes, little information is available on the possible risks of using mechanical room perfumes, although exposure to chemicals in these product types is typically long term. In addition, exposure levels to chemicals in mechanical room perfumes are probably even higher compared to passive room perfumes, since the chemicals are released in an active manner, i.e. via electricity or ventilation. The scent-releasing mechanisms within this product group vary and complicate the exposure assessment. The mass release rate of chemicals in these products is hard to estimate, but crucial for the exposure assessment. In addition, the heating occurring in some electrical plug-in room perfumes may produce potentially harmful by-products. These product types therefore also deserve further investigation.

7.1.2 Heating or burning perfumes

Relatively much scientific research has already been conducted on the use of candles, incense and ethereal oil, given also their wide use in traditional religious rituals and ethereal oil therapies. Many studies found a high release of particulate matter or heavy metals from these products, especially from incense and candles (Fang et al., 2003; Jetter et al., 2002; Lung and Hu, 2003). The Danish EPA performed a survey evaluating the risks of exposure to several substances from burning incense (Pors and Fuhlendorff, 2003). In response to this survey, the RIVM concluded in 2004 that the risk of burning incense warrants further attention. The composition of especially incense and ethereal oils is frequently unknown, but likely varies greatly, and may unduly be assumed safe due to their natural origin. The heating or burning process complicates the exposure assessment since additional by-products will be formed and released.

7.1.3 Home appliance perfumes

Many product types in the group of home appliance perfumes have only been on the market for a short while. Judging from their availability in stores, home appliance perfumes are not used as frequently as other scented products, with the obvious exception of toilet bowl rim hangers. The variation in exposure scenarios for products within this group requires a case by case evaluation of the possible risks associated with each product type.

7.2 Risk assessment considerations for different chemicals

The composition of scented products varies widely both between and within the different product types. For example, perfumes in a spray will always contain some sort of propellant and solvent, but the amount and type of propellant and solvent used may differ significantly between different spray perfumes. In addition, the great number of different scents available in the form of a passive room perfume or a spray is created by an even greater number of fragrance combinations. A further major impediment is the fact that the chemical composition of many product types is unknown. It was impossible within the current project to investigate for individual chemicals the exposure level and potential risk and as explained earlier, the current project focused on allergenic fragrance chemicals. Some considerations for the risk assessment of chemicals other than fragrance chemicals in scented products are discussed below.

7.2.1 Volatile organic chemicals

In 2004, the European Consumer's Union (BEUC) reported possible risks of using different scented product types. It was stated that high concentrations of volatile organic substances such as benzene, formaldehyde, styrene, naphthalene and acetaldehyde were measured. Indeed, many scented products contain volatile organic chemicals for use as a solvent or for other purposes. Examples of volatile organic chemicals used in passive room perfumes and spray perfumes and their concentration ranges are listed in Table 9 and Table 10 (eg. Pors and Fuhlendorff, 2003; Bouma et al., 2005, personal communication manufacturers). In response to the reports from BEUC, the RIVM in collaboration with the Dutch Food and Consumer Product Safety Authority (VWA) evaluated the exposure and risk of benzene, styrene and formaldehyde in a specific passive room perfume and a spray perfume (Bouma et al., 2005). The RIVM concluded that at the estimated exposure levels there was no indication of a health risk associated with the use of these two particular products. However, the study was limited to two product types and three chemicals.

Other product types have been suggested to potentially emit levels of volatile organic chemicals that may indicate a risk. A survey by the Danish EPA on incense indicated that high levels of benzene were emitted while burning incense, approaching levels around the chronic values for acceptable carcinogenic risks (Pors and Fuhlendorff, 2003). It is recommended that volatile organic chemicals are included in the risk assessment of scented products.

Table 9 Volatile organic chemicals in passive room perfumes

Common name	CAS no	Concentration range in products (mg/kg)
Acetaldehyde	75-07-0	5 – 23
Benzene	71-43-2	0.2
Formaldehyde	50-00-0	5 – 35
Naphtalene	91-20-3	0.2 – 0.31

Table 10 Volatile organic chemicals in spray perfumes

Common name	CAS no	Concentration range in products (mg/kg)
Benzene	71-43-2	0.3
Ethanol	64-17-5	250000 – 350000
Formaldehyde	50-00-0	2 - 65
Hexane acid ethylester		unknown
Isopropanol	67-63-0	unknown
Triethylene glycol	112-27-6	60000

It must be emphasized that because of the very limited data sources, these tables should be considered as indicative only.

7.2.2 Heavy metals

Incense in particular have been reported to emit relatively high levels of heavy metals (Lung and Hu, 2003; Lin and Shen, 2003; Jetter et al., 2002; Fang et al., 2003). In addition, relatively high levels of lead and zinc were found to be emitted from burning candles (Wasson et al., 2002; Nriagu and Kim, 2000). Heavy metals may therefore be another group of chemicals to include in the risk assessment of scented products.

7.2.3 By-products

The risk assessment of scented products should not just focus on chemicals reported in the product composition. Some chemicals may only be formed upon exposure to air or after heating or burning of the product. Little information is available on what chemicals may be formed from scented products via these processes. The risk assessment of scented products may need to take in account these possible by-products.

7.2.4 Fine particulate matter

Scientific literature indicates that the use of incense, candles and other scented products may contribute to an increase in the indoor levels of fine particulate matter (< 2.5 µm) (Afshari et al., 2005; Lung and Hu, 2003; Fang et al., 2003; Sorensen et al., 2005). The generation of fine particulate matter may need to be included in the risk assessment of scented products.

8 Conclusions and recommendations

Many scented product types are available on the market, varying greatly in their fragrance release pattern, location of use, and application. These variations in turn lead to a wide variety in exposure scenarios. In addition, the products may contain hundreds of different chemicals, including fragrances that have been listed by the SCCNFP as contact allergens. Measured exposure data to all these chemicals from all product types for every exposure scenario are not available and exposure assessments need to be based on modeled data.

The ConsExpo 4.0 software can model exposure levels for chemicals in passive room perfumes in the form of a gel or a liquid and for chemicals in spray perfumes. However, little information on the use patterns of scented products is available to provide reliable input data for the models in ConsExpo 4.0. Although values for some parameters can be estimated with a certain degree of confidence, more insight in consumer use patterns such as use frequencies and exposure durations would greatly improve the exposure assessment. In addition, information on the use of combinations of products is necessary to determine whether a cumulative risk assessment for one chemical in different scented products is necessary.

Measured exposure data would help to evaluate the ConsExpo 4.0 exposure assessment results. Examples of useful measured exposure data include:

- Air concentrations of fragrances at different time intervals in rooms in which passive room perfumes, spray perfumes or other scented products have been used
- Airborne fractions, mass generation rates and particle distributions of different spray perfumes and the effect of using different solvents and/or propellants on these parameters
- Dermal exposure levels of various chemicals after using spray perfumes
- For product types other than passive room perfumes and spray perfumes, more measured data are needed, such as mass generation rates from mechanical room perfumes, identification and emission rates of (by-)products released from heating or burning incense, ethereal oils and candles

A literature search on absorption of fragrance chemicals would be useful to determine and compare systemic levels of fragrance chemicals via different routes of exposure. However, it is anticipated that little information, particularly on inhalation uptake levels, will be available and more research may be needed in this area.

Another important limitation in the risk assessment of allergenic fragrances in scented products is the limited knowledge on respiratory sensitization. Thresholds and classification of allergenic potency now appear to be possible for skin sensitizers using the LLNA, and a similar approach for respiratory sensitization may be possible. An in-depth literature review on this subject would shed more light on the possibilities for such an approach. In addition, a possible line of research in this area could be:

1) Select a number of fragrance chemicals that have been shown to be skin sensitizing and which induce allergic reactions in humans. A starting point for this selection could be the list drawn up by the SCCNFP
2) Compare the potency of a number of model fragrance chemicals with sensitizing activity by means of the LLNA and dose response relations in respiratory sensitizing tests
3) Compare dose response relations for primary sensitization and allergic reactions
4) Based on the outcome, classify the fragrance chemicals according to the extent to which these chemicals can be sensitizing and determine their thresholds
5) Based on consumer use patterns and exposure data of these fragrance chemicals, assess how many people will be exposed to levels above the thresholds for sensitization and allergic reactions
6) Validate the results of this approach with reported information on the selected fragrance chemicals

In summary, a combination of more data on composition of products, consumer use patterns, uptake levels and allergenic (respiratory) potentials of fragrance chemicals, may help identify the risks in using scented products.

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Appendix I: Suggested ConsExpo 4.0 parameter values for passive room perfumes

This appendix contains suggested parameter values for the exposure assessment of chemicals in passive room perfumes with ConsExpo 4.0. It needs to be emphasized that these values can serve as a starting point for exposure estimation and should be used in the absence of accurate scenario data only. Whenever more detailed information for the product is available, these data should be used instead.

I.a General exposure scenario data

Two examples of exposure scenarios were described in section 5.1.1:

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

Parameters that need to be defined in the exposure scenario section are:

- Bodyweight: Separate exposure assessments should be performed for children and adults. Up to date information on average bodyweights in the Netherlands is available from the Statistics Netherlands (CBS) Statline database[1].
- Use frequency: A passive perfume typically releases its fragrance for several weeks, after which products may be replaced by new ones. A user of passive room perfumes will therefore be exposed every day.

I.b Exposure route data

The exposure model that should be used to describe inhalation exposure to passive room perfumes is the exposure to vapour model. All three modes (instantaneous, constant rate and evaporation) within this model are appropriate to estimate the exposure levels, as explained in more detail in section 5.1.2.

General exposure parameters for all three modes:

- Exposure duration: For the exposure to a passive room perfume in a living room, exposure duration can be assumed 8 hours. For a car, exposure duration can be assumed 3 hours.
- Product amount: The amount of product in a passive room perfume in the form of a gel or liquid ranges from 6 – 75 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

[1] http://statline.cbs.nl/StatWeb

0.1 - 2.5 grams per day, assuming a specific weight of approximately 1 g/cm^3.

- Weight fraction compound: compositions of passive room perfumes may vary greatly. According to the Dutch society of soap manufacturers (NVZ), a typical composition of passive room perfumes in the form of a liquid or a gel is as follows[2]:

Table 11 Indicative composition of passive room perfumes (NVZ)

Component	Weight %
Fragrance	1 – 10%
Solvent	> 50%
Color	< 1%
Conservative	< 1%
Emulsifier/tensid	5 – 50%

However, there are also passive room perfumes on the market which contain > 95% fragrance. As discussed before, it is at all times preferential to use product specific data.

- Room volume and ventilation rate: passive room perfumes can be used in any room throughout the house, in a car, at the office and at stores. Default values for room volumes and ventilation rates in the Netherlands can be found in the General Factsheet belonging to ConsExpo (Bremmer and van Veen, 2000). For a living room, default values are:

Table 12 Default values for living room properties from the general fact sheet belonging to ConsExpo (Bremmer and van Veen, 2000).

	Living room
Room volume [m^3]	58
Ventilation rate [1/hr]	0.5

The volume of a car interior may range from 3 - 6 m3 and ventilation rates may range from 0 – 3/hr.

Constant rate mode parameters

- Emission duration: a passive room perfume will release its fragrance 24 hours per day. The emission duration for a use frequency of every day is therefore 24 hours.

Evaporation mode parameters

- Release area: passive perfumes in the form of a gel or liquid are usually contained in a plastic or glass container with an opening to release the fragrance. The area of this opening typically ranges from 1 – 30 cm^2. This area remains constant throughout the use of the product.
- Application duration: as the products can generally not be switched off, the application duration for passive room perfumes is 24 hours for a use frequency of every day.

[2] http://www.isditproductveilig.nl/was_en_reinigingsmiddelen/index.php?file_id=277

- The physicochemical properties molecular weight and vapour pressure at the application temperature (usually room temperature, 20˚C) of the chemical of interest are evidently chemical-specific.
- Mass transfer rate: the velocity by which a chemical is transferred between the product and the air. ConsExpo 4.0 offers two models to approximate this rate: Langmuir's method and Thibodeaux' method. Langmuir's method generally gives a worst case estimate. If the chemical is contained in a product consisting mostly of water, Thibodeaux' method can be used. For mechanical room perfumes, these methods are not applicable. The mass transfer rate of chemicals in these product types is largely dependent on the mechanism by which the fragrance is released and this should be estimated based on measured emission data.
- Molecular weight matrix: usually, the chemical of interest is part of a liquid or gel product containing many other chemicals. For a liquid or gel, the molecular weight will be approximately 1 g/mol.

Inhalation uptake parameters

- Uptake fraction: when unknown, a worst case value is 1, assuming all the chemical is taken up by the lungs.
- Inhalation rate: a default inhalation rate can be calculated in ConsExpo 4.0 based on bodyweight and exercise level.

Appendix II: Suggested ConsExpo 4.0 parameter values for spray perfumes

This appendix contains suggested parameter values for the exposure assessment of chemicals in spray perfumes with ConsExpo 4.0. It needs to be emphasized that these values can serve as a starting point for exposure estimation and should be used in the absence of accurate scenario data only. Whenever more detailed information for the product is available, these data should be used instead.

II.a General exposure scenario data

Two examples of exposure scenarios were described in section 5.2.1:

1) A user sprays an air spray in a small bathroom.
2) A perfume spray is used to mask unpleasant odors on a couch in a living room. After spraying, a young child crawls on the couch.

Parameters that need to be defined in the exposure scenario section in ConsExpo 4.0 are:

- Bodyweight: separate exposure assessments should be performed for both children and adults. Up to date information on average bodyweights in the Netherlands is available from the Statistics Netherlands (CBS) Statline database[3].
- Use frequency: information on the use frequency of perfume sprays is not available. It can be estimated that a consumer uses a perfume spray 1 – 5 times per day for both scenario examples described above.

II.b Exposure route data

Two exposure routes are relevant for the exposure assessment to chemicals in perfume sprays: the inhalation and dermal route.

II.b.1 Inhalation exposure

The exposure model that should be used to describe inhalation exposure to non-volatile chemicals in spray perfumes is the exposure to spray model, as explained in more detail in section 5.2.2.1.

[3] http://statline.cbs.nl/StatWeb

Exposure parameters of exposure to spray model:

- Spray duration: for a spray bottle mounted on the wall of a bathroom, the spray duration may only be one second. If a spray can is used to treat furniture in the living room, the spray duration may be several seconds.
- Exposure duration: the exposed person may spend several hours in the living room, but generally only spends several minutes in the bathroom.
- Room volume, room height and ventilation rate: default values for these parameters for Dutch rooms are available in the General Fact sheet belonging to ConsExpo (Bremmer and van Veen, 2000):

Table 13 Default values for bathroom and living room properties from the general fact sheet belonging to ConsExpo (Bremmer and van Veen, 2000).

	Bathroom	Living room
Room volume [m^3]	10	58
Room height [m]	2.5	2.6
Ventilation rate [1/h]	2	0.5

- Mass generation rate: experimental results of a study on spray cans and trigger sprays assigned by the RIVM demonstrated that the mass generation rate for sprays ranged from 0.1 – 1.5 g/sec (Delmaar, in preparation). The mass generation rate of a toilet freshener included in the study was 0.5 g/sec, that of a textile freshener was 0.2 g/sec.
- Airborne fraction: if no data is available, the airborne fraction for air sprays can be assumed to be 1. For sprays to treat furniture, this fraction will be much less than 1.
- Weight fractions chemical, propellant, non-volatile and solvent: compositions of sprays may vary greatly. According to the Dutch society of soap manufacturers (NVZ), a typical composition of spray perfumes is as follows:

Table 14 Indicative composition of spray perfumes. Source: NVZ

Component	Weight %
Fragrance	0.5 – 5 %
Solvent	> 50 %
Conservative	< 1 %
Emulsifiers/surfactants	< 5 %

Spray perfumes in the form of spray cans also contain 5 – 75% propellants. As discussed before, it is at all times preferential to use product specific data.

- Density solvent: the solvent used in spray perfumes is generally ethanol. This has a density of 0.8 g/cm^3. For some spray perfumes, water can also be used as a solvent. This has a density of 1.0 g/cm^3.
- Density non-volatile: spray perfumes may contain several non-volatile components, this is very product specific. However, most components will be organic chemicals, which will have a density no higher than 1.3 g/cm^3.

- Initial particle distribution: mean or medium particle sizes from spray cans included in the research on spray cans and trigger sprays assigned by the RIVM ranged from 15 - 200 µm in diameter, with 90th percentiles in the range of 40 – 500 µm (Delmaar, in preparation). The median particle size of a toilet freshener was ±40 µm in diameter, with a 90th percentile of ±100 µm. The median particle size of a textile freshener was ±80 µm, with a 90th percentile of ±155 µm.
- Inhalation cut-off diameter: the diameter of a droplet that can be inhaled rather than deposited in the upper airways (resulting in oral uptake) is usually assumed to be 15 µm.

Spray inhalation uptake model parameters:
- Uptake fraction: in the absence of experimental data, a worst case value is 1, assuming all the chemical is taken up by the lungs.
- Inhalation rate: a default inhalation rate can be calculated in ConsExpo 4.0 based on bodyweight and exercise level.
- Oral uptake fraction: similar to the inhalation uptake fraction, a worst case value is 1, assuming all the chemical is taken up by the gastrointestinal tract.

II.b.2 Dermal exposure

As explained in more detail in section 5.2.2.2 the scenario for both the hands of an air spray user and a crawling child can be described by both the instant application and the constant rate modes. The scenario for the textile freshener can also be described by the rubbing off mode.

General exposure parameter for all modes:
- Exposed area: for the air spray, the exposed area consists of the skin on the hands. For a crawling child, the exposed area can be calculated based on a child wearing a short-sleeved shirt and a napkin, and no socks or shoes. The exposed area then consists of the hands, feet, forearms and lower legs. Default values for surface areas of different body parts for adults and children are given in ConsExpo's general fact sheet (Bremmer and van Veen, 2000).

Instant application parameters:
- Weight fraction chemical: indicative composition of spray perfumes according to the NVZ has been given in Table 14. However, product specific data take preference.
- Product amount: for an air spray, the amount of product available for dermal exposure depends on what is assumed to be the airborne fraction. For example, if the airborne fraction was assumed to be 90%, then the product amount remaining for dermal exposure would be 10% of the total amount of product sprayed.
  For a textile spray, it can be assumed that all of the product sprayed is available for dermal exposure.

Constant rate parameters:

- Weight fraction chemical: indicative composition of spray perfumes according to the NVZ has been given in Table 14. However, product specific data take preference.
- Release duration: dermal exposure to an air spray can be assumed to take place only during spraying. The release duration is in this case equal to the spray duration. For a spray used in a bathroom, the spray duration may only be one second. For a spray used to treat furniture in the living room, the release duration depends on the time spent on the couch, which for a child may be a few minutes to several hours.
- Contact rate: the amount of product available for dermal exposure to an air spray depends on the airborne fraction. The toilet freshener of the RIVM study had a mass generation rate of 0.5g/sec (Delmaar, in preparation). If 10% of the product would be available for dermal exposure, the contact rate would be 0.05g/sec. For a textile spray, the product amount available for dermal exposure is the total amount sprayed on the couch. The textile freshener in the RIVM study had a mass generation rate of 0.2g/sec (Delmaar, in preparation). If this particular spray is used for 1–20 seconds, 0.2-4g is available for dermal exposure. With a release duration of 1–180 minutes, the contact rate may then range from 0.001-4g/minute.