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and Food of Denmark**

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Survey of allergenic substances in products targeted children – toys and cosmetic products

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Consumer Products No. 148, 2016

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Survey of allergenic substances in products
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Foreword

The project "Survey of allergenic substances in products targeted children – toys and cosmetic products" was completed in the period from March 2015 to April 2016. Observations of declarations of contents on cosmetic products for children were conducted in May 2015. The contact to the Toy industry took place in the period from June to August 2015.

This report describes which potentially allergenic substances that are found in toys and cosmetic products for children on the Danish market. An overview of potentially allergenic substances was presented to the Toy industry and a selection of cosmetic products for children was examined for these substances by means of the declarations of content on the products. Based on this survey and in co-operation with the Danish Environmental Protection Agency, a number of products (cosmetic products and toys) were selected and analysed for selected fragrances. The results of the survey and chemical analyses are presented in the report.

The project was carried out for the Danish Environmental Protection Agency by FORCE Technology.

The participants of the project were:

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- Nanna Hundebøll, FORCE Technology (survey)
- Anders Schmidt, FORCE Technology (quality assurance)
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The project was supervised by a group consisting of Shima Dobel and Bettina Ørsnes Larsen from the Chemical unit, the Danish Environmental Protection Agency.

The project was financed by the Danish Environmental Protection Agency.

Summary and Conclusion

Background and purpose

According to the Danish Allergy Research Centre (2015), at least 10% of the Danish population suffers from contact allergy towards one or more chemical substances. Substances with allergenic properties are called allergens. Allergy may be for life when it has first developed.

Contact allergy among children has earlier been considered as rare but data from the last decade indicates an increase in the occurrence of contact allergy among children. A Danish study of more than 2,500 children referred to patch test during the years 2003-2011 showed that the most common allergenic substances were metals, fragrances and colourants (Simonsen et al., 2013).

Therefore, with this project, the Danish EPA wanted to investigate whether toys and cosmetic products addressed to children and in prolonged contact with the skin contain allergenic substances and if corresponding products without allergenic substances are available on the market.

The project has exclusively focused on allergenic substances.

Limitation of cosmetic products for children and toys

In co-operation with the Danish EPA, it was decided to focus on the following sub-group of cosmetic products for children and toys:

- Cosmetic products for children with prolonged skin contact, i.e. products which are targeted children with claims such as “kids”, “children” or pictures which show that they are targeted children.
- Chemical toys where children are expected to have prolonged and direct exposure of allergenic substances. Chemical toys are defined as toys which for instance are in liquid form or powder form as among other things finger paint.

Gross list of allergenic substances

There are many thousands of substances which are considered to be allergenic. According to ECHA's database, there exist more than 1,100 chemical substances with a harmonised classification as allergenic at skin contact, i.e. Skin Sens 1, 1A or 1B. If this search is expanded to chemical substances which are notified with a self-classification as allergenic at skin contact, the result is nearly 12,000 chemical substances (ECHA C&L Inventory, 2015).

Therefore, in the project, there have been a need to focus the effort, among other things by prioritising the allergenic substances which are typically found in cosmetic products and toys. It was decided to focus on allergenic substances from four overall groups:

- Fragrances
- Preservatives
- Colourants
- UV filters

A gross list of allergenic substances, which can occur in cosmetic products for children and in toys, was prepared by making a preliminary list of allowed colourants, preservatives, UV filters and used fragrances in cosmetic products. The substances in the preliminary list were assessed for their potentially allergenic properties based on SCCS opinions, harmonised classifications and other relevant knowledge. Substances which did not have potentially allergenic properties were

eliminated and the remaining substances are substances in the gross list of potentially allergenic substances.

The substances in the gross list may be assumed to be used in cosmetic products and it is assumed that chemical toys can contain the same allergenic substances which are allowed to be used in cosmetic products. This is substantiated by the fact that cosmetic toys have to fulfill the same requirements on composition and labelling which are laid down in the Regulation on cosmetic products.

In total, the gross list contains 191 potentially allergenic substances (also called gross list substances): 2 colourants, 164 fragrances, 19 preservatives, 3 UV filters and 3 adhesives (binders).

Procedure for the survey

Based on the gross list of the potentially allergenic substances, a survey was carried out showing which substances that are used in chemical toys and cosmetic products for children on the Danish market. The survey was carried out by use of the following methods:

- Visits in shops
- Close reading of list of ingredients on products in shops (for cosmetic products)
- Literature search
- Search on the internet
- Contact to the industry (exclusively for toys)

In co-operation with the Danish Toy Sector (“Legetøjsbranchen” – LEG) and the Danish EPA, it was decided that it would be too enormous a task for manufacturer/distributors of toys to go through all of their products for all the 191 potentially allergenic substances from the gross list. For that reason, another approach was chosen. First, a survey was made of which of the 191 gross list substances that were observed in cosmetic products in shops on the Danish market. This shorter list of approx. 30 substances as well as the 26 fragrances subject to declaration from the regulation on cosmetic products was then sent to the members of LEG with the request of sending information on these potentially allergenic substances back to the project group.

The result of the survey

Cosmetic products for children

Lists of ingredients from in total 157 cosmetic products for children on the Danish market were examined for contents of substances from the gross list. The survey shows that a large part (41%) of the cosmetic products for children is eco-labelled (the Swan) and/or allergy-labelled (44%) (The Blue Label). Several of the products have both labels. None of these products contains substances with a harmonised classification as allergenic, as it is not allowed according to the criteria for these labels. In the survey, products without potentially allergenic substances which are neither eco-labelled nor allergy-labelled have been identified.

More than the half (60%) of the 157 investigated cosmetic products for children are produced in the EU while 27% are produced in the East, mainly in China. For the remaining products, the producer country is unknown. In percentages, more of the cosmetic products which are produced in the East (21% or 9 out of 43 products) contain potentially allergenic substances compared to the cosmetic products produced in the EU (12% or 11 out of 94 products).

Out of the in total 157 products, 30 products contained between one and eight substances on the gross list. A content of many potentially allergenic substances is typically due to a content of many different fragrances. The identified potentially allergenic substances in the investigated cosmetic products for children were:

- Two different preservatives (seen in 2 different products – in suntan lotion and face paint)
- Three different UV filters (seen in 2, 6 and 9 products respectively – in lip balm/lip gloss and suntan lotion)
- 8 of the 26 fragrances subject to declaration (seen in 1-3 products – in lip balm/lip gloss and suntan lotion)
- A declared content of "perfume" which might cover for a content of potentially allergenic fragrances (seen in 22 products – in many different types of products)

In relation to the earlier surveys of cosmetic products for children (Poulsen & Schmidt, 2007) and suntan lotions/lotions for children (Tønning et al., 2009), it is mainly the same potentially allergenic substances which were identified in the cosmetic products for children at that time.

Toys

Contact to LEG (the Danish Toy Sector) and selected manufacturers/distributors resulted in information from in total eight manufacturers/distributors on the Danish toy market. Part of the contacted toy distributors and manufacturers has suppliers from the East (as for instance China, Korea, Taiwan and Thailand) but toys are also purchased from European suppliers.

The survey shows that several of the eight companies who have delivered information to the project set requirements on allergenic substances. Among other things, the use of fragrances in chemical toys is unwanted by several companies and several companies make requirements regarding ban on the use of allergenic preservatives or work at replacing allergenic preservatives in their chemical toy products. The contact to the companies shows that chemical toys without any use of potentially allergenic ingredients are found on the Danish market. However, it must be noted that during the project contact was made to toy manufacturers/distributors who did not deliver information to the project. It is possible that the toy products from these companies contain potentially allergenic substances.

No use of either potentially allergenic UV filters or colourants in the chemical toy products was identified. It is primarily potentially allergenic fragrances (mainly in the cosmetic products such as face paint, make-up and perfume sets) and potentially allergenic preservatives (mainly in finger paint, modelling clay and make-up as well as soap bubble products) which seem to be used in chemical toys.

Hazard assessment of identified potentially allergenic substances

A hazard assessment was made of the potentially allergenic substances which were identified in the survey of toys and cosmetic products for children. The hazard assessment focused exclusively on the allergenic properties of the substances, i.e. the allergy potential of the substances and possible levels of elicitation and induction if this information was available. The hazard assessment showed that in general there is limited information on the allergenic properties of the substances. The allergenic potential of the substances is often stated but information about levels of elicitation and induction is only identified for a few substances. This means that a risk assessment of the substances will be difficult to carry out and thus it was not performed in this project.

Focus in the analytical phase

15 out of the in total 157 investigated products had a declared content of perfume but no content of the 26 fragrances subject to declaration in concentrations subject to declaration.

Therefore, it was decided that focus on substances for possible chemical analyses had to be changed to "other" potentially allergenic fragrances, i.e. fragrances which SCCS assesses as allergenic in humans but which are not a part of the 26 fragrances subject to declaration. Focus of the analyses was thus "other" fragrances than the 26 fragrances subject to declaration.

However, the survey has not been able to give any information on which other fragrances that are used as fragrances, as fragrances besides those subject to declaration, exclusively are to be described with the general name "perfume" on the list of ingredients of the cosmetic products. The purpose of analysing cosmetic products with "other" fragrances is thus to examine which "other" fragrances that are used.

Chemical analysis of "other" potentially allergenic fragrances

Initially, it was investigated which of the "other" potentially allergenic fragrances it would be possible to analyse. The basis was SCCS's list of the 82 potentially allergenic fragrances. A search for analytical methods in the literature as well as the possibilities of buying the fragrances as reference substances gave the result that in total 21 (of the 30) "other" potentially allergenic fragrances were selected and for these a SPME Headspace GC-MS analysis was made. Furthermore, it was also possible with the same method to identify some of the 26 fragrances subject to declaration. This qualitative analytical method was chosen due to highest recovery rate of most fragrances and because it is a cheaper analytical method. Through this analytical method, focus is on the substances which, just like perfume, are in the air above the sample. Thus, it is the substances evaporating from the products that are identified by use of the chosen method.

Product selected for chemical analysis

The following products were purchased for analysis of the content of "other" allergenic fragrances:

- 13 pieces of cosmetic products with a declared content of perfume but without a declared content of the 26 fragrances subject to declaration (identified through the survey). However, these products may in principle have a content of fragrances subject to declaration below the concentration subject to declaration. The 13 cosmetic products consisted of in total 23 sub-products as 3 products consisted of a make-up set of different products.
- 10 pieces of modelling clay which smells (of perfume)
- 7 pieces of slime toys which smell (of perfume)
- 4 pieces of other toys which smell (of perfume)

Other toys consisted of a doll with odour, a teddy bear with odour and rubber bands (which for instance may be crocheted together to bracelets) with odour.

Analytical results

The qualitative analysis of the "other" potentially allergenic substances showed that 4 of these substances were identified in both cosmetic products and in toys. All in all, one or several of these 4 "other" allergenic fragrances are identified in 19 of the examined 44 sub-products. These 4 "other" potentially allergenic substances were:

- Terpineol (in 2 cosmetic products (3 sub-products), 2 modelling clays and 1 slime)
- Vanillin (in 2 cosmetic products (3 sub-products), 1 modelling clay and 2 slimes)
- Benzaldehyde (in 2 cosmetic products (4 sub-products), 4 modelling clays and 1 other toy)
- Camphor (in 1 cosmetic product (3 sub-products))

Furthermore, at the qualitative analysis, several of the fragrances subject to declaration were identified. Limonene and linalool are the most frequently used of the fragrances subject to

declaration, and it was also possible to identify them by the used method. Some of the identified fragrances in the toys are not allowed in toys in concentrations above 100 ppm but as the exact concentration is unknown, the product might still be compliant with the legislation. A few of these fragrances subject to declaration were not declared on the cosmetic products. This may be due the fact that they occur in a concentration below 0.001% (10 ppm) for leave-on cosmetic products and below 0.01% (100 ppm) for rinse-off cosmetic products respectively. As no quantitative analyses are made this cannot be confirmed.

Based on the substances which were possible to identify, the analytical results show that 12 out of the in total 34 (35%) analysed products are free from potentially allergenic gross list substances. These products are distributed on 3 of the 13 cosmetic products, 4 of 10 modelling clays and 5 of 7 slimes.

Conclusion

An essential conclusion from the survey is that it is possible to find cosmetic products for children in the Danish shops without potentially allergenic substances (127 out of 157 investigated products are without a content of potentially allergenic substances from the established gross list). It is possible for nearly all the investigated product types (except for the product types hair spray and perfume set) to find products without potentially allergenic substances (from the gross list).

The overall picture from the survey of toys is that alternative products without allergenic substances (based on the gross list) are found on the Danish shop market and that the part of the Danish toy sector who responded to the inquiry is aware of the problem and in general tries to avoid allergenic substances.

Focus in the project was fragrances which during the survey turned out to be that group of substances which could constitute the biggest problem as regards to allergy. In that context, selected cosmetic products with a declared content of perfume as well as toys which smell of perfume were analysed for a content of selected fragrances.

The analyses showed that a relatively large part of the analysed product types (cosmetic products with perfume, modelling clay, slime and other smelling toys) may contain potentially allergenic fragrances. The analysed products were intentionally selected because most probably they could contain potentially allergenic fragrances and the general picture is that both for toys and cosmetic products targeted children, it is possible to find products which do not contain substances on the gross list of potentially allergenic substances.

1. Introduction

1.1 Background

According to the Danish Allergy Research Centre (2015), at least 10% of the Danish population suffers from contact allergy towards one or more chemical substances. Substances with allergenic properties are called allergens and it might be metals, preservatives, fragrances, colourants and other substances (Danish Allergy Research Centre, 2015).

Contact allergy has earlier been considered as rare but data from the last decade indicates an increase in the occurrence of contact allergy among children. A retrospective study of in total 2,594 Danish children between 1 and 17 years referred to patch test (allergy test) in the years 2003-2011 showed that 25.1% had one or more positive reactions. The most common sensitising substances were metals, fragrances and hair dyes (Simonsen et al., 2013). However, the study is not representative for all children in Denmark as children referred to patch test have most probably contact allergy to a greater extent than children who are not referred.

Allergy may be for life when it first has developed. Therefore, the Danish Environmental Protection Agency (Danish EPA) wants to investigate whether toys and cosmetic products addressed to children contain allergenic substances.

1.2 Allergy

Different types of allergy exist – immediate allergy and contact allergy. Immediate allergy is caused by for instance pollen, house dust, animal hair, food products and latex and the symptoms like allergic rhinitis, urticaria and asthma can appear a few minutes after the exposure to the allergen. Contact allergy also called skin allergy occurs through skin contact with chemical substances which can develop allergy, for instance fragrances, metals, colourants and preservatives. The symptoms of contact allergy are eczema which can occur hours to days after the exposure to the allergen (Danish Allergy Research Centre, 2015).

1.2.1 Skin allergy

Skin allergy is a result of an immunological reaction which progresses in two phases. In the first phase, the hypersensitivity is developed. It is also called sensitisation or induction. This phase takes place without any symptoms. If the person is subsequently exposed to the same substance in sufficient amounts, the immunological response is activated and symptoms occur (eczema) (Danish Allergy Research Centre, 2015).

To be able to sensitise, the chemical substance has to be able to penetrate the outermost layer of the skin. At this passage, a conversion of substances can take place which can both increase or reduce the allergenic potential. The allergenic substance is adhered to proteins in the skin and generates a so-called hapten-protein complex. The complex is absorbed by cells from the immune system, Langerhans cells, which are activated and migrate to the nearest lymph nodes. Here, other cells in the immune system are found, the T-cells, which are activated and divided, i.e. many identical cells are generated. These T-cells match precisely to the chemical and will be activated when they get into contact with it again (OECD, 2012; Danish Allergy Research Centre, 2015).

In the second phase, symptoms after skin contact with the same allergen are developed. Again, a generation of a hapten-protein complex takes place and now the T-cells respond to the chemical

substance which they recognise from the sensitisation. Hereafter, a large number of transmitter substances, cytokines, are generated and they attract other cells from the immune system with the purpose to eliminate the penetrating chemical substance. The result is that the blood flow in the skin is increased and the cells migrate to the outermost layer of the skin. This is the beginning of an acute allergic eczema and this is the process which causes that the skin becomes red, swollen, itchy and burning. Normally, the reaction is not visible until after 18-48 hours after the exposure of the allergenic substance as the communication between the cells takes time. The phase is also called elicitation (Danish Allergy Research Centre, 2015; OECD, 2012).

The eczema will initially develop on the skin area where the contact with the allergenic substance has taken place but the allergic eczema will be spread if it is not treated. An untreated allergic eczema can become chronic, i.e. the eczema will be present even if there is no longer any contact with the allergenic substance (Danish Allergy Research Centre, 2015).

The sensitisation depends on several factors such as (WHO, 2008):

- The potency of the allergen, i.e. how large an amount of the substance per unit area that is necessary to sensitise a person not exposed before.
- The exposure conditions, i.e. concentration, frequency and duration of the exposure.

A dose-response relation is found for both sensitisation and elicitation, i.e. in principle, a threshold value can be set for the condition where a chemical exposure will not sensitise or trigger an allergic reaction. However, these threshold values are not absolute values and are not necessarily applicable for a whole population as large differences between individuals are found (WHO, 2008). The general guideline is that the amount of a substance which is necessary to sensitise (phase one) normally is higher than the amount of the same substance which is necessary to trigger allergic symptoms in the already sensitised person (phase two) (Lundov et al., 2010).

1.3 Purpose

The purpose of this project is to provide an overview of which allergenic substances that are found in toys and cosmetic products for children on the Danish market. Focus of the project is allergenic substances in toys and cosmetic products which are in prolonged contact with the skin and which are targeted or appeal to children.

As the project exclusively has focus on allergenic effects it must be noted that effects besides allergenic effects are not assessed or treated in this report.

1.4 Definitions

Here, a number of the terms which are used in this report are defined. Furthermore, a limitation of which allergenic substances being in focus in this project is undertaken.

1.4.1 Cosmetic products

Cosmetic products are defined as in article 2 in the Regulation on cosmetic products EU Regulation no. 1223/2009 (EU, 2009a), i.e. "means any substance or mixture intended to be placed in contact with the external parts of the human body (epidermis, hair system, nails, lips and external genital organs) or with the teeth and the mucous membranes of the oral cavity with a view exclusively or mainly to cleaning them, perfuming them, changing their appearance, protecting them, keeping them in good condition or correcting body odours".

In this project, it is chosen to focus on cosmetic products with a high exposure, i.e. products with a prolonged skin contact. Therefore, the survey of cosmetic products has included the following product types targeted children:

- Face paint
- Baby oil

- Baby powder
- Conditioner (leave in)
- Lotion (body lotion, hand lotion)
- Hair gel
- Hair wax
- Hair spray
- Body glitter
- Lip balm/lip gloss
- Make-up (such as sets consisting of for instance eye shadow, eye pencil, rouge, lipstick, body glitter)
- Nail polish
- Perfume set
- Ointment
- Suntan lotion (including after sun lotion and sun spray)
- Tattooing products
- Towelettes/cleansing tissues

Hair dye products which are a cosmetic product may contain high amounts of allergenic substances. However, hair dye products are not assessed in this project as hair dye products are not recommended to be used by children and young people under 16 years and thus the products are not included in the target group of this project.

1.4.2 Toys

Toys are defined like in the statutory order on safety requirements to toy products (Stat. Ord. No. 13, 2011), i.e. toys which are solely or partly constructed or intended to be used by children under 14 years during playing.

The project solely focuses on toys with an expected prolonged and direct contact with the content of possible allergenic substances. The following types of toys (called “chemical toys” in the report) are included:

- Modelling clay and similar products – for instance formable sand
- Finger paint
- Face paint and make-up
- Slime
- Transferable tattoos or sets to paint own tattoos
- Jewelries (stones) which are glued on the skin as decoration
- Soap bubbles and soap for foam pistols

Focus is on toys which are imported to the EU.

1.4.3 Allergenic substances

Many thousands of substances are considered to be allergenic. According to ECHAs C&L Inventory which is a database with information on classification and labelling of notified and registered substances, there are in total 1,149 chemical substances with a harmonised classification as allergenic at skin contact, i.e. Skin Sens 1, 1A or 1B (as per 22 May 2015 where the database was latest updated). If this search is expanded to chemical substances which are notified with a self classification as allergenic at skin contact, the result is nearly 12,000 chemical substances (ECHA C&L Inventory, 2015).

Therefore, there is a need to select and focus the efforts, among other things by prioritising the allergenic substances which are typically found in cosmetic products and toys. In this project, focus is chosen to be on allergenic substances from four overall groups: Fragrances, preservatives,

colourants and UV filters. In section 3 “Gross list of potentially allergenic substances”, it is described in details which substances that are considered to be allergenic in these overall groups.

1.4.3.1 Fragrances

In this project, fragrances are defined as “scented compounds and the raw materials for this purpose” which according to the regulation on cosmetic products (EU, 2009a) have to be stated on the declaration of contents with the expression “perfume” or “aroma”. As described in a SCCS opinion on fragrances, these are organic compounds with a characteristic and normally pleasant odour (SCCS no. 1459, 2012). SCCS is the EU’s Scientific Committee for Consumer Safety.

1.4.3.2 Preservatives

In this project, preservatives are defined as in the regulation on cosmetic products (EU, 2009a), i.e. *“substances which are exclusively or mainly intended to inhibit the development of micro-organisms in cosmetic products”*. This definition does also apply for substances which have to inhibit development of micro-organisms in toys.

1.4.3.3 Colourants

In this project, colourants are defined as in the regulation on cosmetic products (EU, 2009a), i.e. *“substances which are exclusively or mainly intended to colour the cosmetic product, the body as a whole or certain parts thereof, by absorption or reflection of visible light; in addition, precursors of oxidative hair colorants shall be deemed colorants”*. As this project does not include hair dye products, these products are excluded. This definition does also apply for substances which exclusively or mainly are intended to colour toys.

1.4.3.4 UV filters

In this project, UV filters are defined as in the regulation on cosmetic products (EU, 2009a), i.e. *“substances which are exclusively or mainly intended to protect the skin against certain UV radiation by absorbing, reflecting or scattering UV radiation”*.

1.4.4 Children

In this project, children are defined as children aged 0 to 12 years. There are three age groups:

- 0-3 years
- 4-6 years
- 7-12 years

This division is made as children at different ages will use different types of cosmetic products and toys.

1.4.5 Products for children

In this project, products for children are defined as products which clearly appeal to children; i.e. products which:

- Are claimed with for example the following words: “Baby”, “Kids” or “Children”.
- Are claimed with motives/pictures of babies, children, animals or other figures which appeal to children, for instance through pictures of known cartoon figures or pictures of a baby.
- Otherwise appeal to children through colour, shape etc. or by standing clearly together with other products for children in the shop.

The following considerations are included in the assessment of which products that belong to which age groups:

- Baby products are exclusively categorised in the age group 0-3 years
- If the product can be used by all age groups, as for example Shrovetide/Halloween make-up, the product is noted as relevant for all the three age groups.

- Products with an age indication are noted as relevant for the respective age groups. For instance, products marked with 6+ are indicated as relevant for both the age group 4-6 years and the age group 7-12 years whereas products marked with 8+ are only noted as relevant for the age group 7-12 years.

2. Legislation

In this chapter, the legislation for cosmetic products and toys is described. Focus is on the legislation which is relevant for allergenic substances in these product types.

2.1 Legislation for cosmetic products (EU Regulation no. 1223/2009)

Chemical substances including allergenic substances in cosmetic products are regulated through the Regulation on cosmetic products, EU Regulation no. 1223/2009 (EU, 2009a). The Regulation on cosmetic products is described in details below. Focus is on aspects which are relevant for this project.

The Regulation on cosmetic products contains a number of regulations regarding safety, content of chemical substances in cosmetic products and labelling of the products. Furthermore, the regulation on cosmetic products contains a number of limitations regarding different chemical substances, for instance, it is only allowed to use certain colourants (annex IV), preservatives (annex V) and UV filters (annex VI), and finally 26 fragrances are subject to mandatory declaration and only allowed in accordance with stipulated conditions (annex III).

2.1.1 Safety assessment

According to article 3 in the regulation on cosmetic products, a cosmetic product which is made available on the market in the EU has to be safe for human health when it is used under normal or reasonably foreseeable conditions of use. To demonstrate that a cosmetic product is safe for human health, a safety assessment of the cosmetic products (article 10) has to be performed. The safety assessment is described in a safety report.

2.1.2 Declaration of contents

According to the Regulation on cosmetic products, cosmetic products must be labelled with a complete list of ingredients (article 19). Therefore, it is possible to see the used ingredients on the packaging of the product. In the declaration of contents, the ingredients have to be stated by their INCI name, i.e. the “International Nomenclature for Cosmetic Ingredients”. An INCI name may include several chemical substances. The list of INCI names is indicative which means that it is not a list of approved ingredients in cosmetic products (article 33). If an INCI name of an ingredient does not exist, the chemical name of the substance has to be used (article 19). Ingredients have to be listed in succession according to decreasing weight/content.

It must be noted that special conditions concerning the labelling of colourants (the CI nomenclature) and fragrances (article 19) exist.

- Fragrances (perfume and aromatic compositions) have to be stated by the unified name “aroma” or “perfume”. I.e. the exact fragrance being used is not necessarily a part of the list of ingredients. However, 26 specific fragrances have to be stated in the declaration of contents by their INCI name if their concentration exceeds 0.001% in leave-on products or 0.01% in rinse-off products (annex III).
- Colourants which are not intended for hair colouring can be mentioned in any order after the other ingredients. For make-up products which are marketed in a number of nuances, the applied colourants can be stated in the declaration of contents with the words “may contain”. This means that all the listed colourants in a make-up product are not necessarily in the product.

2.1.3 Colourants

According to the Regulation on cosmetic products (article 14), cosmetic products are only allowed to contain colourants included in annex IV “List of colorants allowed in cosmetic products” and which are used according to the stipulated conditions (such as only for use in certain product types, for use on certain body parts or in a maximum allowed concentration). However, possible colourants included in annex III “List of substances which cosmetic products must not contain except subject to the restrictions laid down” may be used.

2.1.4 Preservatives

According to the Regulation on cosmetic products (article 14), cosmetic products must only contain preservatives included in annex V “List of preservatives allowed in cosmetic products” and which are used according to the stipulated conditions (such as only for use in certain product types, for use on certain body parts or in a maximum allowed concentration). However, possible preservatives included in annex III “List of substances which cosmetic products must not contain except subject to the restrictions laid down” may be used.

2.1.5 UV filters

Similarly, according to the Regulation on cosmetic products (article 14), cosmetic products must only contain UV filters included in annex VI “List of UV filters allowed in cosmetic products” and which are used according to the stipulated conditions (such as only for use in certain product types, for use on certain body parts or in a maximum allowed concentration).

2.1.6 Fragrances

Regarding fragrances, a special obligation to declare the content of these applies for 26 fragrances if they are added above a certain concentration. This is described above in section 2.1.2 “Declaration of contents”.

2.1.7 CMR substances

According to the Regulation on cosmetic products (article 15), cosmetic products must not contain substances which are classified as carcinogenic (Carc), mutagen (Mut) or toxic to reproduction (Repr) (so-called CMR substances) with category 1A, 1B or 2. However, there are exceptions where such substances can be allowed under certain conditions, including that SCCS has evaluated the substances and found them safe for use in cosmetic products. Different requirements apply for substances in category 1 and category 2 respectively for such an exception.

For substances where a harmonised classification has been adopted, a ban on this substance will automatically take effect on the date where the CMR classification applies. This applies to all CMR substances which are classified after 1 December 2010.

2.2 Legislation for toys (Statutory order no. 13/2011)

The Danish statutory order on safety requirements to toy products (Stat. Ord. no. 13, 2011) implements the EU toy safety directive 2009/48/EC (EU, 2009b). According to this statutory order, toy products must be designed and produced in such a way that no risk for harmful effects on human health exists as a result of exposure to the chemical substances and mixtures which the toy product consists of or which the toy product contains when it is used in a way which can be expected from children (annex II, section III, point 1).

Selected allergenic fragrances are directly limited in the toys statutory order. Toy products are not allowed to contain 55 specific allergenic fragrances (see Appendix 1 “Fragrances restricted in toys”, Table 37) in concentrations above 100 mg/kg. In addition to this, 11 other fragrances (see Appendix 1 “Fragrances restricted in toys”, Table 38) shall be listed on the toy, on an affixed label, on the packaging or in an accompanying leaflet, if added to a toy in concentrations which exceed 100 mg/kg in the toy product or the parts of the toy.

However, cosmetic kits (which have the purpose to produce products like for instance fragrances, soap, lotion, make-up and shampoo), olfactory board games (which have the purpose to help the child to recognise different odours) and gustative games (which have the purpose to let the child produce candy or dishes) may contain 15 specific of the banned fragrances in toys and the 11 fragrances subject to labelling (in total the 26 fragrances subject to declaration from the regulation on cosmetic products), if they are labelled so it clearly appears on the packaging. Furthermore, these types of toys containing one or several of the above fragrances must be provided with the warning “Contains fragrances which may be allergenic”. The products which are produced according to the guidelines must comply with the requirements in the regulation on cosmetic products.

In addition to this, cosmetic toys must fulfil the same requirements which are stipulated in the regulation on cosmetic products.

According to the statutory order on toys (annex II, section III “Chemical properties”), substances classified as CMR category 1A, 1B or 2 must not be used in toys. However, CMR substances may be used in concentrations below the classification limits for the individual substances which are stipulated in the CLP¹ regulation (EU, 2008) and in non-accessible parts of the toy. If no specific classification limit has been stipulated, the general classification limits apply as follows:

- Carc and Mut category 1A and 1B: 0.1%
- Repr category 1A and 1B: 0.3%
- Carc and Mut category 2: 1.0%
- Repr category 2: 3.0%

However, CMR substances can be expected and used if they are assessed as safe to use by SCCS and are listed in Appendix A to the statutory order.

In connection with the statutory order on toys, a number of standards (the EN 71 series) have been prepared with a number of requirements for special products – also including few requirements for chemical ingredients relevant for this project.

- In EN 71-5 (2015) “Chemical toys (sets) other than experimental sets”, it is stated that only the preservatives which are allowed in food products (EU Regulation 1333/2008) or in cosmetic products (EU Regulation 1223/2009) must be applied. However, preservatives from the regulation on cosmetic products which are only allowed in rinse-off products must not be applied.
- In EN 71-7 (2014) “Finger paints”, it is stated that only the preservatives which are stated in the standard in the stipulated concentrations must be applied. Furthermore, it is a requirement for finger paints that the applied preservatives have to be declared on the product.

2.2.1 Changes in legislation are pending for certain isothiazolinones

In June 2015, the EU member states decided to ban certain isothiazolinones in toys for children under the age of 3 years. The bans will deal with MI (methylisothiazolinone), MCI (methylchlorisothiazolinone), the mixture MI/MCI (kathon) and BIT (benzisothiazolinone). The bans take effect within 2017 (EU, 2015a; EU, 2015b).

2.3 Ecolabelling of toys and cosmetic products

In this section, the criteria for ecolabelling of toys and cosmetic products are described. Only criteria which make requirements concerning allergenic substances are described.

¹ CLP = Classification, Labelling and Packaging of substances and mixtures

2.3.1 The EU Flower

No criteria for toys under the EU Flower are available but criteria for rinse-off cosmetic products exist. However, this type of products is not in focus in this project.

2.3.2 The Swan

Criteria for Swan labelling of both cosmetics and toys are available. However, it is limited how much Swan labelled toys that can be found in the shops (10 products and primarily products produced in plastic). Therefore, the criteria for Swan labelling of cosmetics are solely described as a wide range of Swan labelled cosmetic products can be found.

2.3.2.1 Relevant criteria for Swan labelled cosmetic products

The Swan labelling criteria for cosmetic products contain the requirement that the ingredients of the product must not be classified with Skin Sens 1 with H317 “May cause an allergic skin reaction”. However, separate requirements for perfumes and enzymes exist (The Nordic Ecolabel, 2015).

It is also required that recommendations from the EU Scientific Committee, SCCS opinions, always must be followed. However, an exception is made for opinion SCCS/1459/2011 (SCCS no. 1459, 2012) which deals with allergenic fragrances. This SCCS opinion is not to be followed; however, the fragrances HICC, chloroatranol and atranol must not be included in the product (The Nordic Ecolabel, 2015).

Fragrances must not be added in products for infants, babies and/or children. This means products which are marketed to or have words like infant, baby and/or children (< 12 years) on the label.

2.3.3 The Blue Label

The allergy label, The Blue Label, of Asthma-Allergy Denmark applies exclusively to products which are in direct contact with the skin and thus have a risk of developing contact allergy (Asthma-Allergy Denmark, 2015).

The following overall requirements are made to have a product declared with the text “Declared in co-operation with Asthma-Allergy Denmark” (Asthma-Allergy Denmark, 2015):

- Asthma-Allergy Denmark, must have knowledge of all the ingredients, their concentrations and functions and based on this knowledge an assessment is made whether there are allergy-causing ingredients.
- Allergenic substances where allergy is seen for several persons are not allowed in products with The Blue Label. This means that the following ingredients are not permitted:
 - Perfume – both natural and synthetic
 - Addition of formaldehyde and formaldehyde releasers
 - Kathon (mixture of MI (methylisothiazolinone) and MCI (methylchloroisothiazolinone))
 - Colophonium
 - Colourants are not allowed in products with skin contact
- Substances which can cause irritation are limited as the risk of allergy is higher if the skin is irritated. However, it is taken into consideration whether it is rinse-off products or leave-on products.
- Asthma-Allergy Denmark continuously keeps up with new knowledge from literature and dermatologists. New knowledge on a substance may mean that according to the criteria, the substance is not allowed to be used in products with The Blue Label. Of such cases can be mentioned that:
 - In 2010, the UV filter octocrylene (in annex VI on allowed UV filters in the regulation on cosmetic products) was phased out in products with The Blue Label and is not allowed anymore due to several observations of allergenic reactions.

3. Gross list of potentially allergenic substances

The gross list of potentially allergenic substances is used to investigate which of these potentially allergenic substances that are an ingredient in toys and cosmetic products targeted children on the Danish market. On the basis of the potentially allergenic substances in toys and cosmetic products to children which are identified in the survey, an assessment of the allergenic properties of the substances has been made in chapter 8 "Hazard assessment of the identified substances" and whether there is evidence to assess them to be allergenic.

The fact, that not all substances being considered to be allergenic by for instance SCCS have a harmonised classification as allergenic, makes the preparation of a gross list of potentially allergenic products difficult. For instance, both resorcinol and lawsone which are used in many hair dye products are stated to be strongly allergenic by SCCS (SCCS no. 1270, 2010; SCCP Memorandum, 2006). However, none of these substances is classified as allergenic as Skin Sens, neither with a harmonised classification nor with a notified self-classification (ECHA C&L Inventory, 2015).

Therefore, it is complicated to describe and analyse all allergenic substances and it is not possible to do this only on basis of the harmonised and/or notified self-classification. In co-operation with the Danish EPA, a specific procedure was chosen for determination of a gross list of possibly allergenic substances which has been used as a basis of the survey in this project.

In the preparation of the gross list, a preliminary list of permitted colourants, preservatives, UV filters and fragrances in cosmetic products was first made. Based on the preliminary list and knowledge of the potentially allergenic properties of substances, a gross list of possibly allergenic substances which are allowed to be used in cosmetic products was made. It is assumed that chemical toys can contain the same allergenic substances which are found in the gross list of possibly allergenic substances which are allowed to be used in cosmetic products. This is based on the fact that cosmetic toys must fulfil the same demands on composition and labelling which are laid down in the regulation on cosmetic products. Furthermore, a previous survey from the Danish EPA on preservatives in chemical toys (Poulsen & Nielsen, 2014) showed that the use of preservatives in chemical toys which are not cosmetics generally contain the same preservatives which cosmetic products are allowed to contain according to the cosmetic legislation. This can be assumed to be applicable for other substance groups as well (such as colourants and UV filters) and it may be supposed that toy producers have an eye to requirements in other legislation too.

The procedure of the setting up of the gross list is described more closely below.

3.1 Preliminary list

The basis of the setting up of the gross list was an identification of all permitted substances in cosmetic products with potentially allergenic properties. According to an agreement with the Danish EPA, potentially allergenic substances were identified from positive lists in the Annex IV to VI of the regulation on cosmetic products (nr. 1223/2009):

- Annex IV is a list of colourants which are allowed in cosmetic products. 153 colourants are on the list (per April 2015)

- Annex V is a list of preservatives which are allowed in cosmetic products and 56 main groups of substances are on the list. Each main group can consist of several CAS numbers and thus Annex V contains a list of approx. 140 different preservatives.
- Annex VI is a list of UV filters which are allowed in cosmetic products. 28 substances are on this list (per April 2015).

Besides the substances in Annex IV to VI, the 26 fragrances, which in article 19(1) in the regulation on cosmetic products are stated to be subject to declaration, are also entered on the preliminary list as these fragrances are considered to be allergenic.

Besides substances from the appendices in the regulation on cosmetic products, allergenic substances stated in the article "Allergic contact dermatitis in Danish children referred for patch testing – a nationwide multicentre study" (Simonsen et al., 2013) are also entered on the preliminary list. The study deals with the prevalence of contact allergy among Danish children and young people based on clinical examinations in Denmark. The article refers to a number of different allergens which, however, not all are used in cosmetic products or in chemical toys. For instance, allergens which may be found in for instance shoes, bijouterie, rubber gloves etc. are also listed in the article. Selected substances from this article are placed on the preliminary list if they are stated to have a frequent use in cosmetic (table 3 in Simonsen et al., 2013). This concerns fragrances, preservatives and adhesives (which are for instance used as binders). The single substances in these three groups were entered on the preliminary list. Some of the substances were stated as a mixture of several different allergenic substances. This concerns fragrance mix I and II and paraben mix and MCI/MI. Fragrance mix I and II are assumed to contain fragrances as stated in table 4-1 and 4-2 in SCCS/1459/11 (see below). In the preliminary list of allowed substances in cosmetic products, the individual substances in these mixtures were registered. In total 30 substances from Simonsen et al. (2013) were entered on the preliminary list.

SCCS has published an opinion (SCCS/1459/11) for a number of fragrances which are used in cosmetic products (SCCS no. 1459, 2012). The 210 fragrances from this opinion were entered on the preliminary list.

Some of the substances from the three different sources (appendices from the regulation on cosmetic products, Simonsen et al. (2013) and SCCS no. 1459 (2012)) are repeated and some of the substances are entered on the preliminary list with more than one CAS number. In total the preliminary list contains 611 different CAS numbers.

3.2 Gross list of potentially allergenic substances

The gross list must exclusively contain potentially allergenic substances which are allowed in cosmetic products. Therefore, the substances on the preliminary list were examined for potentially allergenic properties. The procedure for this is described below.

The substances identified in the article by Simonsen et al. (2013) as well as the fragrances identified as subject to declaration according article 19(1) in the regulation on cosmetic products are already assessed to be allergenic. On the contrary, the substances (colourants, preservatives and UV filters) in the positive lists in Annex IV to VI of the regulation on cosmetic products are not identified as allergenic solely based on their presence in Annex IV to VI. To assess the potentially allergenic properties of these substances, opinions by SCCS for substances on the preliminary list were examined, or the harmonised classification of the substances was looked up in ECHA's C&L inventory (ECHA C&L Inventory, 2015). Furthermore, it was assessed whether the fragrances in SCCS opinion no. 1459/11 (SCCS no. 1459, 2012) are concluded to be allergenic (where the amount of data was concluded to be sufficient).

3.2.1 SCCS opinions for allergenic fragrances

The fragrances assessed in SCCS opinion no. 1459/11 (SCCS no. 1459, 2012) were all entered on the preliminary list. As only potentially allergenic substances are to be entered on the gross list, the opinion was examined and the data material was assessed in order to determine whether the fragrances are allergenic or not. SCCS classified the fragrances in groups, according to the availability and adequacy of the data. The groups are:

1. Established contact allergens in humans
2. Established contact allergens in animals
3. Likely contact allergens by combination of evidence
4. Possible contact allergens
5. Established contact allergens of special concern (12 selected fragrances)

Group 1: Established contact allergens in humans

Fragrances in the list of established contact allergens in humans contain both chemicals and natural extracts. The data material for the individual substances is based on a number of observed positive test reactions where “+” states that up to 10 positive test reactions are reported, “++” states 11-100 positive test reactions, “+++” states 101-1000 positive test reactions, and “++++” states more than 1000 reported positive test reactions. The data material for the individual fragrances does not necessarily cover the same number of tests but it is separately stated (with “r.t.” for “rarely tested”) if the fragrance has been tested in less than 1000 patients. All the substances in this list were entered on the gross list of potentially allergenic substances no matter the number of observed positive tests, as SCCS concludes that these substances are human allergens.

Group 2: Established contact allergens in animals

Fragrances which are established contact allergens in animals were also entered on the gross list. For these fragrances, SCCS has assessed their allergenic properties on basis of EC₃ values from *local lymph node assay* (LLNA) (SCCS no. 1459, 2012). EC₃ values state the amount of substance needed to induce a three-fold increased activity in lymph nodes for an animal exposed to an allergen, compared to the vehicle-treated control animal.

Group 3: Likely a contact allergens by combination of evidence

Substances which are classified as likely contact allergens are based on limited human data as well as *Structural Activity Relationships* (SAR) and assessed by experts. By use of SAR predictions, the allergenic properties of a substance are assessed from the chemical structure of the substance. SCCS assesses these substances to cause allergy in humans if the exposure is sufficient (SCCS nr. 1459, 2012) and therefore the substances are entered on the gross list.

Group 4: Possible contact allergens

Substances which are classified as possible contact allergens are not entered on the gross list. These substances are classified on basis of isolated indications for allergenic properties. It may for instance be either limited human evidence or positive SAR prediction without evidence to be allergenic to human or animals. SCCS concludes that further data is necessary to be able to conclude if the fragrances are allergenic or not.

Group 5: 12 fragrances of special concern

Finally, SCCS lists 12 fragrances of special concern as these fragrances have a specifically high risk of development of contact allergy in humans (i.e. more than 100 cases of contact allergy have been reported). These 12 contact allergens of special concern are already on the gross list as they are among the 26 fragrances subject to declaration stated in article 19(1) of the regulation on cosmetic products.

3.2.2 SCCS opinions for single substances

Furthermore, a search was made for other SCCS opinions on the substances which are not confirmed or denied as being allergenic from SCCS opinion no. 1459/11, Simonsen et al. (2013) or from the fragrances subject to declaration which are entered on appendix III in the declaration on cosmetic products. A search for SCCS opinions on these substances was made on the EU Commission's homepage (EU Commission, 2015). Substances which are stated as allergenic either by having an extreme, strong, moderate or low allergenic potential are entered on the gross list. Substances which were not entered on the gross list are substances where no information regarding the allergenic properties is stated in SCCS opinions, where the property is stated to be "rare contact allergen" or where no SCCS opinion on the substance was found – unless the substance is stated to have a harmonised classification as skin sensitising (see below).

3.2.3 Substances from the C&L Inventory

For a few substances, the harmonised classification of the substances in ECHA's C&L Inventory (ECHA C&L Inventory, 2015) was examined. This applied to substances which were entered on the preliminary list according to the regulation on cosmetic products but where subsequently the examined SCCS opinions did not contain any information on the allergenic properties of the substances. If the substance had a harmonised classification as "Skin Sens. 1" (skin sensitising), it is allergenic and thus entered on the gross list of potentially allergenic substances.

3.2.4 Substances with a special assessment

For a few substances, it was not possible to determine their potentially allergenic properties through examination of the relevant SCCS opinions as these opinions contained ambiguous information regarding the allergenic properties and no harmonised classification as skin sensitising was available. Furthermore, new knowledge or other relevant knowledge is available for some of the substances and this knowledge has been included in the assessment whether the substance is considered to be potentially allergenic or not. This applies for the following substances:

According to the Danish Allergy Research Centre, **parabens** (several CAS numbers) seldom cause allergy and the parabens are considered to be very slightly allergenic (Danish Allergy Research Centre, 2015). According to Simonsen et al. (2013), a mixture of parabens called "Paraben mix" is stated to be allergenic as 13 out of 2,593 (corresponding to 0.5%) tested patients reacted positively towards "Paraben mix". According to Navamedic (2015), "Paraben mix" contains five different parabens: methylparaben, ethylparaben, propylparaben, butylparaben and benzylparaben. SCCS opinion no. 1348/10 (2010) writes nothing about allergenic properties of the parabens and according to ECHA's database of registered substances (ECHA RSD, 2015), methylparaben, ethylparaben or propylparaben is not considered to be allergenic (the remaining parabens are not found in the database). Based on the above information, none of the parabens is entered on the gross list.

CI 19140 also called Acid Yellow 23 and E102 (CAS 1934-21-0) is described in an old opinion no. 0786/04 (SCCNFP no. 0786, 2004). In this opinion, it is described that data is limited regarding the allergenic properties of the substance. A single study with guinea pigs does not indicate allergenic effects but it is concluded that due to lacking human studies, it is not possible to exclude allergenic effects. However, an old French study (Pellegrin, 1979) which is not described in the SCCNFP opinion has described two cases of allergy towards CI 19140 related to skin and mucous membranes and suggests that the colourant is banned in foods where it is called E102. The colourant is still allowed today and is used in foods. In Søstede et al. (2004), an assessment is made of the sensitisation potential of several colourants based on QSAR predictions. CI 19140 is assessed to be a moderate or strong allergen but this assessment is exclusively based on QSAR. In 2010, EFSA concluded that it is improbable that oral intake of E102 will trigger serious negative reactions in humans (EFSA, 2010). The assessment focused on oral intake and not skin allergy as an assessment of the safety of the substance in foods was made.

It has not been possible to identify other sources for the purpose of an assessment of the potentially allergenic properties of the colourant. The substance is not registered and thus no data is available in ECHA's database of registered substances. The Danish Allergy Research Centre has been contacted and has no other information about the colourant. Based on the above information, the colourant is not entered on the gross list of potentially allergenic substances as reports on skin allergy are very few and the substance has been allowed for use in foods for many years.

Triclosan (CAS no. 3380-34-5) has a harmonised classification but not as Skin Sens. Three SCCS opinions on triclosan exist and the newest opinion regarding allergy refers to SCCS opinion no. 1192 (2009). According to this opinion, triclosan is not allergenic in animal experiments but human observations show that triclosan has a low sensitisation potential. Based on this, triclosan is not entered on the gross list of potentially allergenic substances.

Phenoxyethanol (CAS no. 122-99-6) is an ingredient in the mixture Euxyl™ K 400 where the single substances of the mixture were examined for allergenic properties. However, phenoxyethanol is not on the Danish Allergy Research Centre's list of common allergenic preservatives (Danish Allergy Research Centre, 2015) and seven studies in ECHA's registration database (ECHA RSD, 2015) all report that the substance is not skin sensitising. Thus, phenoxyethanol is not entered on the gross list.

Zinc pyrithione (CAS no. 13463-41-7) was stated by SCCS no. 1459/11 (2012) to be non-sensitising for animals but to have a low potential for inducing contact hypersensitisation when it was tested in cosmetic mixtures. ECHA RSD (2015) states three studies which all conclude that zinc pyrithione is not skin sensitising. Therefore, zinc pyrithione is not entered on the gross list.

Benzoic acid (CAS no. 65-85-0) was stated by SCCS no. 1459/11 (2012) to have occasional and sparse positive reactions in patch tests. The potentially allergenic properties of benzoic acid were examined in ECHA's database of registered substances (ECHA RSD, 2015) where seven studies state that the substance is not skin sensitising. Thus, benzoic acid is not entered on the gross list.

Diethylamino hydroxybenzoyl hexyl benzoate (CAS no. 302776-68-7). In SCCS no. 1459/11 (2012), it is stated that it is not possible to evaluate the potentially allergenic properties of the substance based on a study in guinea pigs. ECHA RSD (2015) reports a single study on the allergenic properties of the substance which is negative. Thus, the substance is not entered on the gross list.

Methylene bis-benzotriazolyl tetramethylbutylphenol (CAS no. 103597-45-1) was stated by SCCS no. 1459/11 (2012) to be non-skin sensitising for animals but a few single reports indicated possibly allergenic properties. However, these properties could be due to other allergens in the test agent. ECHA RSD (2015) does not report about skin sensitising studies. The substance is not entered on the gross list due to the weak suspicion of allergenic properties.

Octocrylene (CAS no. 6197-30-4) has been proven to be both a photo-contact allergen and as a contact allergen in a clinical study and in LLNA tests (Karlsson et al., 2011). Therefore, octocrylene is entered on the gross list of potentially allergenic substances.

Drometrizole trisiloxane (CAS no. 155633-54-8) is documented allergenic (Johansen et al., 2011). Therefore, the UV filter is entered on the gross list of potentially allergenic substances.

Benzoisothiazolinone (CAS no. 2634-33-5) is not allowed in cosmetic products but in a former report of the Danish EPA's survey projects "Survey and health assessment of preservatives in toys", it is observed to be used in chemical toy products such as finger paint and hobby paint (Poulsen & Nielsen, 2014). Benzoisothiazolinone (BIT) is assessed by SCCS as a moderate allergen. SCCS

expresses concern about the allergenic properties of the substance at use in cosmetic products as BIT in concentrations of 0.01% can cause allergic reactions in consumers. SCCS concludes that the use of BIT in cosmetic products cannot be considered to be safe with regard to allergy as long as a safe level of BIT is not yet determined (SCCS no. 1482, 2012). Therefore, BIT is not allowed in cosmetic products today. BIT is entered on the gross list of potentially allergenic substances as earlier it has been used in chemical toy products (Poulsen & Nielsen, 2014). However, new regulations for toys for children below three years and toys which are intended to be put into the mouth ban the use of BIT after 24 May 2017 (EU, 2015a).

3.3 Summary

Thus, the gross list contains allowed substances in cosmetic products and toys which are identified as potentially allergenic:

- based on a harmonised classification as skin sensitising,
- based on sufficient knowledge on the allergenic properties assessed in SCCA opinions,
- based on knowledge on allergenic substances listed in Simonsen et al. (2013),
- and based on other relevant knowledge.

Furthermore, the gross list is added a single potentially allergenic preservative (benzisothiazolinone (BIT)) which is not allowed to be used in cosmetic products but has been observed to be used in chemical toy products in a former survey (Poulsen & Nielsen, 2014).

In total, the gross list contains 191 potentially allergenic substances (also called gross list substances). Of these, there are 2 colourants, 164 fragrances, 19 preservatives, 3 UV filters and 3 adhesives (binders) in cosmetic products. The gross list of the 191 potentially allergenic substances is listed in Appendix 2:.

4. Survey – procedure

Based on the prepared gross list of the potentially allergenic substances which are allowed in cosmetic products and toys, a survey was made covering the potentially allergenic substances from the list that are used in chemical toys and cosmetic products for children on the Danish market. The survey has taken place by use of the following methods:

- Visits in shops
- Literature search
- Search on the internet
- Contact to the industrial sector

In the actual context, cosmetic products have the advantage that according to the legislation they are obliged to list the ingredients on the product in question. Therefore, in co-operation with the Danish EPA, it was decided that the survey of the cosmetic products was to be performed through examinations of declarations of contents from a wide choice of cosmetic products for children on the Danish market.

This possibility does not exist for toys. According to the legislation, it is only single substances which have to be declared, for instance if the toy contains some specific fragrances or preservatives in finger paint. Therefore, in the area of toys, the quality of the survey was dependent on the voluntary delivery of information from the toy sector. In co-operation with the Toy Sector (“Legetøjsbranchen – LEG”) and the Danish EPA, it was decided that it would be a too comprehensive task for many of the toy dealers/producers to collect information about the content of all colourants, preservatives, UV filters and fragrances in the toy products and then let the project group examine whether some of these ingredients are on the gross list of potentially allergenic substances. Furthermore, it was decided that it would be too comprehensive for the toy dealers to send the whole gross list of the 191 potentially allergenic substances and let them examine whether some of these many substances are ingredients in their toy products. For this reason, another approach was chosen where initially a survey was made covering which of the 191 gross list substances that were observed in cosmetic products on the Danish market. This shorter list of 30 substances as well as the list of the 26 fragrances subject to declaration from the regulation on cosmetic products, i.e. in total 56 substances, was sent to the members of the Toy Sector with the request to send information on these potentially allergenic substances to the project group.

4.1 Procedure of the survey of cosmetic products

The procedure of the survey of the cosmetic products was exclusively through visits in shops. The industrial sector was not contacted.

4.1.1 Product types investigated

As described in the introduction, focus was chosen to be on cosmetic products with prolonged skin contact. Therefore, the survey of cosmetic products has included the following product types:

- Face paint
- Baby oil
- Baby powder
- Conditioner (leave in)
- Lotion (body lotion, hand lotion)
- Hair gel

- Hair wax
- Hair spray
- Body glitter
- Lip balm/lip gloss
- Make-up
- Nail polish
- Perfume set
- Ointment
- Suntan lotion (including after sun lotion and sun spray)
- Tattooing products
- Towelettes/cleansing tissues

However, at the visits in the shops, it was observed that neither hair gel nor hair wax was distinctly marketed to children for which reason this type of products does not appear in the review in chapter 6 “Results of the survey of cosmetic products”. In this project, cosmetic products for children are defined as cosmetic products which clearly apply to children, i.e. on the product it says “children”, “kids” or similar, or pictures on or design of the product indicates that it applies to children; for instance pictures of Disney figures or pictures of a baby.

4.1.2 Survey in shops

The survey of cosmetic products in shops was chosen as due to the mandatory declaration of contents, it is the fastest procedure to get information about ingredients. In total 21 different shops in the Copenhagen area and North Zealand were visited, distributed on the following types of shops: supermarkets, pharmacies, toy shops, clothing shops, chemists and various shops with primarily cheap products. The visited chains of shops are stated in the fact box below. However, cosmetic products for children were not identified in all shops.

Shops where products were investigated		
<u>Supermarkets</u> Bilka Irma Kvickly Lidl Meny Rema 1000 Netto <u>Hobby stores</u> Panduro Hobby	<u>Pharmacies</u> Apotek Matas Helsemin The Body Shop <u>Various stores</u> Søstre Grene Tiger Glitter	<u>Toy stores</u> Legekæden Toys R Us <u>Clothing shops</u> H&M Magasin <u>Book stores</u> Bog & Ide Arnold Busck

The chosen procedure was that photos of the products were taken so the declaration of contents and other information on the product could be noted subsequently. However, for each product the following information was noted in the shop:

- Product number (for internal use and for comparison with photo)
- Product name
- Cost price
- Price per kg or per litre
- Name of the shop
- Date of identification of the product in the shop
- Country of origin (if this information was available)

Subsequently, the following was noted for each product based on the photo:

- Product type
- The INCI name of the potentially allergenic substance(s)
- The function of the ingredient (i.e. colourant, preservative, fragrance or UV filter)
- Eco-labelled (yes/no)
- Labelled with The Blue Label (yes/no)
- Batch number
- Producer
- The country in which the product was produced – if stated
- The country in which the responsible company belongs (its head office) – if stated
- How the product is marketed to children (claim or type of shop)
- Which of the three age groups the product applies to

Furthermore, the following information was collected:

1. The whole declaration of contents was examined.
2. All colourants, preservatives, fragrances and UV filters were entered for the products in the spreadsheet and the type of substance (function) was stated for the four types.
3. If no ingredients from the four types of substance groups were identified, the word "none" was noted by the product name.
4. If "perfume" was on the list of ingredients, this was noted by the product name.
5. Ingredients with the function "perfuming" according to the CosIng database were also noted.
6. Then all the entered ingredients were compared against the gross list of the potentially allergenic substances and it was stated whether the identified colourants, preservatives, fragrances and UV filters are in the gross list.

4.1.3 Literature search

Finally a literature search was made on the internet for similar surveys which have focus on the content of potentially allergenic substances in cosmetic products for children. This is described in 5.1 "Available surveys of cosmetic products for children".

4.1.4 Contact to the industrial sector

Contact to the industrial sector ("the Association of Danish Cosmetics, Toiletries, Soap and Detergent Industries" – SPT – or selected producers) was not prioritised for the cosmetic products as most information on the ingredients (except for certain fragrances) is found on the products.

4.2 Procedure for the survey of toys

As earlier described, the procedure for the survey of chemical toy products was primarily through contact to the industrial sector. However, toy products, such as face paint, make-up sets, body glitter sets, lip balms/lip gloss, nail polish and sets for production of fragrances, were also investigated through the survey of the cosmetic products via the visits in the shops as the ingredients for these products also have to appear from the declaration of contents as they are cosmetic products too.

4.2.1 Product types investigated

As described in the introduction, focus was exclusively chosen to be on the below types of "chemical toys which have an expected long exposure time, i.e. toys where there is a direct contact with the content of possibly potentially allergenic substances. In other words, toy products of the following types:

- Modelling clay and similar products – for instance, formable sand
- Finger paint
- Face paint and make-up
- Slime
- Transferable tattooing stickers or sets to paint own tattoos

- Jewelries (stones) which are pasted on the skin as a decoration
- Soap bubbles and soap for foam pistols

4.2.2 Contact to producers and dealers of "chemical" toys

Via the Toy Sector LEG, an e-mail was sent to all of their members regarding the project and its purpose as well as a description of the wish to collect information about selected potentially allergenic substance and which of these that might be used in chemical toys.

Selected producers/dealers of toys were also contacted personally to get more information for the survey. The collected information is described in chapter 7 "Results of survey of toys".

4.2.3 Literature search

Finally, a literature search was made on the internet for similar studies which have focused on the content of potentially allergenic substances in chemical toys for children. This is described in section o "

Examinations of toys”.

4.3 Comparison of information with the list of potentially allergenic substances

Based on the collected information on potentially allergenic substances in cosmetic products and toys, a comparison with the gross list of potentially allergenic substances was made.

5. Survey – literature search

In this chapter, the literature search which has focused on content of potentially allergenic substances in cosmetic products for children and in chemical toys for children is described.

5.1 Available surveys of cosmetic products for children

A search was made on the internet for surveys where potentially allergenic substances are identified in cosmetic products or where the use of colourants, preservatives, UV filters or fragrances in cosmetic products is investigated. The identified surveys are described in details below and cover the following reports/tests:

- Various tests of cosmetic products for babies made by the Danish consumer magazine TÆNK (*In English: Think*) (TÆNK, 2015a, 2015b, 2015c and 2014)
- Survey and health and environmental assessment of preservatives in cosmetic products – consumer project no. 138, Danish EPA (Andersen et al., 2015)
- Survey and health assessment of UV filters – consumer project no. 142, Danish EPA (Mikkelsen et al., 2015)
- Colourants in consumer products, including cosmetic products (Poulsen & Hundebøll, 2015)
- Survey of formaldehyde in cosmetic products (Takahiro Doi, 2010)
- Survey and health assessment of the exposure of 2-year-old's to chemical substances in consumer products – consumer project no. 103, Danish EPA (Tønning et al., 2009)
- Cosmetic products for children – consumer project no. 88, Danish EPA (Poulsen & Schmidt, 2007)

5.1.1 Various tests of cosmetic products for babies from the Danish consumer magazine TÆNK (2015)

The Danish consumer magazine TÆNK (*“THINK”*) has carried out various examinations of cosmetic products for babies from which it also appears whether the products contain fragrances and possibly allergenic preservatives. The examinations are based on an assessment of declarations of content of various products. It is not stated which ingredients that are identified but exclusively whether they are allergenic substances or not. According to TÆNK², a declared content of “perfume”, fragrances subject to declaration and certain plant extracts (from SCCS opinion no. 1459 (2012)) is considered as a content of allergenic substances.

- Baby lotion: In total 37 baby lotions were examined in June 2015. 14 of the 37 products contained perfume or one or more of the fragrances subject to declaration (TÆNK, 2015a)
- Baby ointments: In total 30 baby ointments were examined in May 2015. 8 of the 30 products contained perfume or one or more of the fragrances subject to declaration (TÆNK, 2015b)
- Baby oils: In total 37 baby oils were examined in May 2015. 13 of the 37 products contained perfume or one or more of the fragrances subject to declaration (TÆNK, 2015c)
- Toweleaves: In total 33 toweleaves were examined in April 2014. 8 out of the 33 toweleaves contained allergenic substances (in the form of perfume, allergenic preservatives or chamomile extract), (TÆNK, 2014)

² Correspondance with Stine Müller, TÆNK.

5.1.2 Survey of preservatives in cosmetic products (2015)

In this report prepared for the Danish EPA, more than 600 cosmetic products were in 2013 examined via the declaration of contents for their content of preservatives. The survey included both products for children and adults. An extraction was made of the 21 leave-on products for children identified in this project. The identified preservatives which at the same time appear in the gross list are stated in Table 1 below.

Type of substance	Potentially allergenic substances from the gross list	Identified in number of products (out of a total number of this type)
Preservative	Benzyl alcohol	1 suntan lotion/suntan oil (out of 6)
	Methylisothiazolinone	1 towelette (out of 10)

TABLE 1
IDENTIFIED ALLERGENIC PRESERVATIVES IN COSMETIC PRODUCTS FOR CHILDREN (ANDERSEN ET AL., 2015)

5.1.3 Survey of UV filters (2015)

In this survey, based on declarations of contents, 291 cosmetic products with a content of UV filters were identified on the Danish market. A survey of products for both children and adults was made. The identified UV filters, which at the same time are seen in the gross list, are stated in Table 2 below.

Type of substance	Potentially allergenic substances from the gross list	Identified in number of products (out of a total number of this type)
UV filters	Benzophenone-3	17 out of 291
	Drometrizole trisiloxane	27 out of 291
	Octocrylene	76 out of 291

TABLE 2
IDENTIFIED POTENTIALLY ALLERGENIC UV FILTERS IN COSMETIC PRODUCTS (MIKKELSEN ET AL., 2015)

5.1.4 Colourants in consumer products including cosmetic products (2015)

In a literature study on colourants in different consumer products, among others cosmetic products, the use of colourants was investigated (Poulsen & Hundebøll, 2015). The study showed that none of the two potentially allergenic colourants from the gross list was used in cosmetic products.

5.1.5 Survey of formaldehyde in cosmetic products (2010)

A Japanese survey has analysed in total 92 different cosmetic products for a content of free formaldehyde (however, not specifically for children). The 92 products were selected so they all contained one or more formaldehyde-releasers, i.e. some of the preservatives mentioned below. Of the 92 products, 31 were lotions. The remaining products were rinse-off products which have not been in focus in this project. The following formaldehyde-releasers were identified:

- Imidazolidinyl urea in 9 lotions
- Dimethyldimethyl hydantoin in 7 lotions
- Diazolidinyl urea in 9 lotions
- Bronopol in 1 lotion

In the 92 products, the concentration of free formaldehyde was measured to between 2.7 ppm and 876 ppm. Products from the USA (65), Europe (9), Canada (8) and Japan (7) were purchased. The

European products had the lowest content of free formaldehyde (on average below 100 ppm) whereas the American products had the largest content of free formaldehyde (on average below 300 ppm) (Takahiro Doi, 2010).

5.1.6 2-year-old's exposure to chemical substances (2009)

This report carried out for the Danish EPA investigated in total 32 different lotions and 28 suntan lotions for children on the Danish market in 2008. Relevant gross list substances which were identified via the declaration of contents are stated in Table 3.

Type of substance	Potentially allergenic substances from the gross list	Number out of 32 lotions where the substance is found	Number out of 28 suntan lotions where the substance is found
Colourants	<i>No colourants in the gross list were identified in this project</i>		
UV filters	Octocrylene	0	4
	Drometrizole siloxane	0	2
Preservatives	Imidazolidinyl urea	1	0
Fragrances	Perfume	6	7
	<u>Of the fragrances subject to declaration:</u>		
	Benzyl alcohol	2	0
	Benzyl benzoate	1	2
	Benzyl salicylate	1	3
	Butylphenyl methylpropional	0	3
	Cinnamyl alcohol	0	1
	Citral	0	5
	Citronellol	0	6
	Coumarin	0	3
	Eugenol	0	3
	Geraniol	2	5
	Hexyl cinnamal	0	1
	Hydroxyisohexyl-3-cyclohexene carboxaldehyde (HICC)	0	2
	Limonene	6	6
	Linalool	5	5

TABLE 3
IDENTIFIED POTENTIALLY ALLERGENIC SUBSTANCES IN COSMETIC PRODUCTS FOR CHILDREN (TØNNING ET AL., 2009)

5.1.7 Cosmetic products for children (2008)

This survey carried out for the Danish EPA investigated in total 208 cosmetic products for children on the market in Denmark in 2007. Gross list substances which were identified via the declaration of contents in this project are stated in Table 4.

Type of substance	Potentially allergenic substances from the gross list	Number of identified out of 17 lotions	Number of identified out of 9 perfumes	Number of identified out of 2 hair styling products
Colourants	<i>No colourants in the gross list were identified in this project</i>			
UV filter	<i>No UV filters in the gross list were identified in this project</i>			
Preservative	Methylchloroisothiazolinone (MCI)	1	1	0
	Methylisothiazolinone (MI)	1	0	0
	Imidazolidinyl urea	1	0	0
Fragrances	Perfume	13	9	2
	<u>Of the fragrances subject to declaration:</u>	0	3	0
	Alpha-isomethyl ionone	1	0	0
	Amyl cinnamal	1	1	0
	Benzyl alcohol	2	2	0
	Benzyl benzoate	2	3	0
	Benzyl salicylate	0	3	0
	Butylphenyl methylpropional	2	2	0
	Citral	2	4	0
	Citronellol	1	3	0
	Coumarin	0	1	0
	Eugenol	2	6	0
	Geraniol	1	1	0
	Hexyl cinnamal	1	2	0
	Hydroxycitronellal	0	4	0
	Hydroxyisohexyl-3-cyclohexene carboxaldehyde (HICC)	1	0	0
	Isoeugenol	5	3	0
	Limonene	4	5	0
	Linalool			

TABLE 4
IDENTIFIED ALLERGENIC SUBSTANCES IN COSMETIC PRODUCTS FOR CHILDREN (POULSEN & SCHMIDT, 2007)

5.2 Examinations of toys

A search was made on the internet for examinations where potentially allergenic substances were identified in toys or which investigated the use of colourants, preservatives, UV filters or fragrances in toys. The identified examinations are described in details below and cover the following examinations/reports:

- Colourants in consumer products, including toys (Poulsen & Hundebøll, 2015)
- Preservatives in toys – consumer project no. 123, Danish EPA (Poulsen & Nielsen, 2014)
- Chemicals in toys (KEMI, 2012)
- Fragrances in toys - consumer project no. 68, Danish EPA (Glensvig & Pors, 2006)
- Colourants in tattooing stickers - consumer project no. 61, Danish EPA (Rastogi et al. 2005)

5.2.1 Colourants in consumer products, including toys (2015)

Poulsen & Hundebøll (2015) have made a literature study for the Consumer Council at the Austrian Standards Institute on the use of colourants in different types of consumer products, among others toys. The literature study identified approx. 90 different colourants which are used in toys but none of the two potentially allergenic substances from the gross list was a part of the 90 identified colourants. The literature study on colourants in toys is primarily based on an old source (more than 10 years old) which is based on reports from the toy sector on used substances in toys (CEN/TC 52, 2002). Nearly 70 of the identified 90 colourants come from this source. Another substantial source to colourants was a literature study from KEMI (2012) on chemicals in toys. This report is separately described below.

5.2.2 Preservatives in toys (2014)

In 2014, the Danish EPA published a survey on the use of preservatives in chemical toys (Poulsen & Nielsen, 2014). In this survey, the used preservatives were identified through a combination of literature searches, contact to producers/dealers and via study of declarations of contents on products where preservatives must appear (cosmetic products and finger paint). The preservatives, which were identified in this survey (table 22 in the report), are stated in Table 5. However, there are only stated preservatives which are in the gross list of potentially allergenic substances and for the product types which are included in the survey in the present project. Table 5 covers both results from literature as well as analysed products in this project. In the project, analyses were made for free formaldehyde, which most probably comes from one of the formaldehyde-releasing preservatives, as for instance DMDM hydantoin (see Appendix 2: “Gross list of potentially allergenic substances” for other formaldehyde-releasing preservatives).

Product type	Preservative	Highest concentration
Modelling clay	Free formaldehyde Bronopol	0.122% (analysis) 0.0305% (analysis)
Finger paint	1,2-benzisothiazol-3(2H)-one (BIT) MCI MI Kathon (mixture of MI and MCI) Bronopol Diazolidinylureum Free formaldehyde	Approx. 0.00018% 0.0031% 0.0095% 0.0095% <i>No information</i> <i>No information</i> 0.069%
Face paint and make-up	DMDM hydantoin Iodopropynyl butylcarbamate (IPBC)	<i>No information</i> <i>No information</i>
Slime	Preventol D7 (is a mixture of isothiazolinones) Free formaldehyde	0.0025% 0.0335% (analysis)

Product type	Preservative	Highest concentration
Soap bubbles	Methylisothiazolinon (MI) DMDM Hydantoin Free formaldehyde Bronopol	<i>No information</i> 0.3034% 0.0025% 0.004% (analysis) 0.1% (analysis)

TABLE 5
POTENTIALLY ALLERGENIC PRESERVATIVES AND THEIR IDENTIFIED CONCENTRATION IN CHEMICAL TOY PRODUCTS (POULSEN & NIELSEN, 2014). ONLY THE TYPES OF CHEMICAL TOY PRODUCTS FROM THE SURVEY WHICH ARE RELEVANT IN THIS PROJECT ARE LISTED.

5.2.3 Chemical in toys (2012)

In 2012, the Swedish Chemicals Agency (KEMI) has published a report which has studied different literature and scientific databases for descriptions of chemicals in toys. Besides the literature study, the toy sector was also contacted with regard to input. The survey resulted in a list of 388 classified substances which somehow are a part of the life cycle in the production of toys. 149 of these substances are a part of the final toy. Relevant gross list substances which were identified as a part of the final toy product by KEMI (2012) are stated in Table 6.

Type of substance	Potentially allergenic substances from the gross list	Identified in the following materials
Colourants	<i>No colourants in the gross list were identified</i>	
UV filters	<i>No UV filters in the gross list were identified</i>	
Preservatives	Kathon	Chemical products*
Fragrances	Citral	Chemical products*

TABLE 6
IDENTIFIED ALLERGENIC SUBSTANCES IN TOYS (KEMI, 2012)
* THE TYPE OF TOY IS NOT STATED

5.2.4 Fragrances in toys (2006)

An older study investigated the use of fragrances in toys for children at the age of 0-10 years (Glensvig & Pors, 2006). Added fragrances were identified in 15 different types of products for children while 10 products were chemically analysed for the content of the 26 fragrances subject to declaration (cosmetic). In total 18 fragrances subject to declaration were identified in the 10 products. Only one of the analysed toy products was of the type chemical toy which is in focus in the present project. This product was a soap bubble product. The identified fragrances subject to declaration (two in total) and the identified levels in the soap bubble product are stated in Table 7. Generally, it is described in the project that fragrances might be added toys to camouflage unwanted odour from the products. Examples are given, among other things slime which is added fragrances.

Fragrances	Measured concentration (mg/kg)
Citral	27
D-limonene	7

TABLE 7
IDENTIFIED FRAGRANCES SUBJECT TO DECLARATION IN ONE SOAP BUBBLE PRODUCT

5.2.5 Colourants in tattooing stickers (2005)

In an older survey study from 2005, 36 transmittable tattooing stickers were chemically analysed for 129 colourants (Rastogi et al. 2005). The results showed that only 11 different colourants were found. In the report, based on the measured concentrations of the colourants, it was concluded that the potential risk of allergy by using the tested transmittable tattooing stickers was limited. None of the two gross list colourants was identified in this survey, neither through a chemical analysis of contents nor the declarations of contents.

6. Results of the survey of cosmetic products

This chapter deals with the results reached through the survey of potentially allergenic substances which are found in the gross list and which are used in cosmetic products for children on the Danish market. The results cover exclusively products in shops in the retail trade. A search for the corresponding products on the internet was made and a few other products for children were also identified but the declaration of contents was not available on the homepage for any of these. The survey was carried out during May 2015,

In total, information on ingredients for 157 different cosmetic products for children distributed on 15 different types of cosmetic products was collected. These 157 different cosmetic products for children cover products from at least 37 different producers/importers as in some cases no name of the producer/importer was identified because this could not be read from the photos taken of the products.

The survey is considered to be representative of the Danish shop market as nearly all relevant products from shops were included in the survey. In cases where more similar products from the same producer were identified – for instance face paint sets for painting of cat, tiger, pirate etc. or suntan lotions with factor 10, 15, 30 and 50, only a few of these products were selected and thus not all which were identified. As described in section 4.1.2 “Survey in shops”, search for relevant products in a large range of shops on the Danish market was made. However, the survey has exclusively included products in physical shops and not from internet shops, due to the chosen procedure by taking photos of the list of ingredients.

Furthermore, the collected information on fragrances, colourants, preservatives and UV filters is assessed to cover a broad extract of products on the Danish market. The registered products cover both cheap products (7.25 DKK for a packet of towelettes) and expensive products (399.95 DKK for a set with several types of nail polish for children) and all between these prices. The kilo price of the products varies between 200 DKK/kilo (baby powder) for the cheapest and 36,700 DKK/kilo (tattooing product) for the most expensive products. The price per litre of the products varies between 75.80 DKK/litre (lotion) for the cheapest and 17,800 DKK/litre (tattooing product) for the most expensive products. For towelettes, the price per piece varies between 0.08 DKK and 0.90 DKK per towelettes.

6.1.1 Shops included in the survey

The 157 cosmetic products for children are gathered from the following shops (see Table 8) which are distributed as follows:

- 1 pharmacy
- 1 book shop
- 6 different supermarkets
- 1 clothing shop
- 2 toy shops
- 2 shops with primarily cheap products
- 1 hobby shop

- 1 special shop with cosmetic products

In addition to this, a few other shops have been visited (for instance, another type of bookshop) but no new relevant products were found.

Shop/supermarket	Number of products
Pharmacy	18
Bilka (supermarket)	42
Bog & Ide (book shop)	10
Hennes & Mauritz (clothing shop)	7
Irma (supermarket)	2
Kvickly (supermarket)	16
Legekæden (toy shop)	14
Lidl (supermarket)	4
Matas ("pharmacy" only with cosmetic products)	10
MENY (supermarket)	3
Panduro Hobby (hobby shop)	15
Rema1000 (supermarket)	5
Søstrene Grene (shop with mostly cheap products)	1
Tiger (shop with mostly cheap products)	2
Toys R Us (toy shop)	8

TABLE 8
OVERVIEW OF SHOPS AND SUPERMARKETS WHERE IN TOTAL 157 COSMETIC PRODUCTS ARE SEEN

6.1.2 Product types included in the survey

In total, 15 different types of cosmetic products with prolonged skin contact (leave-on products) were identified.

Product type	Number of products
Face paint	26
Baby oil	10
Baby powder	4

Product type	Number of products
Conditioner, leave on	3
Lotion	18
Hair spray (colour)	2
Body glitter	1
Lip balm/lip gloss	8
Make-up	4
Nail polish	15
Perfume set	1
Ointment	13
Suntan lotion	30
Tattooing product	5
Towelettes	17

TABLE 9
OVERVIEW OF PRODUCT TYPES

6.1.3 Where are the products produced?

The investigated cosmetic products are produced in the countries which are stated in Table 10. However, the producer country does not appear for all the products, either because it does not appear from the product or of the photos which were taken. This is marked as “unknown” for the products in question. According to the regulation on cosmetic products, it must appear from the labelling if the product is produced outside the EU.

Produced in	Number of products
Unknown country	21 (13%)
Within Europe (in total)	94 (60%)
Germany	17
Denmark	54
Finland	1
France	7
Switzerland	1

Produced in	Number of products
UK	7
EU	7
Outside Europe (in total)	42 (27%)
China	34
Korea	1
Taiwan	6
Thailand	1

TABLE 10
OVERVIEW OF THE COUNTRY WHERE THE PRODUCTS ARE PRODUCED

The overview in Table 10 shows that 27% of the cosmetic products for children are produced outside Europe and that 60% are produced inside Europe. No information is available about the remaining 13%.

6.1.4 Producers

The 157 products are produced by at least 37 different producers. However, there are a number of products (24 in total) where the producer does not appear from the product or clearly from the photos.

6.1.5 Products for the three age groups

Products for children at the age 0-12 years are divided into three age groups: 0-3 years, 4-6 years and 7-12 years. The grouping is based on the claim of the product, for instance stated by “baby lotion” or “4+”, which informs that the product is intended for children at the age of 4 years or older. Several of the investigated products can be used by all age groups. The distribution is stated in the table below and is divided into the different product types.

Product type	Products in total	0-3 years	4-6 years	7-12 years
Face paint	26		22	26
Baby oil	10	10		
Baby powder	4	4		
Conditioner, leave in	3	3	3	3
Lotion	18	18	4	4
Hair spray	2		2	2
Body glitter	1			1

Product type	Products in total	0-3 years	4-6 years	7-12 years
Lip balm/lip gloss	8		2	8
Make-up	4		1	4
Nail polish	15		1	15
Perfume set	1			1
Ointment	13	13	1	1
Suntan lotion	30	30	28	28
Tattooing product	5		4	5
Towelettes	17	17		
Products in total	157	95	68	98

TABLE 11
THE 157 INVESTIGATED PRODUCT TYPES DISTRIBUTED ON THE THREE AGE GROUPS. MANY OF THE PRODUCTS CAN BE USED BY MORE AGE GROUPS.

6.1.6 Eco-labelled and allergy-labelled products

A potential eco-label (the Swan) or allergy-label (The Blue Label) is noted for all products (see Table 12). It is seen that a large part of the 157 investigated products is eco-labelled and/or allergy-labelled, 41% and 44% respectively. All in all, it is the same products which have both the Swan-label and The Blue Label. One single product is Swan-labelled without having The Blue Label and five products have The Blue Label without being Swan-labelled. In total, 64 products are both eco-labelled with the Swan and have The Blue Label.

It is seen that none of the Swan-labelled products or products labelled with The Blue Label have a content of allergenic substances which also is in accordance with the criteria to obtain the Swan and The Blue Label.

Eco-label	Labelled (yes/no)	Number of products	Products with a content of potentially allergenic substances
The Swan	Yes	65	0
	No	92	54
The Blue Label	Yes	69	0
	No	88	54

TABLE 12
THE SHARE OF ECO-LABELLED AND ALLERGY-LABELLED PRODUCTS

6.1.7 Identified potentially allergenic substances

In this section, the colourants, preservatives, fragrances and UV filters identified in the 157 investigated products are presented. Three different tables for three of the four groups of substances are presented. No table for the group of colourants is presented as none of the identified colourants in the survey is on the gross list. In Appendix 3 “Identified colourants, preservatives, fragrances and UV filters in the cosmetic products”, the total list of all the identified substances can be found (distributed on the four groups of substances). Below in Table 13 to Table 15, the presentation is exclusively of the substances which are considered to be potentially allergenic (this appears from the prepared gross list). In total, the following was identified:

- 55 different colourants
- 15 different preservatives
- 30 different substances with a perfuming function:
 - of these, one entrance is the generic term “perfume”,
 - 8 are some of the 26 fragrances subject to declaration,
 - and 21 are substances which are listed with the function “perfuming” in the CosIng database. None of these 21 substances is found on the gross list of potentially allergenic substances,
- 14 different UV filters.

In total, 30 products out of 157 contain one or up to 8 potentially allergenic substances. A content of many allergenic substances is typically due to a content of many different fragrances.

Colourants

In total, 55 different colourants were identified in 126 of the 157 investigated products. In total, 29 cosmetic products were marketed to be free from colourants. A few products were free from colourants without promoting it on the packaging. Nearly all product types contain colourants, however, with the exception of baby oil and conditioner (leave in) where all the identified products are free from colourants. Other products contain for instance often titanium dioxide to give the lotion a whiter colour.

None of the 55 used colourants is on the gross list of potentially allergenic substances.

Preservatives

In total, 15 different preservatives were identified in 139 of the 157 investigated products. Preservatives were seen in nearly all product types, however, with the exception of baby oil, baby powder and hair spray. This is product types where preservation should not be necessary as typically the product type does not contain water.

Two of the 15 different used preservatives are on the gross list of potentially allergenic substance (see Table 13). The two preservatives are found in suntan lotion and in face paint. Please note that benzyl alcohol is stated both under preservatives and fragrances as the substance has both functions. However, in the suntan lotion, benzyl alcohol has probably a function as fragrance as the suntan lotion contains other preservatives (which are not on the gross list).

Preservatives	Seen in number of products	Identified in the following products
Benzyl alcohol	1	Suntan lotion
Imidazolidinyl urea	1	Face paint

TABLE 13
USED POTENTIALLY ALLERGENIC PRESERVATIVES IN THE 157 INVESTIGATED COSMETIC PRODUCTS

Fragrances

Substances with the function "perfuming" were identified in 43 products. According to the definition in the CosIng database, "perfuming" is used for perfume and aromatic raw materials but some of the substances with the property "perfuming" also have other functions, such as "skin conditioning" or solvent. The majority of the investigated cosmetic products, 83 products out of 157, are marketed as free from perfume. Fragrances are seen in nearly all product types; however, with the exception of conditioner (leave on) and body glitter.

Besides the general description "perfume", in total 29 different substances with the function "perfuming" are identified. All the 8 of the 26 fragrances subject to declaration identified during the survey are considered to be potentially allergenic but none of the 21 other identified substances with the function "perfuming" is found on the gross list of potentially allergenic substances. The fragrances which are on the gross list and which are identified in the survey are stated in Table 14 below. It must be noted that the common description "perfume" can cover many different fragrances and it is unknown which ones, unless one or several of the 26 fragrances subject to declaration are contained in the product. In total, 15 products are identified where solely "perfume" is declared but no declaration of the 26 fragrances subject to declaration.

Fragrances	Potentially allergenic, i.e. on the gross list	Seen in number of products	Identified in the following products
Benzyl alcohol	Yes	1	Suntan lotion
Citral	Yes	1	Suntan lotion
Citronellol	Yes	1	Suntan lotion
Coumarin	Yes	1	Lip balm/lip gloss
Eugenol	Yes	1	Lip balm/lip gloss
Geraniol	Yes	2	Lip balm/lip gloss (1), suntan lotion (1)
Limonene	Yes	3	Lip balm/lip gloss (2), suntan lotion (1)
Linalool	Yes	2	Lip balm/lip gloss (1), suntan lotion (1)
Perfume	(perhaps)	22	Lip balm/lip gloss (4), face paint (3), suntan lotion (3), make-up (3), hair spray (2),

Fragrances	Potentially allergenic, i.e. on the gross list	Seen in number of products	Identified in the following products
			towelettes (2), baby oil (1), baby powder (1), lotion (1), nail polish (1), perfume set (1)

TABLE 14
USED ALLERGENIC FRAGRANCES IN THE 157 INVESTIGATED COSMETIC PRODUCTS

Please note, that benzyl alcohol is stated both under preservatives and fragrances as the substance has both functions. However, in the suntan lotion, benzyl alcohol has probably a function as fragrance as the suntan lotion contains other preservatives (which are not on the gross list).

UV filters

In total, 14 different UV filters were identified in 75 of the 157 investigated products. Besides in suntan lotions, the UV filters are seen in face paint, lotion, lip balm/lip gloss, make-up (eye shadow), nail polish and tattooing products.

3 of the 14 different used UV filters are on the gross list of potentially allergenic substances (see Table 15). The UV filters are identified primarily in suntan lotion, but also in lip balm/lip gloss.

UV filter	Seen in number of products	Identified in the following products
Benzophenone-3	2	Lip balm/lip gloss (2)
Drometrizole trisiloxane	6	Suntan lotion (6)
Octocrylene	9	Suntan lotion (9)

TABLE 15
USED POTENTIALLY ALLERGENIC UV FILTERS IN THE 157 INVESTIGATED COSMETIC PRODUCTS

6.1.8 Products without potentially allergenic substances

One purpose with this project was to investigate whether corresponding products without potentially allergenic substances are available on the Danish market. Therefore, the number of products without substances on the gross list distributed on the different product types and age groups was investigated. The overview shows that for nearly all product types, products without a content of one or more potentially allergenic substances are available – and for most product types, the main part is without a content of potentially allergenic substances. However, there are the following exceptions:

- For hair spray, both identified products are with potentially allergenic substances, i.e. here no typically child product without potentially allergenic ingredients was identified.
- For lip balm/lip gloss, in total 8 products were identified. Two of these products have not a content of potentially allergenic substances but these products are not assessed to be targeted the age group 4-6 years. Both identified lip balm/lip gloss products in this age group are with a content of one or more potentially allergenic substances.
- For the product type perfume sets, the only product which was identified in the survey contains potentially allergenic substances (fragrances).

Product type*	Products in total	0-3 years	4-6 years	7-12 years
Face paint (in total)	26		22	26
Face paint (without)	23		19	23
Baby oil (in total)	10	10		
Baby oil (without)	9	9		
Baby powder (in total)	4	4		
Baby powder (without)	3	3		
Conditioner, leave in (in total)	3	3	3	3
Conditioner, leave in (without)	3	3	3	3
Lotion (in total)	18	18	4	4
Lotion (without)	17	17	4	4
Hair spray (in total)	2		2	2
Hair spray (without)	0		0	0
Body glitter (in total)	1			1
Body glitter (without)	1			1
Lip balm/lip gloss (in total)	8		2	8
Lip balm/lip gloss (without)	2		0	2
Make-up (in total)	4		1	4
Make-up (without)	3		1	3
Nail lacquer (in total)	15		1	15
Nail lacquer (without)	15		1	15
Perfume set (in total)	1			1
Perfume set (without)	0			0
Ointment (in total)	13	13	1	1
Ointment (without)	13	13	1	1

Product type*	Products in total	0-3 years	4-6 years	7-12 years
Suntan lotion (in total)	30	30	28	28
Suntan lotion (without)	18	18	17	17
Tattooing product (in total)	5		4	5
Tattooing product (without)	5		4	5
Towelettes (in total)	17	17		
Towelettes (without)	15	15		
<i>Products in total</i>	<i>157</i>	<i>95</i>	<i>68</i>	<i>98</i>
<i>Products in total (without)</i>	<i>127</i>	<i>78</i>	<i>50</i>	<i>73</i>

TABLE 16
THE 157 INVESTIGATED PRODUCT TYPES DISTRIBUTED ON THE THREE AGE GROUPS AND * DISTRIBUTED ON ALL INVESTIGATED PRODUCTS (WHITE BACKGROUND) AND PRODUCTS WITHOUT POTENTIALLY ALLERGENIC SUBSTANCES (GREEN BACKGROUND). MANY PRODUCTS CAN BE USED BY MORE AGE GROUPS.

Based on the survey of the cosmetic products for children, it can thus be concluded that for nearly all the investigated product types, products without potentially allergenic substances are found. Only for the product types, hair spray and perfume set, products (two products and one product in total, respectively) with a content of potentially allergenic substance were identified.

6.2 Discussion and summary

In the survey of the cosmetic products for children in the Danish shops, knowledge of the ingredients for in total 157 products has been collected. More than the half of these products (60%) is produced in the EU while 27% is produced in the East, mainly in China. For the remaining products, the producer country is unknown or could not be identified through the photos which were taken of the products. In percentages, more of the cosmetic products which are produced in the East (21% or 9 out of 43 products) contain potentially allergenic substances compared to the cosmetic products produced in the EU (12% or 11 out of 94 products).

The survey shows that a large part of the cosmetic products for children is eco-labelled (the Swan) and/or the allergy label (The Blue Label). In total, 41% of the products are eco-labelled and 44% of the products are allergy-labelled. Several products had both labels. None of these products contain allergenic substances as it is not allowed according to the criteria for these labels. There are products without potentially allergenic substances which are neither eco-labelled nor allergy-labelled.

Out of the in total 157 products, 30 products contained between one and eight potentially allergenic substances. A content of many potentially allergenic substances is typically due to a content of many different fragrances. The identified potentially allergenic substances in the investigated cosmetic products for children are stated in Table 17 below.

Type of substance	Potentially allergenic substances	Seen in number of products	Identified in the following products
Colourants	<i>No colourants in the gross list were identified in this project</i>		
Preservatives	Benzyl alcohol	1	Suntan lotion
	Imidazolidinyl urea	1	Face paint
Fragrances	Benzyl alcohol	1	Suntan lotion
	Citral	1	Suntan lotion
	Citronellol	1	Suntan lotion
	Coumarin	1	Lip balm/lip gloss
	Eugenol	1	Lip balm/lip gloss
	Geraniol	2	Lip balm/lip gloss (1), suntan lotion (1)
	Limonene	3	Lip balm/lip gloss (2), suntan lotion (1)
	Linalool	2	Lip balm/lip gloss (1), suntan lotion (1)
	Perfume (perhaps allergenic)	22	Lip balm/lip gloss (4), face paint (3), suntan lotion (3), make-up (3), hair spray (2), towelettes (2), baby oil (1), baby powder (1), lotion (1), nail lacquer (1), perfume set (1)
UV filters	Benzophenone-3	2	Lip balm/lip gloss (2)
	Drometrizole trisiloxane	6	Suntan lotion (6)
	Octocrylene	9	Suntan lotion (9)

TABLE 17
USED POTENTIALLY ALLERGENIC SUBSTANCES IN 30 OUT OF 157 INVESTIGATED COSMETIC PRODUCTS WHICH CONTAIN ALLERGENIC SUBSTANCES

In relation to the earlier surveys of cosmetic products for children (Poulsen & Schmidt, 2007) and suntan lotions/lotions for children (Tønning et al., 2009), it is mainly the same potentially allergenic substances which were identified in the cosmetic products for children at that time. However, more of the 26 fragrances subject to declaration were identified and furthermore, MI as well as MCI were identified in the earlier surveys but not in the present survey.

In relation to the Danish consumer magazine TÆNK's surveys of different baby products, it is worth noting that in percentages TÆNK has identified more products with a content of allergenic substances than identified in this survey. TÆNK has examined far more products (between 30 and 37 products) within the different product types for babies (lotions, ointments, oils and towelettes) than included in this survey (between 11 and 18 products). It is not clear which criteria TÆNK uses regarding the definition of allergenic substances. Possible explanations of the difference between the share of products which contain allergenic substances in TÆNK's survey and this survey might be the following:

- In this survey, only products from physical shops are included as no products have been purchased in connection with the survey. Only photos of declarations of contents have been taken in shops.
- TÆNK has purchased products from both physical shops and internet shops. There are perhaps more allergenic ingredients in products purchased on the internet. TÆNK's surveys show that many products in "English" (not Danish language) contain allergenic substances.
- In this survey, products are exclusively regarded as containing potentially allergenic substances if the substances are included in the gross list of potentially allergenic substances. Several substances with the function "perfuming" are not in the gross list according to CosIng. It might be considered that TÆNK regards these substances to be potentially allergenic. For instance, TÆNK states that chamomile extract is considered to be allergenic which is not in the gross list of potentially allergenic substances in this project.

An essential conclusion from the survey is that it is possible to find cosmetic products for children without potentially allergenic substances (127 out of 157 investigated products are without a content of potentially allergenic substances). It is possible for nearly all the investigated product types (except for hair spray and perfume set) to find products without potentially allergenic substances.

7. Results of survey of toys

In this chapter, the results, which are obtained during the survey of which potentially allergenic substances on the gross list that are used in toys for children on the Danish market, are presented. The results are primarily achieved through contact with the industrial sector.

As described in the introduction, focus has exclusively been on chemical toys which have an expected prolonged skin contact.

7.1 Contact to the industrial sector

The main part of the information regarding content of potentially allergenic substances from the gross list is collected via contact to the industrial sector. As described in chapter 4 “Survey – procedure”, an email was sent out in co-operation with the Toy Sector (Legetøjsbranchen – LEG) to the members of the sector. The email was an inquiry on which of selected substances from the gross list (see Table 18), that are present in their chemical toy products; i.e. toy products of the following types:

- Modelling clay and similar products – for instance formable sand
- Finger paint
- Face paint and make-up
- Slime
- Transferable tattoos or sets to paint own tattoos
- Jewellery (stones) which are glued on the skin as decoration
- Soap bubbles and soap for foam pistols

Besides an email from the Toy Sector, selected toy retailers and producers were contacted via telephone.

Type	CAS no.	INCI name
Colourant	1064-48-8	CI 20470
Colourant	846-70-8	CI 10316
UV filter	131-57-7	BENZOPHENONE-3
UV filter	6197-30-4	OCTOCRYLENE
UV filter	155633-54-8	DROMETRIZOLE TRISILOXANE
Preservative	50-00-0	FORMALDEHYDE
Preservative	30525-89-4	PARAFORMALDEHYDE
Preservative	52-51-7	2-BROMO-2-NITROPROPANE-1,3-DIOL
Preservative	59-50-7	P-CHLORO-M-CRESOL

Type	CAS no.	INCI name
Preservative	88-04-0	4-chloro-3,5-dimethylphenol
Preservative	1321-23-9	Chloroxylenol
Preservative	39236-46-9	IMIDAZOLIDINYL UREA
Preservative	32289-58-0	POLYAMINOPROPYL BIGUANIDE*
Preservative	100-97-0	METHENAMINE
Preservative	4080-31-3	QUATERNIUM-15*
Preservative	51229-78-8	QUATERNIUM-15*
Preservative	38083-17-9	CLIMBAZOLE
Preservative	6440-58-0	DMDM HYDANTOIN
Preservative	55965-84-9	Kathon
Preservative	26172-55-4	METHYLCHLOROISOTHIAZOLINONE
Preservative	2682-20-4	METHYLISOTHIAZOLINONE
Preservative	79-07-2	CHLOROACETAMIDE
Preservative	78491-02-8	DIAZOLIDINYL UREA
Preservative	111-30-8	GLUTARAL
Preservative	70161-44-3	SODIUM HYDROXYMETHYLGLYCINATE
Preservative	55406-53-6	IODOPROPYNYL BUTYLCARBAMATE
Preservative	2634-33-5	BENZISOTHIAZOLINONE**
Adhesive (binder)	25085-50-1	p-tert-Butyl formaldehyde resin
Adhesive (binder)		Epoxy resin
Fragrances		The 26 fragrances subject to declaration from the regulation on cosmetic products

TABLE 18

THE SELECTED SUBSTANCES FROM THE GROSS LIST WHICH WAS SENT TO THE TOY SECTOR FOR COMMENTS.

* THESE PRESERVATIVES ARE NOT LONGER ALLOWED IN COSMETIC PRODUCTS BUT ARE ALLOWED FOR USE IN TOYS AND THUS ON THE LIST TO THE TOY SECTOR.

** THIS PRESERVATIVE IS NOT ALLOWED IN COSMETIC PRODUCTS BUT IN AN EARLIER SURVEY IT WAS SEEN IN CHEMICAL TOYS AND THUS ON THE LIST TO THE TOY SECTOR.

7.2 Results from the survey – information from companies

In this section, the information which was received from several dealers and producers of toys is presented. The information was received through an inquiry which was sent from the Toy Sector in Denmark (LEG) to their members as well as via telephone calls to selected toy dealers or producers. The results are presented anonymously below.

7.2.1 Information from dealers, importers and producers of toys

7.2.1.1 Company no. 1

Toy dealer no. 1 commented on the forwarded gross list and gave the following comments which are inserted in Table 19 below.

The company writes that the comments apply for both the toy and the cosmetic products (toy products) which they sell. An overall comment is that some of the substances are substances which they do not see very often. Generally, they do not accept a number of the substances on the forwarded gross list in the mentioned product types. For instance, in general, they do not allow perfume in their toys and they normally test for content of the 26 fragrances subject to declaration from the regulation on cosmetic products. However, there may be exceptions for products with a bad smell where perfume can be accepted.

The company informs that formaldehyde releasing preservatives are not accepted in products with predictable prolonged skin contact (which the mentioned products are). However, they are accepted in a few products with a very limited skin contact on the condition that they comply with the test in EN 71-9 on organic chemical compounds. Especially for preservatives, the general challenge is that the raw materials may be preserved, i.e. information on preservatives has to be found several steps back in the production chain.

Generally, the company informs that it is a challenge to provide information on ingredients in toy products as it depends on the individual supplier and their policy. Not all suppliers/producers allow full information on the used ingredients.

7.2.1.2 Company no. 2

Primarily, the company does business with the big producers of toys or makes sure that they buy toys from European suppliers. In general, the company has not access to knowledge on ingredients and therefore they refer to the producers of toys for further information.

7.2.1.3 Company no. 3

The company is not in possession of any information regarding ingredients in their toy products. They do not get access to this information from their suppliers. However, they test the toys but only for ingredients which are not allowed to be used according to the statutory order on toys.

The company seeks knowledge on which ingredients that can be used safely (a positive list) or which ingredients that should not be used (besides the requirements from legislation) so they have a possibility to make demands to their suppliers. Recently, due to the discussion about MI (methylisothiazolinone), they have asked about the content of this preservative in their toy products and found out that it is not found in any of their products. Otherwise, it is very limited knowledge which they have about the ingredients in their toy products.

7.2.1.4 Company no. 4

Due to busyness and replacement of the staff, only information on the use of preservatives in their products was given. The information which they have sent comes from similar surveys from the Danish EPA on preservatives in toys from 2012 and the use of MI in consumer products in 2013 respectively. According to their former survey of their products, it is the use of Kathon and BIT

(benzisothiazolinone) which are used in their finger paints. However, they point out that since then their suppliers have worked hard on replacing certain preservatives. This is due to the CLP regulation coming into force and the fact that they want to avoid the labelling requirement of EUH208 “Contains (name of the sensitizing substance). May cause an allergic reaction”.

The company is aware of the discussion which takes place on allergens and preservatives. Due to the risk of allergy, the allowed levels of the preservatives are continuously reduced through legislation. However, the company feels that there is not enough attention to the risk of infection when it comes to certain types of toys. Finger paint is a typical product which consistently gets into contact with virus and bacteria through children’s hands. Here it is clear that a use of preservatives is needed, and according to the company the risk of infection ought to be more important. The company is of the opinion that it is necessary with a market with many different alternatives to preservation in order to be able to reduce the risk of allergy. In the course of time, a large consumption of a certain preservative will increase the risk of allergy by using this preservative if it is allergenic.

7.2.1.5 Company no. 5

The company delivers a number of soap bubble products to different shops which sell toys. These soap bubble products are purchased from a European supplier. The supplier states that all the soap bubble products contain a preservative but which preservative is confidential information. However, Kathon is not used (is stated on the producer’s homepage). The soap bubble products are tested for the content of a number of substances from the statutory order on toys. These tests show that there is no content of MI, MCI or MI/MCI (Kathon) as preservative in concentrations above 10 ppm (or corresponding to 0.001%). The content of formaldehyde has also been tested and the concentration is below 0.01%. However, from another toy distributor, it is known that this preservative, which this European supplier uses in the soap bubble products, is the gross list substance bronopol.

7.2.1.6 Company no. 6

The company has inquired for information on ingredients from their three Chinese suppliers. Regarding the Chinese soap bubble products, they have been informed that there is no content of any of the potentially allergenic substances in the list sent to the toy sector (Table 18).

From another Chinese supplier, who delivers modelling clay, finger paints and cosmetic products, they have been informed that of the substances in the list (Table 18), the preservative DMDM hydantoin is used in finger paints. No other substances from the list (Table 18) are used in the finger paints or in any of their other products.

From the third Chinese supplier, who delivers two types of modelling clay and finger paints, they have received the information that polyaminopropyl biguanide³ (in a modelling clay), Kathon (in another type of modelling clay) and DMDM hydantoin (in finger paints) from the gross list are used.

Generally, the company has the opinion that they do not buy toy products with a content of fragrances as their customers do not want products with a content of fragrances.

The company also has a European supplier of soap bubble products. This supplier states that all the soap bubble products are free from Kathon and that the used preservative is the gross list substance bronopol.

³ Polyaminopropyl biguanide is allowed to use in toys in a maximum concentration of 1% due to the classification as Carc. 2. As a preservative, the substance is typically used in a concentration lower than 1%.

7.2.1.7 Company no. 7

The company informs that they have made a ban on the use of a large part of the preservatives which are on the list that was sent to the toy sector (Table 18).

The company's Chinese supplier of the soap bubble products informs that from the list of substances, the preservative DMDM hydantoin is used in a concentration of approx. 0.29% in the products they sell to the company. No fragrances are used in any of the soap bubble products.

7.2.1.8 Company no. 8

The company delivers toys to supermarkets in Denmark and other smaller shops/chains. The products in question are of the following types: tattooing sets, tattooing pens, transmittable tattooing marks, magic sand, make-up products, nail polish products, modelling clay, various soap bubble products and various slime products.

The company has examined all of the toy products (in total more than 40 different products) which are in focus in this project and which they have in their assortment. They inform that none of the stated potentially allergenic ingredients (from Table 18) is found in their products.

Type	CAS no.	INCI name	Company information regarding use of possible potentially allergenic substances from the forwarded list					
			No. 1	No. 4	No. 5	No. 6	No. 7	No. 8
Colourant	1064-48-8	CI 20470	No info	No info	<i>No use</i>	<i>No use</i>	No info	<i>No use</i>
Colourant	846-70-8	CI 10316	No info	No info	<i>No use</i>	<i>No use</i>	No info	<i>No use</i>
UV filter	131-57-7	BENZOPHENONE-3	No info	No info	<i>No use</i>	<i>No use</i>	No info	<i>No use</i>
UV filter	6197-30-4	OCTOCRYLENE	Is not accepted for the listed products	No info	<i>No use</i>	<i>No use</i>	No info	<i>No use</i>
UV filter	155633-54-8	DROMETRIZOLE TRISILOXANE	No info	No info	<i>No use</i>	<i>No use</i>	No info	<i>No use</i>
Preservative	50-00-0	FORMALDEHYDE*	Is not accepted for the listed products	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>
Preservative	30525-89-4	PARAFORMALDEHYDE	Is not accepted for the listed products	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>
Preservative	52-51-7	2-BROMO-2-NITROPROPANE-1,3-DIOL	Is not accepted for the listed products	<i>No use</i>	Yes, in soap bubble products (EU)	Yes, is present in some soap bubble products (EU)	<i>No use</i>	<i>No use</i>
Preservative	59-50-7	P-CHLORO-M-CRESOL	No info	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>
Preservative	88-04-0	4-chloro-3,5-dimethylphenol	No info	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>
Preservative	1321-23-9	Chloroxylenol	No info	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>

Type	CAS no.	INCI name	Company information regarding use of possible potentially allergenic substances from the forwarded list					
			No. 1	No. 4	No. 5	No. 6	No. 7	No. 8
Preservative	39236-46-9	IMIDAZOLIDINYL UREA	Is not accepted for the listed products	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>
Preservative	32289-58-0	POLYAMINOPROPYL BIGUANIDE**	Is not accepted for the listed products	<i>No use</i>	<i>No use</i>	Yes, in some modelling clays	<i>No use</i>	<i>No use</i>
Preservative	100-97-0	METHENAMINE	Is not accepted for the listed products	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>
Preservative	4080-31-3	QUATERNIUM-15**	Is not accepted for the listed products	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>
Preservative	51229-78-8	QUATERNIUM-15**	Is not accepted for the listed products	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>
Preservative	6440-58-0	DMDM HYDANTOIN	Is not accepted for the listed products	<i>No use</i>	<i>No use</i>	Yes, in finger paint	Yes, in soap bubble products in conc. of 0.29%	<i>No use</i>
Preservative	55965-84-9	Kathon	Is not accepted for the listed products	Is present in glitter and finger paint in conc. of 0.00098% and 0.0009% respectively	<i>No use</i>	Yes, in some modelling clays	<i>No use</i>	<i>No use</i>

Type	CAS no.	INCI name	Company information regarding use of possible potentially allergenic substances from the forwarded list					
			No. 1	No. 4	No. 5	No. 6	No. 7	No. 8
Preservative	26172-55-4	METHYLCHLORO-ISOTHIAZOLINONE	Is not accepted for the listed products	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>
Preservative	2682-20-4	METHYLI-SOTHIAZOLINONE	Is not accepted for the listed products	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>
Preservative	79-07-2	CHLOROACETAMIDE	No info	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>
Preservative	78491-02-8	DIAZOLIDINYL UREA	Is not accepted for the listed products	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>
Preservative	111-30-8	GLUTARAL	Is not accepted for the listed products	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>
Preservative	70161-44-3	SODIUM HYDROXYMETHYL-GLYCINATE	Is not accepted for the listed products	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>
Preservative	55406-53-6	IODOPROPYNYL BUTYLCARBAMATE	Is not accepted for the listed products	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>
Preservative	2634-33-5	BENZISOTHIAZOLINONE	Is not accepted for the listed products	Is present in one single finger paint in a conc. of 0.00018%	<i>No use</i>	<i>No use</i>	<i>No use</i>	<i>No use</i>

Type	CAS no.	INCI name	Company information regarding use of possible potentially allergenic substances from the forwarded list					
			No. 1	No. 4	No. 5	No. 6	No. 7	No. 8
Adhesive (binder)	25085-50-1	p-tert-Butyl formaldehyde resin	No restrictions in our system – is this substance documented as being allergenic?	No info	<i>No use</i>	<i>No use</i>	No info	<i>No use</i>
Adhesive (binder)		Epoxy resin	No restrictions in our system – is this substance documented as being allergenic?	No info	<i>No use</i>	<i>No use</i>	No info	<i>No use</i>
Fragrances		The 26 fragrances subject to declaration according to the Regulation on cosmetic products	Is not accepted for the listed products in conc. above 0.001%	No info	<i>No use</i>	<i>No use</i>	No info	<i>No use</i>

TABLE 19

COMMENTS FROM THE COMPANIES REGARDING THE SUBSTANCES IN TABLE 18

“NO INFO” = NO INFORMATION

“NOT USED” = THE SUBSTANCE IS NOT USED ACCORDING TO THE TOY DISTRIBUTOR OR PRODUCER IN THEIR CHEMICAL TOY PRODUCTS

* FORMALDEHYDE IS NO LONGER ALLOWED TO BE USED IN COSMETIC PRODUCTS AS OF 1.1.2016 BECAUSE OF ITS CLASSIFICATION AS CMR

** SUBSTANCES ARE NOT ALLOWED IN COSMETIC PRODUCTS BECAUSE OF THEIR CMR CLASSIFICATION, BUT ARE ALLOWED IN TOYS IN A MAXIMUM CONCENTRATION OF 0.1 TO 3% DEPENDANT OF THE CLASSIFICATION CATEGORY (1A/1B OR 2) OR THE EFFECT (CM OR R)

7.2.2 Shops included in the survey

The toy dealers who have delivered information to the project inform that the toy products which they resell are sold to both small and big toy shops/chains as well as various supermarkets.

7.2.3 Where are the products produced?

From the information received from the toy dealers who have delivered information to the project, it seems as if most of the toy products are produced in the East (primarily China). However, some soap bubble products are produced in South Europe.

The toy products, which at the same time also have been a part of the survey of the cosmetic products as they also are comprised by the regulation on cosmetic products, are primarily produced in China (approx. 63% of the investigated products) and approx. 22% are produced within the EU (in Germany, France or the UK). For 14% of the products, the origin of the producer was not described on the product.

7.2.4 Products for the three age groups

The types of chemical toys which have been included in the survey are presented in Table 20 below and it is stated to which age group the products typically address. This is based on the products from the survey of the cosmetic products as well as from information from these product types observed in shops and on the internet.

Product type	0-3 years	4-6 years	7-12 years
Modelling clay, formable sand and similar products	Yes/No	Yes	Yes
Finger paint	Yes	Yes	Yes
Face paint	No	Yes	Yes
Make-up	No	Yes	Yes
Slime	No	Yes	Yes
Transferable tattooing stickers/tattooing sets	No	Yes	Yes
Soap bubbles and soap for foam pistols	Yes/No	Yes	Yes

TABLE 20

CHEMICAL TOYS WHICH ARE A PART OF THE SURVEY, DISTRIBUTED ON THE THREE AGE GROUPS. MANY PRODUCTS CAN BE USED BY MORE AGE GROUPS.

"YES/NO" = SOME PRODUCTS SHOULD NOT BE USED BY CHILDREN AT THE AGE OF 0-3 YEARS, WHILE OTHER PRODUCTS OF THE SAME TYPE ARE FOR CHILDREN AT ANY AGE.

7.2.5 Identified potentially allergenic substances in chemical toys

Table 21 is a presentation of the colourants, the preservatives, the fragrances and the UV filters which are identified in chemical toys. The identification is based on responses from the toy sector as well as earlier surveys (literature). It appears that preservatives and fragrances are most relevant when it comes to chemical toy products.

Substance type	Potentially allergenic substances	Identified in the following toy products
Colourants	<i>None observed</i>	<i>No potentially allergenic colourants are observed in this project</i>
Preservatives	Bronopol	Soap bubbles (0.1%) Finger paint (literature) Modelling clay (0.0305%) (analysis)
	Kathon (MI/MCI)	Finger paint (0.0009% and in higher concentrations in the literature) Modelling clay
	Benzisothiazolinone	Finger paint (0.00018%)
	Preventol D7 (a mixture of isothiazolinones)	Slime (0.0025%) (literature)
	Iodopropynyl butylcarbamate	Face paint and make-up (literature)
	Free formaldehyde	Modelling clay (0.122%) (analysis) Finger paint (0.069%) (literature) Slime (0.0335%)
	DMDM hydantoin	Finger paint Soap bubbles (0.29%) Face paint and make-up (literature)
	Diazolidinyl urea	Finger paint (literature)
	Imidazolidinyl urea	Face paint (see chapter 6)
Fragrances	The 26 fragrances subject to declaration	In general, the sector seems to avoid these
	Perfume	Face paint (see chapter 6) Make-up (see chapter 6) Perfume set (see chapter 6) Chemical toy products which smell bad (for instance modelling clay and slime) (see chapter 5 and 6)
UV filters	<i>None observed</i>	Is not used – is not seen in the survey of cosmetic toy products (make-up or face paint)

TABLE 21
USED ALLERGENIC SUBSTANCES IN CHEMICAL TOYS
“(LITERATURE)” = MEANS THAT INFORMATION ABOUT THE USE IS EXCLUSIVELY BASED ON LITERATURE WHICH MAY BE OF AN EARLIER DATE

7.2.6 Products without potentially allergenic substances

Based on the contact to toy dealers and producers as well as the survey of the cosmetic toy products, it can be demonstrated that in most of the investigated product categories, chemical toys without a content of potentially allergenic substances (from the list based on the gross list which was sent to the sector) do exist. The product type finger paint contains preservative and several responses from toy dealers and producers show that their finger paints contain a potentially allergenic preservative. The earlier survey of preservatives in chemical toys carried out for the Danish EPA (Poulsen & Nielsen, 2014) also showed that finger paints on the Danish market (in 2012) often contained potentially allergenic preservatives from the gross list.

Generally, for chemical toys, it is not possible to see in the purchase situation whether the product contains potentially allergenic substances. However, preservatives used in finger paint must be declared (according to EN 71-7) and on cosmetic sets which are intended to produce products like for instance fragrances, soap, lotion, make-up and shampoo it must clearly appear from the packaging if they contain one of the stated allergenic fragrances in the statutory order on toy products (the 26 fragrances subject to declaration from the regulation on cosmetic products). Furthermore, the cosmetic sets must be provided with the warning "Contain fragrances which may be allergenic". Toy products which at the same time are cosmetic products must be labelled according to the regulation on cosmetics, i.e. a list of ingredients.

7.3 Summary

During the survey of chemical toys for children, knowledge on possibly used potentially allergenic substances was collected through contact to the toy sector. Eight companies have given responses about their use of possibly potentially allergenic substances in chemical toys which are sold on the Danish market. A number of the toy dealers and producers have suppliers from the East (such as China, Korea, Taiwan and Thailand) but toys are also purchased from European suppliers.

The survey shows that several of the eight companies who have delivered information to the project make requirements concerning allergenic substances. Among other things, the use of fragrances in chemical toys is unwanted by several companies and several companies make requirements regarding ban on the use of allergenic preservatives or are working at replacing allergenic preservatives in their chemical toy products. The contact to the companies shows that chemical toys without any use of potentially allergenic ingredients are found on the Danish market.

The identified potentially allergenic substances are stated in Table 21 above. The table shows that no use is identified of either potentially allergenic UV filters or colourants in the chemical toy products. It is primarily potentially allergenic fragrances (mainly in the cosmetic products such as face paint, make-up and perfume sets) and potentially allergenic preservatives (mainly in finger paint, modelling clay and make-up as well as soap bubbles) which seem to be used in chemical toys.

8. Hazard assessment of the identified substances

In this chapter, a hazard assessment of the identified substances from the survey of the potentially allergenic substances in cosmetics and toys targeted children has been carried out. The hazard assessment is exclusively focusing on describing the allergenic properties of the substances, i.e. the allergenic potential of the substances and possible levels for elicitation and induction, if these data is available. Data regarding the allergenic potential has only been searched for in easy accessible sources such as SCCS opinions or the ECHA database of registered substances. Levels for induction and elicitation are described, if information about this exists in the SCCS opinions.

8.1 Allergy potential for the identified substances

In Table 17 in chapter 5, an overview of the potentially allergenic substances that were identified in the survey of the cosmetic products is presented. Table 19 in chapter 6 shows the potentially allergenic substances, which were identified in chemical toys. These potentially allergenic substances, which are described with respect to their allergy potential, are aggregated in Table 22 to Table 24 below.

The following aspects are described for each of the identified substances:

- INCI name or chemical name (CAS no. is listed in brackets after the INCI name)
- Which products the substance is identified in (number of products is listed in brackets)
- Allergy potential
 - Here the assessment of the allergenic properties carried out by SCCS is listed, if such an assessment exists. In some cases, it is only stated if the substance has allergenic properties, while in other cases, the allergy potential of the substance is listed, i.e. if the substance is a ‘moderate’, ‘strong’ or an ‘extreme’ sensitiser. Finally, information about levels for induction and elicitation is listed, if such information exists in a possible SCCS opinion of the substance.
 - The rate of sensitisation is given as listed in Simonsen et al. (2013), if such information exists for the substances. The rate of sensitisation is the percentage of tested persons that developed allergic reactions towards the substance. The substance is a stronger allergen, the higher the percentage.
- LLNA EC₃ value⁴, if such a value can be found for the substance. A search has been performed in SCCS opinions, in the ECHA database of registered substances (ECHA RSD, 2015) and the report “Allergens in Consumer Products” (RIVM, 2008) has been used as a reference.
 - An EC₃ value above 2% means that the substance is a moderate sensitiser; whereas an EC₃ value of less than 0.2 means that the substance is an extreme sensitiser. Values in between are regarded as strong sensitising substances (Table R. 8-23 ECHA, 2012).
- Harmonised classification according to ECHA C&L Inventory (2015), and if a harmonised classification does not exist, the most frequent notified classification is listed (if any) (ECHA C&L Inventory, 2015).
- Reference.

⁴ EC₃ value is the estimated concentration of a chemical necessary to give a 3-fold increase in lymph node cell proliferative activity (stimulation index SI ≥ 3) in animals exposed to an allergen compared to the vehicle-treated control (SCCS nr. 1459, 2012).

The types of potentially allergenic substances identified in cosmetics and in chemical toys are (Table 22, Table 23 and Table 24):

- 3 UV filters
 - The result of the survey indicates that these UV filters exclusively are found in cosmetics and primarily in suntan lotions. One UV filter is, however, only observed in a few lip balm/lip gloss products.
- 10 preservatives
 - The result from the survey indicates that the preservatives primarily are found in chemical toys such as finger paint, slime, modelling clay and face paint/make-up. Face paint and make-up, which also are cosmetic products, are the only type of cosmetics which contain the potentially allergenic preservatives.
- 8 fragrances
 - The result of the survey indicates that the use of the fragrances is limited. In chemical toys, the use of the fragrances are avoided as far as possible, but they may be present in products that beforehand have a nasty smell (e.g. modelling clay and slime) in order to conceal the smell. In cosmetics the 8 fragrances are observed in suntan lotion and lip balm/lip gloss products. The 8 fragrances were found in 1-3 different products depending on the fragrance.

The hazard assessment of these three types of potentially allergenic substances is given in the three tables below (Table 22, Table 23 and Table 24).

Levels for induction and elicitation

As mentioned above, a search has been made in possible available SCCS opinions for the substances for levels of induction and elicitation. The result of the search is listed in Table 22, Table 23 and Table 24 below.

According to ECHA (2012), a LLNA EC₃ value can be regarded as a LOAL value for induction. LLNA (Local Lymph Node Assay) EC₃ ('3-fold Effect Concentration') stands for the amount of substance needed to induce a three-fold increased activity (stimulation index SI ≥ 3) in lymph nodes for an animal exposed to an allergen, compared to the control animal (SCCS no. 1459, 2012). According to ECHA (2012), EC₃ values are often given as a percentage and are representing the used concentration of the substance in percent. Based on the standard conditions for the LLNA animal experiment, where a dose volume of 25 µl and an estimated application area of 1 cm² of the ears of the mouse are used, the percentage can be converted by using the following formula:

$$EC3 (\%) \times 250 \frac{\mu g}{cm^2} / \% = EC3 (\frac{\mu g}{cm^2})$$

A LOAL value for induction has been calculated based on the lowest identified EC₃ value, where possible.

If no values for induction based on e.g. human observations exist, it will be possible to calculate a DNEL or DMEL for the substances where LLNA EC₃ values exist by use of assessment factors (safety factors).

A similar approach is described in the SCCS Notes of Guidance (SCCS no. 1051, 2012) for cosmetics and in the SCCS opinion on fragrances (SCCS no. 1459, 2012), where a safety margin is used to establish an acceptable exposure level for induction of allergy based on LLNA values.

INCI name UV-filters	Identified in	Classification (ECHA C&L)	Allergy potential (according to SCCS, if not otherwise stated)	LLNA EC ₃ - value (ECHA RSD or RIVM)	Level of induction/elicitation	Reference
BENZOPHENONE-3 (131-57-7)	Lip balm (2)	<p><u>Harmonised:</u></p> <p>None</p> <p><u>Notified:</u></p> <p>Skin Irrit. 2, H315; Eye Irrit. 2, H319; STOT SE 3, H335</p>	<p>LLNA: not sensitising</p> <p>SCCS concludes: can cause photo-allergic reactions.</p> <p>100 documented cases of contact allergy (from 30 studies)</p> <p>318 documented cases of photo-contact allergy (from 43 studies)</p>	No data (cannot be calculated, not sensitising)	<p><u>Induction:</u></p> <p><i>No data</i></p> <p><u>Elicitation:</u></p> <p><i>No data</i></p>	SCCP/1069/06; SCCP/1201/08; ECHA RSD, 2015; Heurung et al., 2014
OCTOCRYLENE (6197-30-4)	Suntan lotion (9)	<p><u>Harmonised:</u></p> <p>None</p> <p><u>Notified:</u></p> <p>Aquatic Chronic 4, H413</p>	<p>'Moderate sensitiser'</p> <p>Photo-contact allergen and contact allergen</p> <p>69 documented cases of contact allergy (from 9 studies)</p> <p>81 documented cases of photo-contact allergy (from 7 studies)</p>	<p>No skin reactions (ECHA RSD)</p> <p>7.7% (de Groot)</p>	<p><u>Induction:</u></p> <p>AEL = 4-9 µg/cm²</p> <p>Calculated LOAL = 7.7 x 250 = 1925 µg/cm²</p> <p><u>Elicitation:</u></p> <p><i>No data</i></p>	Karlsson et al., 2011; Asthma-Allergy Denmark, 2015; Manova et al., 2014; de Groot & Roberts, 2014; Heurung et al., 2014

INCI name UV-filters	Identified in	Classification (ECHA C&L)	Allergy potential (according to SCCS, if not otherwise stated)	LLNA EC ₃ - value (ECHA RSD or RIVM)	Level of induction/elicitation	Reference
DROMETRIZOLE TRISILOXANE (155633-54-8)	Suntan lotion (6)	<u>Harmonised:</u> None <u>Notified:</u> Not listed in C&L Inventory	Regularly causes cases of photo-allergy. Rarely causes contact dermatitis. 2 documented cases of contact allergy (from 2 reports). 1 documented case of photo-contact allergy (from 1 study).	No data Not registered in ECHA	<u>Induction:</u> <i>No data</i> <u>Elicitation:</u> <i>No data</i>	Johansen et al., 2011; Saraswat, 2012; Heurung et al., 2014

TABLE 22
THE IDENTIFIED POTENTIALLY ALLERGENIC UV-FILTERS IN COSMETICS AND CHEMICAL TOYS.

RATE OF SENSITISATION = NUMBER OF POSITIVE REACTIONS PER NUMBER OF TESTED PERSONS (IN PERCENT). AEL = ACCEPTABLE EXPOSURE LEVEL. NO DATA (ECHA RSD) = NO DATA CONCERNING LLNA EC₃-VALUES IN THE DATABASE OF REGISTERED SUBSTANCES EXISTS. NOT REGISTERED = THE SUBSTANCES ARE NOT REGISTERED AND CANNOT BE FOUND IN THE DATABASE OF REGISTERED SUBSTANCES (ECHA).

INCI name Preservatives	Identified in	Classification (ECHA C&L)	Allergy potential (according to SCCS, if not otherwise stated)	LLNA EC3- value (ECHA RSD or RIVM)	Level of induction/elicitation	Reference
FORMALDEHYDE (50-00-0)	Modelling clay, finger paint, slime	<u>Harmonised:</u> Acute Tox. 3, H301; Acute Tox. 3, H311; Skin Corr. 1B, H314; Skin Sens. 1, H317; Acute Tox. 3, H331; Carc. 2, H351	'Strong sensitiser' Rate of sensitisation = 0.7%	3.8 – 12.3% (ECHA RSD) 0.96% (RIVM) 0.29% (SCCS)	<u>Induction:</u> < 200-300 ppm free formaldehyde in cosmetics will induce allergy. Calculated LOAL = 0,29 x 250 = 72.5 µg/cm ² <u>Elicitation:</u> Levels between 0.2 ppm and 300 ppm have been observed. Threshold values of 30 ppm for aquatic solutions and 60 ppm for products that contain formaldehyde have been suggested (SCCS).	Simonsen et al., 2013; ECHA C&L Inventory, 2015; SCCS/1538/14; ECHA RSD, 2015; de Groot et al., 2009; Johansen et al. (year unknown)
2-BROMO-2- NITROPROPANE- 1,3-DIOL (Bronopol) (52-51-7)	Soap bubbles, finger paint, modelling clay	<u>Harmonised:</u> Acute Tox. 4, H302; Acute Tox. 4, H312; Skin Irrit. 2, H315; Eye Dam. 1, H318; STOT SE 3, H335; Aquatic Acute 1, H400	Formaldehyde releaser Rate of sensitisation = 0.2% Not sensitising (ECHA RSD)	No data (not sensitising)	<i>No data, but releases formaldehyde</i>	Simonsen et al., 2013; SCCNFP/0125/99; Danish Allergy Research Centre, 2015

INCI name Preservatives	Identified in	Classification (ECHA C&L)	Allergy potential (according to SCCS, if not otherwise stated)	LLNA EC3- value (ECHA RSD or RIVM)	Level of induction/elicitation	Reference
IMIDAZOLIDINYL UREA (39236-46-9)	Face paint (1)	<u>Harmonised:</u> None <u>Notified:</u> Not classified	Formaldehyde releaser Rate of sensitisation = 0.3%	> 2	<i>No data, but releases formaldehyde</i> In the SCCS opinion, it is stated that a concentration of 0.6% Imidazolidinyl urea corresponds to a concentration of free formaldehyde of 0.186%.	Simonsen et al., 2013; Danish Allergy Research Centre, 2015; SCCNFP/586/02, final
DMDM HYDANTOIN (6440-58-0)	Finger paint, soap bubbles, face paint and make-up (lit.)	<u>Harmonised:</u> None <u>Notified:</u> Acute Tox. 4, H302	Formaldehyde releaser Not sensitising (ECHA RSD)	No data (not sensitising)	<u>Induction:</u> <i>No data, but releases formaldehyde</i> <u>Elicitation:</u> 0.25% in lotion gives allergic reactions in already sensitised individuals	Danish Allergy Research Centre, 2015; de Groot et al., 1988
DIAZOLIDINYL UREA (78491-02-8)	Finger paint (lit.)	<u>Harmonised:</u> None <u>Notified:</u> Skin Sens. 1, H317	Formaldehyde releaser Rate of sensitisation = 0.3%	No data (unequivocal regarding sensitisation)	<i>No data</i> In the SCCS opinion, it is stated that a concentration of 0.6% Diazolidinyl urea corresponds to a concentration of free formaldehyde of 0.215%.	SCCNFP/586/02; Simonsen et al., 2013

INCI name Preservatives	Identified in	Classification (ECHA C&L)	Allergy potential (according to SCCS, if not otherwise stated)	LLNA EC3- value (ECHA RSD or RIVM)	Level of induction/elicitation	Reference
POLYAMINOPRO PYL BIGUANIDE* (32289-58-0)	Face paint (3) Modelling clay	<u>Harmonised:</u> None <u>Notified:</u> Skin Irrit. 2, H315; Skin Sens. 1, H317 ; Eye Irrit. 2, H319	'Moderate to strong sensitiser in animals'	No data Not registered (ECHA)	<u>Induction:</u> SCCS concludes that a 2% solution can cause sensitisation in humans. <u>Elicitation:</u> Threshold value is stated to be about 1% for guinea pigs. SCCS concludes that elicitation in humans can occur at concentrations from 0.2%.	SCCS/1535/14
Kathon (55965-84-9) Consisting of a mixture of MI and MCI	Finger paint	<u>Harmonised:</u> Acute Tox. 3, H301; Acute Tox. 3, H311; Skin Corr. 1B, H314; Skin Sens. 1, H317 ; Acute Tox. 3, H331; Aquatic Acute 1, H400; Aquatic Chronic 1, H410	'Extreme sensitiser' Rate of sensitisation = 0.8%	Not registered (ECHA) 0.01% (RIVM) 30 ppm (0.003%) = 0.75 µg/cm ² (SCCS)	<u>Induction:</u> > 58 ppm (> 0.7 µg/cm ²) Calculated LOAL = 0.003 x 250 = 0.75 µg/cm ² <u>Elicitation:</u> < 2 ppm corresponding to < 0.025 µg/cm ²	SCCS/1238/09; Simonsen et al., 2013; Zachariae et al., 2006

INCI name Preservatives	Identified in	Classification (ECHA C&L)	Allergy potential (according to SCCS, if not otherwise stated)	LLNA EC3- value (ECHA RSD or RIVM)	Level of induction/elicitation	Reference
METHYLCHLORO ISOTHIAZOLI- NONE (MCI) (26172-55-4)	Finger paint	<u>Harmonised:</u> None <u>Notified:</u> Acute Tox. 2, H300; Acute Tox. 2, H310; Skin Corr. 1B, H314; Skin Sens. 1, H317; Eye Dam. 1, H318; Acute Tox. 2, H330; Aquatic Acute 1, H400	Potent allergen. MCI seem to be a more potent allergen compared to MI in LLNA. The mixture MCI/MI is an 'extreme sensitiser' Rate of sensitisation = 0.8%	Not registered (ECHA) 81 ppm (0.0081%) = 2 µg/cm ² (SCCS)	Calculated LOAL = 2 µg/cm ²	SCCS/1238/09; Simonsen et al., 2013
METHYL- ISOTHIA- ZOLINONE (MI) (2682-20-4)	Finger paint	<u>Harmonised:</u> None <u>Notified:</u> Acute Tox. 3, H301; Acute Tox. 3, H311; Skin Corr. 1B, H314; Skin Sens. 1, H317; Eye Dam. 1, H318; STOT SE 3, H335; Aquatic Acute 1, H400	'Strong sensitiser' Increasing occurrence of contact allergy Rate of sensitisation = 0.8%	Not registered (ECHA) 0.8% = 200 µg/cm ² (SCCS, 2013) 0.4% (SCCS, 2015)	<u>Induction:</u> Threshold value: 15 ppm is considered to be safe for the consumer from the view of induction of contact allergy for rinse-off products. No safe concentration for leave-on products (SCCS). Induction at 20 -25 µg/cm ² . AEL = 15 µg/cm ² . Calculated LOAL = 0.4 x 250 = 100 µg/cm ² . <u>Elicitation:</u> No safe concentration for leave-on products. No data for rinse-off products (SCCS).	SCCS/1238/09; SCCS/1521/13; SCCS/1557/15; Simonsen et al., 2013

INCI name Preservatives	Identified in	Classification (ECHA C&L)	Allergy potential (according to SCCS, if not otherwise stated)	LLNA EC ₃ - value (ECHA RSD or RIVM)	Level of induction/elicitation	Reference
BENZISOTHIA- ZOLINONE (2634-33-5)	Finger paint	<u>Harmonised:</u> Acute Tox. 4, H302; Skin Irrit. 2, H315; Skin Sens. 1, H317; Eye Dam. 1, H318; Aquatic Acute, H400	'Moderate sensitiser'	Not registered (ECHA) 10.4% (RIVM, SCCS) 2.3% (SCCS)	<u>Induction:</u> Calculated acceptable concentration in suntan lotion is 0.0075%. AEL: An estimate of the NOEL value is listed by SCCS (2004), as "in the region of 500 ppm". Calculated LOAL = 2.3 x 250 = 575 µg/cm ² <u>Elicitation:</u> Sensitising at 20 ppm in gloves (SCCS, 2012).	SCCNFP/0811/04; SCCS/1482/12; Novick et al., 2013
IODOPROPYNYL BUTYL- CARBAMATE (55406-53-6)	Face paint and make-up (lit.)	<u>Harmonised:</u> Acute Tox. 4, H302; Skin Sens. 1, H317; Eye Dam. 1, H318; Acute Tox. 3, H331; STOT RE 1, H372; Aquatic Acute 1, H400; Aquatic Chronic 1, H410	<i>No information</i>	No data Not registered (ECHA)	<u>Induction:</u> <i>No data</i> <u>Elicitation:</u> <i>No data</i>	SCCNFP/0826/04

TABLE 23

THE IDENTIFIED POTENTIALLY ALLERGENIC PRESERVATIVES IN COSMETICS AND CHEMICAL TOYS.

* = THE SUBSTANCES ARE RESTRICTED IN COSMETICS (ARE NOT ALLOWED AS A PRESERVATIVE), BUT ARE ALLOWED TO BE USED IN CHEMICAL TOYS.

RATE OF SENSITISATION = NUMBER OF POSITIVE REACTIONS PER NUMBER OF TESTED PERSONS (IN PERCENT). AEL = ACCEPTABLE EXPOSURE LEVEL. NO DATA (ECHA RSD) = NO DATA CONCERNING LLNA EC₃ VALUES IN THE DATABASE OF REGISTERED SUBSTANCES EXISTS. NOT REGISTERED = THE SUBSTANCES ARE NOT REGISTERED AND CANNOT BE FOUND IN THE DATABASE OF REGISTERED SUBSTANCES (ECHA).

INCI name Fragrances	Identified in	Classification (ECHA C&L)	Allergy potential (according to SCCS, if not otherwise stated)	LLNA EC ₃ -value (ECHA RSD or RIVM)	Level of induction/elicitation	Reference
Benzyl alcohol (100-51-6)	Suntan lotion (1)	Harmonised: Acute Tox. 4, H302; Acute Tox. 4, H332	Established contact allergen in humans. Listed as “+” in SCCS opinion, i.e. up to 10 positive test reactions reported.	> 50% (RIVM; SCCS) No data in ECHA RSD (sensitising)	Induction: <i>No data</i> Elicitation: <i>No data</i> SCCS concludes that in the absence of adequate substance specific data, it is possible to use a general threshold of 0.8 µg/cm ² (based on a concentration of 100 ppm).	SCCS/1459/11
Citral (5392-40-5)	Suntan lotion (1)	Harmonised: Skin Irrit. 2, H315; Skin Sens. 1, H317	Established contact allergen in humans. Listed as “+++” in SCCS opinion, i.e. 101 – 1000 positive test reactions reported. Rate of sensitisation = 2.4%	6.3 – 15% (ECHA RSD) 5.6% (RIVM) 1.2% (SCCS) 8.9% (Picotti & Kawabata)	Induction: NOEL for patch test is 1400 µg/cm ² (ECHA RSD) Calculated LOAL = 1.2 x 250 = 300 µg/cm ² . IFRA gives an AEL of 0.05% in deodorants based on induction based experiments. SCCS points out that there is no guarantee for this value being safe for the consumers. Elicitation: <i>No data</i> SCCS concludes that in the absence of adequate substance specific data, it is possible to use a general threshold of 0.8 µg/cm ² (based on a concentration of 100 ppm).	SCCS/1459/11; Simonsen et al., 2013; Picotti & Kawabata, 2008; Lalko & Api, 2008
Citronellol	Suntan lotion (1)	Harmonised:	Established contact	43.5% (ECHA RSD;	Induction:	SCCS/1459/11;

INCI name Fragrances	Identified in	Classification (ECHA C&L)	Allergy potential (according to SCCS, if not otherwise stated)	LLNA EC3-value (ECHA RSD or RIVM)	Level of induction/elicitation	Reference
(106-22-9)		None <u>Notified:</u> Skin Irrit. 2, H315; Skin Sens. 1B, H317 ; Eye Irrit. 2, H319	allergen in humans. Listed as “++” i SCCS opinion, i.e. 11 – 100 positive test reactions reported. Rate of sensitisation = 2.4%	RIVM; SCCS)	<i>No data</i> Calculated LOAL = 43,5 x 250 = 8700 µg/cm². <u>Elicitation:</u> <i>No data</i> SCCS concludes that in the absence of adequate substance specific data, it is possible to use a general threshold of 0.8 µg/cm² (based on a concentration of 100 ppm).	Simonsen et al., 2013
Citronellol (1117-61-9)	Suntan lotion (1)	<u>Harmonised:</u> None <u>Notified:</u> Skin Irrit. 2, H315; Skin Sens. 1, H317		43.5% (RIVM; SCCS) Not registered (ECHA)		SCCS/1459/11; Simonsen et al., 2013
Citronellol (7540-51-4)	Suntan lotion (1)	<u>Harmonised:</u> None <u>Notified:</u> Skin Irrit. 2, H315; Skin Sens. 1, H317		43.5% (RIVM; SCCS) Not registered (ECHA)		SCCS/1459/11; Simonsen et al., 2013

INCI name Fragrances	Identified in	Classification (ECHA C&L)	Allergy potential (according to SCCS, if not otherwise stated)	LLNA EC3-value (ECHA RSD or RIVM)	Level of induction/elicitation	Reference
Coumarin (91-64-5)	Lip balm (1)	<p><u>Harmonised:</u></p> <p>None</p> <p><u>Notified:</u></p> <p>Acute Tox. 4, H302; Skin Sens. 1, H317</p>	<p>Established contact allergen in humans. Listed as “+++” in SCCS opinion, i.e. 101 – 1000 positive test reactions reported.</p> <p>Rate of sensitisation = 2.4%</p>	<p>No data in ECHA RSD (sensitising)</p> <p>Negative (RIVM)</p> <p>> 50% (SCCS)</p>	<p><u>Induction:</u></p> <p>IFRA gives an AEL of 0.13% in deodorants based on induction based experiments. SCCS points out that there is no guarantee for this value being safe for the consumers.</p> <p><u>Elicitation:</u> <i>No data</i></p> <p>SCCS concludes that in the absence of adequate substance specific data, it is possible to use a general threshold of 0.8 µg/cm² (based on a concentration of 100 ppm).</p>	SCCP/0935/05; SCCS/1459/11; Simonsen et al., 2013
Eugenol (97-53-0)	Lip balm (1)	<p><u>Harmonised:</u></p> <p>None</p> <p><u>Notified:</u></p> <p>Skin Sens. 1, H317; Eye Irrit. 2, H319</p>	<p>Established contact allergen in humans. Listed as “+++” in SCCS opinion, i.e. 101 – 1000 positive test reactions reported.</p> <p>Rate of sensitisation = 2.5%</p>	<p>5.4% (ECHA RSD)</p> <p>5.3% (SCCS)</p> <p>10.1% (RIVM)</p>	<p><u>Induction:</u></p> <p>IFRA gives an AEL of 0.2% in deodorants based on induction based experiments. SCCS points out that there is no guarantee for this value being safe for the consumers.</p> <p>Calculated LOAL = 5.3 x 250 = 1325 µg/cm².</p> <p><u>Elicitation:</u></p> <p><i>No data</i></p> <p>SCCS concludes that in the absence of adequate substance specific data, it is possible to use a general threshold of 0.8 µg/cm² (based on a concentration of 100 ppm).</p>	SCCS/1459/11; Simonsen et al., 2013

INCI name Fragrances	Identified in	Classification (ECHA C&L)	Allergy potential (according to SCCS, if not otherwise stated)	LLNA EC ₃ -value (ECHA RSD or RIVM)	Level of induction/elicitation	Reference
Geraniol (106-24-1)	Lip balm (1), suntan lotion (1)	<u>Harmonised:</u> None <u>Notified:</u> Skin Irrit. 2, H315; Skin Sens. 1, H317; Eye Dam. 1, H318	Established contact allergen in humans. Listed as “+++” in SCCS opinion, i.e. 101 – 1000 positive test reactions reported. Rate of sensitisation = 2.5%	11.4% (ECHA RSD) 5.6% (SCCS) 22.4% (RIVM)	<u>Induction:</u> IFRA gives an AEL of 0.4% in deodorants based on induction based experiments. SCCS points out that there is no guarantee for this value being safe for the consumers. Calculated LOAL = 5.6 x 250 = 1400 µg/cm ² . <u>Elicitation:</u> <i>No data.</i> SCCS concludes that in the absence of adequate substance specific data, it is possible to use a general threshold of 0.8 µg/cm ² (based on a concentration of 100 ppm).	SCCS/1459/11; Simonsen et al., 2013
Limonene (138-86-3)	Lip balm (2), suntan lotion (1)	<u>Harmonised:</u> Flam. Liq. 3, H226; Skin Irrit. 2, H315; Skin Sens. 1, H317; Aq. Acute 1, H400; Aq. Chronic 1, H410	Established contact allergen in humans. Listed as “+++” in SCCS opinion, i.e. 101 – 1000 positive test reactions reported.	69% (RIVM) Not registered (ECHA)	<u>Induction:</u> <i>No data</i> <u>Elicitation:</u> <i>No data.</i>	SCCS/1459/11
Limonene (5989-27-5)	Lip balm (2), suntan lotion (1)	<u>Harmonised:</u> Flam. Liq. 3, H226; Skin Irrit. 2, H315; Skin Sens. 1, H317; Aq. Acute 1, H400; Aq. Chronic 1, H410	Established contact allergen in humans. Listed as “+++” in SCCS opinion, i.e. 101 – 1000 positive test reactions reported.	22% (ECHA RSD) < 10% (SCCS) 69% (RIVM)	SCCS concludes that in the absence of adequate substance specific data, it is possible to use a general threshold of 0.8 µg/cm ² (based on a concentration of 100 ppm).	SCCS/1459/11

INCI name Fragrances	Identified in	Classification (ECHA C&L)	Allergy potential (according to SCCS, if not otherwise stated)	LLNA EC ₃ -value (ECHA RSD or RIVM)	Level of induction/elicitation	Reference
Linalool (78-70-6)	Lip balm (1), suntan lotion (1)	<u>Harmonised:</u> None <u>Notified:</u> Skin Irrit. 2, H315; Eye Irrit. 2, H319	Established contact allergen in humans. Listed as “+++” in SCCS opinion, i.e. 101 – 1000 positive test reactions reported.	30 – 55% (ambiguous results) (ECHA RSD) 30% (SCCS) 46.2% (RIVM)	<u>Induction:</u> <i>No data</i> Calculated LOAL = 30 x 250 = 7500 µg/cm ² . <u>Elicitation:</u> <i>No data</i> SCCS concludes that in the absence of adequate substance specific data, it is possible to use a general threshold of 0.8 µg/cm ² (based on a concentration of 100 ppm).	SCCS/1459/11

TABLE 24
THE IDENTIFIED POTENTIALLY ALLERGENIC FRAGRANCES IN COSMETICS AND CHEMICAL TOYS.

AEL = ACCEPTABLE EXPOSURE LEVEL

RATE OF SENSITISATION = NUMBER OF POSITIVE REACTIONS PER NUMBER OF TESTED PERSONS (IN PERCENT)

NO DATA (ECHA RSD) = NO DATA CONCERNING LLNA EC₃-VALUES IN THE DATABASE OF REGISTERED SUBSTANCES EXISTS

NOT REGISTERED = THE SUBSTANCES IS NOT REGISTERED AND CANNOT BE FOUND IN THE DATABASE OF REGISTERED SUBSTANCES (ECHA)

8.2 Assessment of the identified allergy potential of the substances

The overviews presented in Table 22, Table 23 and Table 24 show that data regarding the allergy potential of the substances is limited. The identified data (for LLNA EC₃ values), however, shows that Kathon is the most potent allergen with an allergy potential categorised as an extreme sensitiser. Additionally, MCI, MI and formaldehyde are strong sensitisers, whereas the rest of the substances seems to be moderate sensitisers.

For the two UV filters (octocrylene and drometrizole trisiloxane), which are used in suntan lotion, it is primarily reporting of allergic reactions when using suntan lotions that has resulted in these substances being on the gross list of potentially allergenic substances. No SCCS opinions exist for these substances, but an American article has in 2014 reviewed the available information (in English) on allergic reactions from UV filters including octocrylene and drometrizole trisiloxane. For octocrylene, which was identified in 8 products in the survey of cosmetic products for children, 69 documented cases of contact allergy and 81 documented cases of photo-contact allergy have been reported. For drometrizole trisiloxane, which was identified in 6 products in the survey, the equivalent numbers are: 2 cases of contact allergy and 1 case of photo-contact allergy (Heurung et al., 2014).

For the UV filter benzophenone-3, an SCCS opinion exists which concludes that the UV filter can cause photo-allergic reactions. Heurung et al. (2014) describes that 100 documented cases of contact allergy have been reported for benzophenone-3 and more than 300 cases of photo-contact allergy. This UV filter is also stated to be the most allergenic and photo-allergenic of the UV filter used (Heurung et al. (2014)). Benzophenone-3 was, however, only observed in two products (both were lip glosses) in the survey of the cosmetic products for children. The American review of the allergenic properties of UV filters generally states that the incidence of allergy towards UV filters in individuals where patch testing have been performed is generally low and probably less than 1% (Heurung et al., 2014).

Professor Klaus Ejner Andersen from the Department of Dermatology and Allergy Centre at Odense University Hospital was contacted in order to hear about his experiences with UV filters and allergic reactions. Klaus Ejner Andersen declares that they have observed a few cases of allergic reactions caused by UV filters, but not to such an extent that it can be defined as a problem. Klaus Ejner Andersen informed that they in USA (Heurung et al., 2014) come to the same conclusion for many of the UV filters – cases of allergy have been observed, but not to such an extent that it is regarded as a problem with regard to allergy.

For the preservatives, a few more data on their allergy potential exists. The information originates from the SCCS opinions or studies of allergic reactions in humans (e.g. Simonsen et al. (2013)). In the survey, the isothiazolinones methylchloroisothiazolinone (MCI), methylisothiazolinone (MI), Kathon (MCI and MI) as well as benzisothiazolinone (BIT) are found to be used in finger paints and they are all potent allergens. Kathon (the mixture of MCI and MI) is regarded as an extreme sensitiser.

Formaldehyde is a strong sensitiser. However, it is rarely added intentionally but comes from several preservatives that release formaldehyde (formaldehyde releasers). Four preservatives which release formaldehyde were identified, but there is limited data on the allergy potential for these preservatives. The formaldehyde releasers bronopol and DMDM hydantoin seem to be the preservatives which most often are used in chemical toys, but there is limited data on the allergy potential of these substances. The formaldehyde releasing preservatives work by releasing the strong sensitiser formaldehyde in small amounts.

Many of the 11 identified fragrances are part of Fragrance mix I and II which are used in patch testing when examining for allergic responses towards fragrances. According to Simonsen et al.

(2013), more than 2% of the examined patients are allergic to these fragrances despite the fact that the identified LLNA values do not suggest that the fragrances are that potent sensitisers (moderate). However, the fragrances are all assessed by SCCS to be established contact allergens in humans, even though differences in the number of positive test reactions for the individual substances exist. The main part of the listed fragrances is listed as “+++” in SCCS no. 1459 (2012) which means that 101 – 1000 positive test reactions in humans have been reported (published) for the substance. Benzyl alcohol is listed as only “+” which means that up to 10 positive test reactions in humans have been reported. However, none of the fragrances has a widespread use in neither cosmetics nor toys according to the survey.

8.3 Considerations regarding focus on substances for analysis of selected products

In the second phase of the project chemical analysis of selected toys and cosmetic products for children was to be carried out. Here focus was on the most potent substances, i.e. the identified substances being most sensitising. Based on the above review of the allergy potential of the identified substances, the focus was therefore to be on the following substances as the largest allergic reactions are observed for these according to literature:

- Isothiazolinones – primarily Kathon (MI/MCI), MI and MCI
- Formaldehyde
- Polyaminopropyl biguanide
- A selection of the 26 fragrances subject to declaration

As described, the isothiazolinones are identified in finger paint and were reviewed and analysed in a former survey project from the Danish EPA regarding preservatives in toys (Poulsen & Nielsen, 2014). Moreover, the EU members decided in June 2015 to restrict certain isothiazolinones in toys for children under the age of 3. The restriction will apply to MI (methylisothiazolinone), MCI (methylchlorisothiazolinone), the mixture MI/MCI (kathon) and BIT (benzisothiazolinone). The restriction will take effect during 2017 (EU, 2015a; EU, 2015b). As the Danish EPA does not wish to repeat the former survey project on preservatives in toys and as a restriction has been adopted for these substances, it was decided not to perform chemical analyses of these substances in this project.

Formaldehyde is rarely intentionally added but originates from several preservatives which release formaldehyde (formaldehyde releasers). Four preservatives which release formaldehyde are identified (bronopol (found in soap bubbles, finger paint and modelling clay), imidazolidinyl urea (face paint), DMDM hydantoin (finger paint, soap bubbles, face paint and make-up) and diazolidinyl urea (finger paint)), but the amount of data regarding the allergy potential for these substances is limited. The only information found is that they release small amounts of the strong sensitiser formaldehyde. In the mentioned earlier survey from the Danish EPA regarding preservatives in toys (Poulsen & Nielsen, 2014), products were analysed for free formaldehyde and bronopol. As the Danish EPA does not wish to repeat the former survey project on preservatives in toys and as there is limited information regarding the allergy potential of these formaldehyde releasers, it was decided not to perform chemical analysis of these substances in this project.

Polyaminopropyl biguanide is regarded as a moderate to strong sensitiser (SCCS no. 1535, 2014). In the survey, the preservative was identified to be used in three different face paints (out of 26 different face paints) and was used by a single producer in some modelling clays. The use of the preservative is not particularly widespread (it is restricted today in cosmetic products but is allowed to be used in toys under the classification limit of 1%). A possible more in-depth investigation is complicated by the fact that no easy way to analyse for this substance seems to exist at first glance. SCCS concludes in an opinion of the substance (SCCS no. 1535, 2014) that polyaminopropyl biguanide is not safe for consumers when used in cosmetic products in the former allowed concentration of 0.3%. The substance has not been allowed to be used in cosmetics since January 1

2015 (the date of effect of the Carc. 2 classification) due to a classification as Carc. 2 and because SCCS has concluded that the substance is not safe to use in cosmetics. A new opinion on the substance may be prepared during 2016 which may lead to a permission to use the substance again in cosmetic products. The substance may be used in toys, but only in concentrations below 1% (because of its Carc. 2 classification).

The 11 of the 26 fragrances subject to declaration which were identified in suntan lotions or lip balms are all established contact allergens in humans, and for most of them many examples of allergic reactions in humans have been observed. However, none of the 11 fragrances subject to declaration has a particularly widespread use according to the survey. The 11 fragrances subject to declaration were identified in either 1 or 2 suntan lotions or lip balms out of 30 and 8 products in total respectively. Therefore, the use of the fragrances subject to declaration is not particularly widespread in cosmetic products for children.

Because of the above observations, it was therefore decided not to perform analyses of any of the observed potential allergic substances in neither toys nor cosmetic products for children.

8.3.1 Changed focus on substances for analyses of selected products

Even though the number of cosmetic products containing fragrances subject to declaration was not that high, 15 of the total of 157 products in the survey contained perfume according to the declaration, but no content of the 26 fragrances subject to declaration.

Therefore it was decided that the focus of substances for the chemical analyses should be changed to 'other' potentially allergenic fragrances, i.e. fragrances which SCCS assesses as established contact allergens in humans, but not as a part of the 26 fragrances subject to declaration.

However, the survey has not stated which of the other fragrances that are used, as fragrances other than the fragrances subject to declaration exclusively are to be described with the general term "perfume" on the declaration. The purpose with the analyses of cosmetic products containing 'other' fragrances is therefore to investigate which 'other' fragrances that are used. The first phase in such a task is to examine, partly which 'other' potentially allergenic fragrances that exist and partly whether it is possible to analyse for these 'other' potentially allergenic fragrances. This is described in more details in the succeeding chapter.

9. Screening for analytical methods for "other" fragrances

In co-operation with the Danish EPA, it was decided that focus for the analytical phase of the project was to be on "other" allergenic fragrances as the survey in the project had identified 15 out of the in total 157 identified products where a declared content of perfume was found but no content of the 26 fragrances subject to declaration in amounts subject to declaration. By "other" potentially allergenic fragrances is meant other fragrances than the 26 fragrances subject to declaration in cosmetic and at the same time being assessed as allergenic by SCCS.

Before chemical analyses were made, it was examined:

1. which "other" allergenic fragrances to focus on, and
2. whether analytical methods for these "other" allergenic fragrances already exist.

9.1 'Other' allergenic fragrances

In an opinion on fragrances in cosmetic products (SCCS no. 1459, 2012), SCCS has prepared a list of 82 established contact allergens in humans (Table 13-1 from SCCS no. 1459, 2012). The list of the 82 established contact allergens covers 54 individual chemicals and 28 natural extracts. For all these fragrances, human cases of contact allergy to these substances have been published, and SCCS has therefore assessed these 82 fragrances to be established contact allergens in humans. SCCS states with one to four "+" how many cases of positive test reactions to the substance in humans that are reported. A "+" states up to 10 reported positive test reactions and "++++" states more than 1000 reported positive test reactions. Among these 82 fragrances, the 26 fragrances subject to declaration are also found and they are distributed on 24 individual chemicals and 2 natural extracts.

As fragrances in the form of natural extracts can consist of a large number of different chemicals, it was decided in advance to exclude these substances due to analytical reasons as a quantitative analysis of not pure substances is difficult. Therefore, it was decided that focus was to be on the 54 individual fragrances deducted the 24 fragrances subject to declaration. These in total 30 fragrances (which cover more than in total 42 different CAS numbers because different isomers of the substance occur for several fragrances) are listed in Table 25 below. In the table the information which is available regarding their allergenic properties in SCCS opinion no. 1459 (2012) and via ECHA's database of registered substances (ECHA RSD, 2015) is stated. ECHA's database was used if no specific data is stated in SCCS opinion no. 1459 (2012).

INCI name Fragrances	CAS number	Allergy potential Human evidence according to SCCS	LLNA EC ₃ value (primarily SCCS)	Levels for induction/elicitation
Acetylcedrene	32388-55-9	+	13.9%	<p>Induction: <i>No data</i></p> <p>Calculated LOAL = 13.9 x 250 = 3475 µg/cm².</p> <p>Elicitation: <i>No data</i></p> <p>SCCS concludes that in the absence of adequate substance specific data a general threshold of 0.8 µg/cm² (based on a concentration of 100 ppm) can be used.</p>
Amyl salicylate	2050-08-0	+ (r.t.)	No data (SCCS) Not registered (ECHA)	<p>Induction: <i>No data</i></p> <p>Elicitation: <i>No data</i></p> <p>SCCS: A general threshold of 0.8 µg/cm² (100 ppm) can be used in the absence of adequate substance specific data.</p>
trans-Anethole	4180-23-8	+	No data (SCCS) Sensitising, but no EC ₃ value listed (ECHA RSD)	
Benzaldehyde	100-52-7	+	No data (SCCS) Not sensitising (ECHA RSD)	
Camphor	76-22-2	+ (r.t.)	No data (SCCS) Not sensitising by use of read across (ECHA RSD)	<p>Induction: <i>No data</i></p> <p>Elicitation: <i>No data</i></p> <p>SCCS: A general threshold of 0.8 µg/cm² (100 ppm) can be used in the absence of adequate substance specific data.</p>
Camphor	464-49-3	+ (r.t.)	<i>No data (SCCS)</i> <i>Not registered (ECHA)</i>	

INCI name Fragrances	CAS number	Allergy potential Human evidence according to SCCS	LLNA EC ₃ value (primarily SCCS)	Levels for induction/elicitation
beta-Caryophyllene	87-44-5	non-ox.: + ox.: +	No data (SCCS) Not registered (ECHA)	Induction: No data Elicitation: No data SCCS: A general threshold of 0.8 µg/cm ² (100 ppm) can be used in the absence of adequate substance specific data.
Carvone	99-49-0	+ (r.t.)	No data (SCCS) Not registered (ECHA)	Induction: No data Calculated LOAL = 5.7 x 250 = 1425 µg/cm ² . Elicitation: No data SCCS concludes that in the absence of adequate substance specific data a general threshold of 0.8 µg/cm ² (based on a concentration of 100 ppm) can be used.
Carvone	6485-40-1	+ (r.t.)	5.7%	
Carvone	2244-16-8	+ (r.t.)	No data (SCCS) Not registered (ECHA)	
Rose Ketone-4	23696-85-7	+ (r.t.)	No data (SCCS) Not registered (ECHA)	Induction: No data Elicitation: No data SCCS: A general threshold of 0.8 µg/cm ² (100 ppm) can be used in the absence of adequate substance specific data.
alpha-Damascone (TMCHB)	43052-87-5	++	No data (SCCS) Not registered (ECHA)	Induction: No data Elicitation: No data SCCS: A general threshold of 0.8 µg/cm ² (100 ppm) can be used in the absence of adequate substance specific data.
alpha-Damascone (TMCHB)	23726-94-5	++	No data (SCCS) Not registered (ECHA)	

INCI name Fragrances	CAS number	Allergy potential Human evidence according to SCCS	LLNA EC ₃ value (primarily SCCS)	Levels for induction/elicitation
cis-beta-Damascone	23726-92-3	+	No data (SCCS) Not registered (ECHA)	<p>Induction: <i>No data</i></p> <p>Elicitation: <i>No data</i></p> <p>SCCS: A general threshold of 0.8 µg/cm² (100 ppm) can be used in the absence of adequate substance specific data.</p>
delta-Damascone	57378-68-4	+	No data (SCCS) Not registered (ECHA)	
Dimethylbenzyl carbinyl acetate	151-05-3	+++	No data (SCCS) Not registered (ECHA)	
Hexadecanolactone	109-29-5	+ (r.t.)	No data (SCCS) Not registered (ECHA)	
Hexamethylindanopyran	1222-05-5	++	No data (SCCS) Not sensitising (ECHA RSD)	
Linalyl acetate	115-95-7	non-ox.: + ox.: ++	3.6% (ox.)	<p>Induction:</p> <p><i>No data</i></p> <p>Calculated LOAL = 3.6 x 250 = 900 µg/cm².</p> <p>Elicitation:</p> <p><i>No data</i></p> <p>SCCS concludes that in the absence of adequate substance specific data a general threshold of 0.8 µg/cm² (based on a concentration of 100 ppm) can be used.</p>

INCI name Fragrances	CAS number	Allergy potential Human evidence according to SCCS	LLNA EC ₃ value (primarily SCCS)	Levels for induction/elicitation
Menthol	1490-04-6	++	No data (SCCS) Not sensitising (ECHA RSD)	<p>Induction: <i>No data</i></p> <p>Elicitation: <i>No data</i></p> <p>SCCS: A general threshold of 0.8 µg/cm² (100 ppm) can be used in the absence of adequate substance specific data.</p>
Menthol	89-78-1	++	No data (SCCS) Not sensitising (ECHA RSD)	
Menthol	2216-51-5	++	No data (SCCS) Not sensitising (ECHA RSD)	
6-Methyl coumarin	92-48-8	++	No data (SCCS) Not registered (ECHA)	
Methyl salicylate	119-36-8	+	No data (SCCS) 15% (ECHA RSD)	<p>Induction:</p> <p><i>No data</i></p> <p>Calculated LOAL = 15 x 250 = 3750 µg/cm².</p> <p>Elicitation:</p> <p><i>No data</i></p> <p>SCCS: A general threshold of 0.8 µg/cm² (100 ppm) can be used in the absence of adequate substance specific data.</p>

INCI name Fragrances	CAS number	Allergy potential Human evidence according to SCCS	LLNA EC ₃ value (primarily SCCS)	Levels for induction/elicitation
3-Methyl-5-(2,2,3-trimethyl-3-cyclopentenyl)pent-4-en-2-ol	67801-20-1	++ (r.t.)	No data (SCCS) Not sensitising (ECHA RSD)	Induction: <i>No data</i> Elicitation: <i>No data</i> SCCS: A general threshold of 0.8 µg/cm ² (100 ppm) can be used in the absence of adequate substance specific data.
alpha-Pinene	80-56-8	++	No data (SCCS) 29% via read across from beta-pinene (ECHA RSD)	Induction: <i>No data</i> Calculated LOAL = 29 x 250 = 7250 µg/cm ² . Elicitation: <i>No data</i> SCCS concludes that in the absence of adequate substance specific data a general threshold of 0.8 µg/cm ² (based on a concentration of 100 ppm) can be used.
beta-Pinene	127-91-3	++	No data (SCCS) 29% (ECHA RSD)	
Propylidene phthalide	17369-59-4	+ (r.t.)	No data (SCCS) Not registered (ECHA)	Induction: <i>No data</i> Elicitation: <i>No data</i>
Salicylaldehyde	90-02-8	++	No data (SCCS) Not sensitising (ECHA RSD)	SCCS: A general threshold of 0.8 µg/cm ² (100 ppm) can be used in the absence of adequate substance specific data.

INCI name Fragrances	CAS number	Allergy potential Human evidence according to SCCS	LLNA EC ₃ value (primarily SCCS)	Levels for induction/elicitation
alpha-santalol	115-71-9	++	No data (SCCS) Not registered (ECHA)	Induction: <i>No data</i> Elicitation: <i>No data</i>
beta-santalol	77-42-9	++	No data (SCCS) No data (ECHA RSD)	SCCS: A general threshold of 0.8 µg/cm ² (100 ppm) can be used in the absence of adequate substance specific data.
Sclareol	515-03-7	+	No data (SCCS) Not registered (ECHA)	Induction: <i>No data</i> Elicitation: <i>No data</i> SCCS: A general threshold of 0.8 µg/cm ² (100 ppm) can be used in the absence of adequate substance specific data.
Terpineol (mixture of isomers)	8000-41-7	+	No data (SCCS) Not sensitising (ECHA RSD)	Induction: <i>No data</i> Elicitation: <i>No data</i> SCCS: A general threshold of 0.8 µg/cm ² (100 ppm) can be used in the absence of adequate substance specific data.
alpha-Terpineol	10482-56-1	+	No data (SCCS) Not registered (ECHA)	
alpha-Terpineol	98-55-5	+	No data (SCCS) Not sensitising (ECHA RSD)	

INCI name Fragrances	CAS number	Allergy potential Human evidence according to SCCS	LLNA EC ₃ value (primarily SCCS)	Levels for induction/elicitation
Terpinolene	586-62-9	+	No data (SCCS) 8% (ECHA RSD)	<p>Induction:</p> <p><i>No data</i></p> <p>Calculated LOAL = 8 x 250 = 2000 µg/cm².</p> <p>Elicitation:</p> <p><i>No data</i></p> <p>SCCS concludes that in the absence of adequate substance specific data a general threshold of 0.8 µg/cm² (based on a concentration of 100 ppm) can be used.</p>
Tetramethyl acetyloctahydronaphtalenes	54464-57-2	+	25.1%	<p>Induction:</p> <p><i>No data</i></p> <p>Calculated LOAL = 25.1 x 250 = 6275 µg/cm².</p> <p>Elicitation:</p> <p><i>No data</i></p> <p>SCCS concludes that in the absence of adequate substance specific data a general threshold of 0.8 µg/cm² (based on a concentration of 100 ppm) can be used.</p>
Tetramethyl acetyloctahydronaphtalenes	54464-59-4	+	No data (SCCS) Not registered (ECHA)	<p>Elicitation:</p> <p><i>No data</i></p> <p>SCCS concludes that in the absence of adequate substance specific data a general threshold of 0.8 µg/cm² (based on a concentration of 100 ppm) can be used.</p>
Tetramethyl acetyloctahydronaphtalenes	68155-66-8	+	No data (SCCS) Not registered (ECHA)	
Tetramethyl acetyloctahydronaphtalenes	68155-67-9	+	No data (SCCS) Not registered (ECHA)	

INCI name Fragrances	CAS number	Allergy potential Human evidence according to SCCS	LLNA EC ₃ value (primarily SCCS)	Levels for induction/elicitation
Trimethyl-benzenepropanol	103694-68-4	++	30%	<p><u>Induction:</u></p> <p><i>No data</i></p> <p>Calculated LOAL = 30 x 250 = 7500 µg/cm².</p> <p><u>Elicitation:</u></p> <p><i>No data</i></p> <p>SCCS concludes that in the absence of adequate substance specific data a general threshold of 0.8 µg/cm² (based on a concentration of 100 ppm) can be used.</p>
Vanillin	121-33-5	++	> 50%	<p><u>Induction:</u></p> <p><i>No data</i></p> <p>Calculated LOAL = > 50 x 250 = > 12.500 µg/cm².</p> <p><u>Elicitation:</u></p> <p><i>No data</i></p> <p>SCCS concludes that in the absence of adequate substance specific data a general threshold of 0.8 µg/cm² (based on a concentration of 100 ppm) can be used.</p>

TABLE 25
SELECTED 'OTHER' ALLERGENIC FRAGRANCES.

THE REFERENCES USED ARE SCCS NO. 1459, 2012 AND ECHA'S DATABASE OF REGISTERED SUBSTANCES (ECHA RSD, 2015).

+ = UP TO 10 POSITIVE TEST REACTIONS REPORTED FOR THE SUBSTANCE. ++ = 11-100, +++ = 101 – 1000, AND ++++ = OVER 1000 POSITIVE TEST REACTIONS REPORTED FOR THE SUBSTANCE.

R.T = RARELY TESTED

NON-OX. = NON-OXIDISED

OX. = OXIDISED

9.1.1 Assessment of the "other" fragrances

SCCS has assessed all these "other" fragrances (Table 25) to be established contact allergens in humans as human cases of contact allergy towards these substances are reported for all these fragrances. Generally, there is few data of experiments on animals for the substances (LLNA EC₃ values) and generally, there is no information on levels for neither induction nor elicitation. As described earlier, the available LLNA EC₃ can be regarded as a LOAEL value for induction (ECHA, 2012). Therefore, a LOAEL value for induction has been calculated in those cases where an EC₃ value exists. Furthermore, SCCS concludes in opinion no. 1459 (2012) that in the absence of substance specific data, a general threshold value for elicitation of 0.8 µg/cm² (based on a concentration of 100 ppm) can be used. I.e. SCCS assesses that at a threshold value of 100 ppm, persons who have already developed allergy towards the fragrance will not develop an allergic reaction. However, SCCS stresses that if specific data for the individual substances is available and indicates that the threshold value is lower, this lower value has to be used (SCCS no. 1459, 2012).

9.2 Screening for analytical methods for these 'other' fragrances

For the 30 "other" allergenic fragrances (in total 42 different CAS numbers), a screening for possible analytical methods was made as no standard analytical methods for these "other" fragrances exist. The screening was made through an internet search and the following is described for each individual substance (CAS number):

- Synonyms
- Chemical structure of the substance
- Molecular weight/molecular formula
- Analytical methods
- Matrix
- Availability of reference substance as well as a possible price of the reference substance

This data is reported in Appendix 4 "Screening for analytical methods for 'other' fragrances" for the individual substances (CAS numbers). It has not been possible to find analytical methods for all substances and it has especially been difficult to find methods for different relevant matrices for this project, such as cosmetics or slime/modelling clay. Furthermore, several of the substances are not immediately available as a reference substance which means that an analysis cannot be made (a final identification of the substance cannot be made).

Based on the identified information, an assessment was subsequently made to determine which analytical methods that can be used to make a quantitative analysis of the individual "other" fragrances.

9.2.1 Description and assessment of analytical methods for "other" fragrances

In general, when searching for analytical methods, not many methods for analysis of the substances are identified. Several articles on analysis of the raw materials exist, i.e. the essential oils, while only a few articles are identified where the cosmetic products have been the examined products (the matrix). No other matrices which are relevant for this project have been identified.

The "common denominator" for the identified analytical methods is that they are typically based on the GC-MS technique. This analytical technique is mentioned for all the "other" fragrances for which an analytical method has been identified in the literature. Headspace SPME GC-MS is also mentioned as an applicable analytical technique for some of the fragrances. This analytical method combines a solid phase extraction with GC-MS. The extraction takes place in the following way: a fibre coated with for instance PDMS (the same type of coating like in general GC columns) collects substances in an aqueous solution or in the gas phase over a product after which the collected substances are desorbed thermally in the GC injector. It may be very sensitive to specific substances with a specific SPME fibre and has a different sensitivity to different groups of substances for the same fibre.

Many of the fragrances seem to have several CAS numbers but the search shows that usually it is different CAS numbers for different stereoisomers. Within a short period, it is not realistic to develop an analytical method which can separate these isomers, as different isomers of the same substance have the same molecular weight and thus they will coelute in the chromatogram, having identical retention time, when using usual GC-MS equipment (with non chiral⁵ column). The search on these 30 “other” substances shows that the molecular weights of the substances (see Table 26) vary between 106 g/mole as the lowest (benzaldehyde) and 308 g/mole as the highest molecular weight (sclareol). This means that both lightly volatile and more heavily volatile fragrances must be included in the same analytical method. However, the advantage of this uneven distribution of the molecular weight of the “other” fragrances is that they can be distinguished from each other as the tops will be separated in a chromatogram (different retention times). However, several of the fragrances (which are not stereoisomers of each other) lie relatively close to each other in molecular weight which will complicate an identification of the individual fragrances. Furthermore, the 26 fragrances subject to declaration are also in this mass area and it is possible that other organic substances will be found in the same area of the chromatograms and coelute with fragrances, having similar retention times. This will normally mean that the mass spectra of the overlapping tops do not correspond to the reference substances.

The literature search shows that it is probably possible to establish a method which can separate most of the possible fragrances, provided that the reference substances can be procured and that they are substances with different molecular weight (so they can be separated in a chromatogram with higher certainty). For most of the fragrances, the reference substances can be provided (see Table 26) but these vary a lot in price.

In general, the following challenges/”problems” are found in connection with chemical analysis of these ”other” fragrances:

- Generally, many different isomers are found for the individual fragrances which complicate the identification of the fragrances at isomer level (e.g. menthol has 46 different isomers).
- Not all fragrances have easily accessible reference substances. That reason alone makes an identification and a quantification difficult/impossible.
- Other conditions might complicate identification, such as interference and overlapping tops in the chromatograms of similar substances or for substances with the same molecular weight, which also makes an identification and quantification difficult. The mass spectra for this type of substances (terpenoids) are relatively identical and cannot be used as a reliable identification, but with access to a reference substance, the possibility of identification will be increased as the retention time also is an identification parameter. For instance, the spectra of menthol and citronellol (one of the fragrances subject to declaration) are almost identical but the tops come approx. 0.8 minutes from each other so the two substances can be separated.
- The few analytical methods which are identified in the literature most often describe only matrices as cosmetic products, i.e. typically “fatty substance” but in this project, more different types of matrices are included (textile from teddy bears, rubber, plastic from dolls etc.).

The reference ”Determination of Safrole and 6-methyl Coumarin in Cosmetics Using GC and GC-MS” (Xing et al., 1992) describes extraction of cosmetic products with methanol. This method is assessed to be realistic as it will be possible to determine a realistic recovery rate. Methanol will hardly dissolve all fatty substances in the matrices and therefore it will hardly create technical challenges for the equipment.

Alternatively, the common analytical method for the 26 fragrances subject to declaration could be used (which for instance Eurofins uses), i.e. a method with extraction in MTBE from an aqueous suspension followed by GC-MS.

⁵ Column that do not distinguish between stereoisomers.

The vast majority of the identified analytical methods is based on the GC-MS technique. It is assessed that it will be possible to develop a GC-MS method for analysis of most of the substances. However, it will be necessary, as stated in the article "Solid-phase microextraction gas chromatography-mass spectrometry determination of fragrance allergens in baby bathwater" (Lamas et al., 2009), to use an extra long column (50 m DB Wax column) for the GC-MS equipment to ensure that the individual fragrances, which are close to each other in molecular weight in the chromatograms, are separated.

Furthermore, it will be possible – instead of quantifying substances – to perform a screening in the form of a qualitative analysis with SPME Headspace GC-MS. This method has the advantage that various softeners and other non volatile substances, which may contaminate the system, are not extracted so only the substances which, just like perfume, are in the air above the sample are examined. In this way, the substances that evaporate from the products are identified. The samples are typically heated up to force evaporation. However, with SPME Headspace GC-MS it will be extremely difficult to quantify and assure a realistic recovery rate for several of the requested matrices (cosmetic products). With this method, a qualitative screening can show whether there is any reason for a quantitative analysis.

Based on the above conditions, it was decided that the best procedure would be to make a qualitative screening by means of SPME Headspace GC-MS. A qualitative screening via headspace has also the advantage that it is a far cheaper analytical method compared to making a quantitative analysis of more fragrances where initially it would be necessary to make a validation of the analytical methods (i.e. establishment of recovery rates, detection threshold and uncertainties) to be able to make a quantitative determination of the fragrances. Furthermore, SPME Headspace GC-MS has the advantage that the same sample preparation is used, independently from the different product matrices which again makes the method cheaper. With this qualitative screening method via SPME Headspace GC-MS, it will be possible to carry out a screening for many fragrances in several toy products and cosmetic products for children.

An overall assessment of which of these "other" fragrances it will be possible to make the described qualitative headspace analysis for can be seen in Table 26 below. A few of the "other" fragrances were in advance deselected as it was not possible to provide the substances as reference substances, i.e. a reliable identification would not be possible. These fragrances are marked with a "no" in Table 26 below.

Other fragrances were assessed to be particularly difficult to make a reliable identification of, primarily for the reason that these fragrances are similar to each other with regard to structure which makes identification difficult. The mass spectra for this type of substances (terpenoids) are relatively alike and cannot be used as a reliable identification. These fragrances are marked with a "difficult" in Table 26 below.

It ought to be possible to distinguish the remaining fragrances from each other in a chromatogram with the suggested method (SPME Headspace GC-MS with polar long column and use of DVB/PDMS fibre, which has been found to have the best retrieval for most of the examined fragrances by Lamas et al. (2009)). Therefore, these fragrances were chosen for qualitative screening analysis of selected pieces of toys and cosmetic toys for children. These fragrances are marked with "should be possible" in Table 26 below.

Therefore, it was assessed as possible to make a headspace screening of in total 21 different fragrances (consisting of 29 different CAS numbers).

CAS no.	Name	Molecular weight (g/mole)	Reference substance available	Price for reference substance	Assessment: Is an analysis possible?
32388-55-9	ACETYLCEDRENE	246	No	-	No, because of missing reference substance
2050-08-0	AMYL SALICYLATE	208	No	-	No, because of missing reference substance
4180-23-8	trans-ANETHOLE	148	Sigma-Aldrich	210 DKK	Should be possible
100-52-7	BENZALDEHYDE	106	Sigma-Aldrich	474 DKK	Should be possible
76-22-2	CAMPHOR, DL	152	Sigma-Aldrich	135 DKK	Should be possible
464-49-3	CAMPHOR	152	Sigma-Aldrich	313 DKK	Should be possible
87-44-5	beta-CARYOPHYLLENE (ox.)	204	Sigma-Aldrich, sum of enantiomers	838 DKK	Should be possible
99-49-0	CARVONE	150	Racemic, not at Sigma-Aldrich	?	Should be possible
6485-40-1	CARVONE	150	Sigma-Aldrich	209 DKK	Should be possible
2244-16-8	CARVONE	150	Sigma-Aldrich	155 DKK	Should be possible
23696-85-7	(DAMASCENONE) ROSE KETONE-4	190	Sigma-Aldrich, natural product	626 DKK	Difficult
43052-87-5	alpha-DAMASCONE (TMCHB)	192	Sigma-Aldrich	208 DKK	Difficult
23726-94-5	alpha-DAMASCONE (TMCHB)	192	No, but with another CAS no. as listed above	-	Difficult
23726-92-3	cis-beta-DAMASCONE	192	Sigma-Aldrich	705 DKK	Difficult
57378-68-4	delta-DAMASCONE	192	Sigma-Aldrich	230 DKK	Difficult
151-05-3	DIMETHYLBENZYL CARBINYL ACETATE (DMBCA)	192	Sigma-Aldrich	446 DKK	Should be possible
109-29-5	HEXADECANOLACTONE	254	Sigma-Aldrich	337 DKK	Should be possible
1222-05-5	HEXAMETHYLINDANOPYRAN	258	Sigma-Aldrich	418 DKK	Should be possible
115-95-7	LINALYL ACETATE	196	Sigma-Aldrich	221 DKK	Should be possible

CAS no.	Name	Molecular weight (g/mole)	Reference substance available	Price for reference substance	Assessment: Is an analysis possible?
1490-04-6	MENTHOL	156	Sigma-Aldrich, EP reference	868 DKK	Should be possible. Notice that NIST lists 46 isomers
89-78-1	MENTHOL	156	Sigma-Aldrich (DL product)	221 DKK	Should be possible
2216-51-5	MENTHOL	156	Sigma-Aldrich	533 DKK	Should be possible
92-48-8	6-METHYL COUMARIN	160	Sigma-Aldrich	410 DKK	Should be possible
119-36-8	METHYL SALICYLATE	152	Sigma-Aldrich	216 DKK	Should be possible
67801-20-1	3-METHYL-5-(2,2,3-TRIMETHYL-3-CYCLOPENTENYL)PENT-4-EN-2-OL	208	Sigma-Aldrich	273 DKK	Should be possible
80-56-8	CYCLOPENTENYL)PENT-4-EN-2-OL alpha-PINENE	136	Sigma-Aldrich	1213 DKK	Should be possible
127-91-3	CYCLOPENTENYL)PENT-4-EN-2-OL beta-PINENE	136	SBT (USA)	960 USD	Should be possible
17369-59-4	PROPYLIDENE PHTHALIDE	174	Sigma-Aldrich	266 DKK	Should be possible
90-02-8	SALICYLALDEHYDE	122	Sigma-Aldrich	200 DKK	Should be possible
115-71-9	alpha-SANTALOL	220	? not for this CAS no. at SBT	-	Difficult
77-42-9	beta-SANTALOL	220	SBT (USA)	440 USD	Difficult
515-03-7	SCLAREOL	308	Sigma-Aldrich	337 DKK	Should be possible
8000-41-7	TERPINEOL (mixture of isomers)	154	Sigma-Aldrich, mixture	228 DKK	Should be possible, but notice the isomers
10482-56-1	alpha-TERPINEOL	154	Sigma-Aldrich, Two CAS numbers, but one substance	252 DKK	Should be possible, but notice the isomers

CAS no.	Name	Molecular weight (g/mole)	Reference substance available	Price for reference substance	Assessment: Is an analysis possible?
98-55-5	alpha-TERPINEOL	154	Sigma-Aldrich	252 DKK	Should be possible, but notice the isomers
586-62-9	TERPINOLENE	136	Sigma-Aldrich	418 DKK	Should be possible, but notice the isomers
54464-57-2	TETRAMETHYL ACETYLOCTAHYDRONAPHTHALENES	234	Not pure, only as part of a perfume raw material	48 USD	No
54464-59-4	TETRAMETHYL ACETYLOCTAHYDRONAPHTHALENES	234	Not pure, only as part of a perfume raw material	-	No
68155-66-8	TETRAMETHYL ACETYLOCTAHYDRONAPHTHALENES	234	Not pure, only as part of a perfume raw material	195 USD	No
68155-67-9	TETRAMETHYL ACETYLOCTAHYDRONAPHTHALENES	234	Not pure, only as part of a perfume raw material	195 USD	No
103694-68-4	TRIMETHYL-BENZENEPROPANOL (Majantol)	178	Sigma-Aldrich	238 DKK	Should be possible
121-33-5	VANILLIN	152	Sigma-Aldrich	168 DKK	Should be possible

TABLE 26
OVERVIEW OF THE ASSESSMENT OF THE ANALYTICAL METHODS FOR 'OTHER' POTENTIALLY ALLERGENIC FRAGRANCES.

SHOULD BE POSSIBLE = BASED ON THE AVAILABLE INFORMATION, WE HAVE ASSESSED THAT IT SHOULD BE POSSIBLE TO BE ABLE TO CARRY OUT THE CHEMICAL ANALYSIS. HOWEVER, UNEXPECTED CONDITIONS MAY CAUSE COMPLICATIONS FOR THE ANALYSIS.

DIFFICULT = HERE TOO MANY POSSIBILITIES OF CONFUSIONS EXIST (SUBSTANCES WHERE SPECTRA LOOK ALIKE OR LOOK LIKE OTHER SIMILAR SUBSTANCES), AND THEREBY HAVE CHROMATOGRAMS THAT WILL OVERLAP, WHICH WILL MAKE AN IDENTIFICATION EXTREMELY DIFFICULT.

NO = AN ANALYSIS IS NOT OBVIOUSLY POSSIBLE, AS IT DOES NOT SEEM POSSIBLE TO OBTAIN THE REFERENCE SUBSTANCE.

10. Selection of substances and products for analysis

In co-operation with the Danish EPA, it was decided that focus of the analytical phase in this project was to be on “other” potentially allergenic fragrances, i.e. other fragrances than the 26 fragrances subject to declaration in cosmetic products and which at the same time are assessed to be allergenic by SCCS. The presence of these “other” potentially allergenic fragrances was examined in the 15 (out of 157) investigated cosmetic products where a declared content of perfume was found, but not the 26 fragrances subject to declaration, above the concentration subject to declaration. Furthermore, it was decided that analyses were to be made for the same “other” fragrances in scented toys where the survey showed that fragrances might be used. This is described in details below.

10.1 Selection of substances

The in total 21 different “other” fragrances, which in section 9.2.1 “Description and assessment of analytical methods for “other” fragrances” were assessed possible to make a screening analysis of, are listed in Table 27 below. However, when shopping it turned out that it was not possible to provide all isomers (CAS numbers) as reference substance for some of the fragrances. In total three CAS numbers are listed in Table 26 but not in Table 27 below.

For these 21 substances (26 CAS numbers), it was decided that a qualitative screening by means of SPME Headspace GC-MS was to be carried out, because it, in a search for applicable analytical methods, turned out to be the best possible method for identification of most of the “other” fragrances and at the same time a relatively cheap method which made it possible to analyse for more “other” fragrances in more products within the budget frame.

CAS no.	Name	CAS no.	Name
4180-23-8	trans-ANETHOLE	119-36-8	METHYL SALICYLATE
100-52-7	BENZALDEHYDE	67801-20-1	3-METHYL-5-(2,2,3-TRIMETHYL-3-CYCLOPENTENYL)PENT-4-EN-2-OL
76-22-2 464-49-3	CAMPOR, DL CAMPOR	80-56-8 127-91-3	CYCLOPENTENYL)PENT-4-EN-2-OL (alpha-PINENE) CYCLOPENTENYL)PENT-4-EN-2-OL (beta-PINENE)
87-44-5	beta-CARYOPHYLLENE (ox.)	17369-59-4	PROPYLIDENE PHTHALIDE
6485-40-1 2244-16-8	CARVONE	90-02-8	SALICYLALDEHYDE

CAS no.	Name	CAS no.	Name
151-05-3	DIMETHYLBENZYL CARBINYL ACETATE (DMBCA)	515-03-7	SCLAREOL
109-29-5	HEXADECANOLACTONE	8000-41-7 98-55-5	TERPINEOL (mixture of isomers) alpha-TERPINEOL
1222-05-5	HEXAMETHYLINDANOPYRAN	586-62-9	TERPINOLENE
115-95-7	LINALYL ACETATE	103694-68-4	TRIMETHYLBENZENEPROPANOL (Majantol)
1490-04-6 2216-51-5	MENTHOL	121-33-5	VANILLIN
92-48-8	6-METHYL COUMARIN		

TABLE 27
OVERVIEW OF THE "OTHER" POTENTIALLY ALLERGENIC FRAGRANCES FOR WHICH A SCREENING ANALYSIS WAS CARRIED OUT. THE CAS NUMBERS FOR WHICH REFERENCE SUBSTANCES WERE PURCHASED ARE LISTED.

10.2 Selection of products

In the survey of the cosmetic products for children, in total 15 (out of the 157) investigated cosmetic products were identified where a declared content of perfume was found but none of the 26 fragrances subject to declaration above the concentration subject to declaration. It was decided that these 15 products were to be purchased and analysed for the above selected "other" fragrances. It must be noted that some of the 15 products in fact consisted of several sub-products as for instance a make-up set consisting of eye shadow, lip gloss and blush, each with their own declaration of contents (and with perfume but without any fragrances subject to declaration above the concentration subject to declaration) was counted as three sub-products in the survey.

Furthermore, the survey of toys showed that in general fragrances are avoided (especially the fragrances subject to declaration) but that in some cases fragrances are used in toy products with a bad smell. In other words, it is primarily the more "chemical" products such as modelling clays and slimes which are added fragrances to hide/mask a possible bad chemical odour. Therefore, in co-operation with the Danish EPA it was decided that different modelling clays and slimes also were to be selected for chemical analysis for the selected "other" fragrances.

Finally it was decided that, if available, some ordinary toy products, such as teddy bears, dolls or similar which were purposely added perfume (i.e. sold with a certain odour), were to be purchased and analysed for the selected "other" fragrances too.

10.3 Purchase of products

According to an agreement with the Danish EPA, the following products were to be purchased for analysis of "other" fragrances:

- Cosmetic products with a declared content of perfume but without a declared content of the 26 fragrances subject to declaration (identified via the survey). However, these products might in principle have a content of fragrances subject to declaration below the concentration subject to declaration.
- Modelling clay which smells (of perfume)

- Slime which smells (of perfume)
- Other toy which smells (of perfume)

Before products were purchased an internet search was made. The purpose was to find which kind of “smelling” toys, modelling clay and slime that is available on the Danish market. Based on this survey, the result showed that a few products within the category of other toys which smell or which are sold with odour were identified. These products were prioritised in the analytical phase.

However, on the basis of the descriptions on the internet of modelling clay and slime, it was not possible to see whether these were added fragrances or not. Therefore, an inquiry was sent to the different internet shops to ask whether their modelling clay and slimes smelled “of chemistry” or if perfume was added to the products. Based on the responses and the description of the odour from the internet shops (not all answered), it was decided whether the products were to be purchased or not. Products which according to the internet shops did not smell were not purchased.

In general, toy products were purchased according to the following guidelines:

- Basically, the products must have a scented smell. In the purchase situation, it turned out that it was not easy to identify the smell, as many products were wrapped in cardboard, plastic or other packaging material that it was impossible to smell to the content. Thus, a few products were purchased even if they did not have a scented smell in the purchase situation.
- Products from different producers were purchased. However, not all internet shops state the producers and therefore it has not been possible take this into consideration in all cases.
- Both cheap and expensive products were purchased.
- Products from both the internet and in physical shops were purchased.

For the cosmetic products, products from the survey were as a basis purchased. These cosmetic products with a declared content of perfume, but without a declared content of the 26 fragrances subject to declaration – could theoretically contain fragrances subject to declaration below the concentration subject to declaration. However, it turned out that six of these products from the survey were not longer available on the market when the products were to be purchased approx. 5 months after the survey took place. Therefore, similar cosmetic products identified in physical shops were purchased as supplement and these products had a declared content of perfume too but no declared content of the fragrances subject to declaration. In the survey, 15 products with a declared content of perfume but no declared content of the fragrances subject to declaration were identified, but for the chemical analysis only 13 products were purchased. This is due to the fact that some of the newly purchased products contained several different sub-products (for instance lip gloss, blush and eye shadow in a make-up set) so that the total number of sub-analyses was identical (in total 23 sub-samples).

The following products for analysis of “other” fragrances were purchased:

- 13 cosmetic products for children consisting of in total 23 sub-samples (CP)
- 10 modelling clays (MO)
- 7 slimes (SL)
- 4 other types of toys (OT)

A more detailed description of the different products (sub-samples) is found in Table 28 to Table 31 below. Thus, in total 44 sub-samples from 34 different products were analysed.

For the cosmetic products, analyses of the individual sub-products were made, i.e. when a make-up product contained more different parts (for instance eye shadow, blush and lip gloss), all sub-products were analysed if the declaration of contents was different for these parts. However, no analysis of all the nail polish in one product consisting of several nail polishes was made.

Product no. (sub-sample)	Product type	Price	Purchased at
CP1	Baby oil	33 DKK	Supermarket
CP2	Baby powder	33 DKK	Supermarket
CP3	Suntan lotion	123 DKK	Supermarket
CP4	Suntan lotion	123 DKK	Supermarket
CP5	Hair spray with colour	59 DKK	Hobby shop
CP6	Hair spray with glitter	59 DKK	Hobby shop
CP7.1*	Blush	80 DKK for the whole set	Toy shop
CP7.2*	Eye shadow		
CP7.3*	Glitter lip gloss		
CP7.4*	Lipstick		
CP8	Lip gloss	15DKK	Clothes shop
CP9.1*	Lip gloss	300 DKK for the whole set	Toy shop
CP9.2*	Nail polish		
CP9.3*	Blush		
CP9.4*	Eye shadow		
CP9.5*	Glitter gel		
CP10.1*	Lip gloss	495 DKK for the whole set	Toy shop
CP10.2*	Lip gloss		
CP10.3*	Lip gloss		
CP10.4*	Lipstick		
CP11	Lotion	38 DKK	Supermarket
CP12	Towelettes	14 DKK	Supermarket
CP13*	Nail polish (set with three pcs.)	70 DKK	Toy shop

TABLE 28
COSMETIC PRODUCTS WHICH WERE ANALYSED FOR "OTHER" FRAGRANCES. COSMETIC PRODUCTS WHICH ALSO ARE TOYS ARE MARKED WITH A *

The purchased modelling clays were most often sets consisting of 3 to 12 different colours. Only one random colour was analysed as it was assumed that the same fragrances would be added to the different colours of modelling clays, if perfume was added.

It must be noted that extra modelling clay was purchased (an extra product) as it was difficult to assess whether they smelled before the package was opened. Therefore, before the chemical

analysis, it was decided to leave one modelling clay product out as this product did not have a smell of perfume (MO6).

Product no. (sub-sample)	Product type	Price	Purchased at
MO1	Modelling clay (set of 4 colours)	60 DKK	Internet shop
MO2	Modelling clay (set of 3 small rolls)	20 DKK	Supermarket
MO3	Modelling clay (set of 12 tubs)	150 DKK	Toy shop
MO4	Soft modelling clay (set of 6 tubs)	50 DKK	Bookshop
MO5	Modelling clay (set of 6 tubs)	20 DKK	Cheap shop
MO7	Modelling clay	16 DKK	Cheap shop
MO8	Soft modelling clay (set of 5 tubs)	69 DKK	Bookshop
MO9	Formable sand	129 DKK	Hobby shop
MO10	Soft modelling clay	30 DKK	Bookshop
MO11	Modelling clay	20 DKK	Toy shop

TABLE 29
MODELLING CLAYS WHICH WERE ANALYSED FOR "OTHER" FRAGRANCES

The purchased slime consisted of both tubs exclusively with slime as well as different toys where slime was included. In all cases, it was only the actual slime which was analysed.

Product no. (sub-sample)	Product type	Price	Purchased at
SL1	Snot sucker monster with slime	38 DKK	Supermarket
SL2	Slime powder which transforms bath water into slime	48 DKK	Supermarket
SL3	Toy figure which shoots with slime	100 DKK	Toy shop
SL4	Slime in tub	15 DKK	Toy shop
SL5	Slime with a figure inside	22 DKK	Internet shop
SL6	Skeleton head with slime	40 DKK	Toy shop
SL7	Slime in tub	10 DKK	Toy shop

TABLE 30
SLIMES WHICH WERE ANALYSED FOR "OTHER" FRAGRANCES

For the group of other toys, the part of the toy which scented most was analysed.

Product no. (sub-sample)	Product type	Price	Purchased at
OT1	Doll with an odour of vanilla	390 DKK	Internet shop
OT2	Rubber bands with an odour of vanilla (rubber bands which are "crocheted" together to e.g. a bracelet)	15 DKK	Internet shop
OT3	Rubber bands with an odour (rubber bands which are "crocheted" together to e.g. a bracelet)	15 DKK	Internet shop
OT4	Teddy bear (soft toy) with candy floss odour	250 DKK	Toy shop

TABLE 31
OTHER TOYS WHICH WERE ANALYSED FOR "OTHER" FRAGRANCES

11. Analytical method and results

In this section, the analytical method used for determination of the presence of the “other” fragrances and the results of the analyses are described.

11.1 Analytical method

A qualitative screening method is used on the basis of the SPME Headspace GC-MS technique inspired by the article “Solid-phase microextraction gas chromatography-mass spectrometry determination of fragrance allergens in baby bathwater” (Lamas et al., 2009) where an extra long column (50 m DB Wax column) is used for the GC-MS equipment to be sure of being able to separate the individual fragrances which is close to each other in molecular weight in the chromatograms. In the article, several different SPME fibres are examined and the conclusion was that a DVB/PDMS fibre was the one on which most of the examined substances could be concentrated.

The method has the advantage that various plasticisers and other non-volatile substances which can contaminate the system are not extracted so the only focus will be on the substances which, just like perfume, are in the air above the sample. Therefore, it is the substances evaporating from the products that are identified. Typically, the samples are heated up to force evaporation. With SPME Headspace GC-MS it is difficult to quantify and assure a realistic recovery rate in several of the wanted matrices (cosmetic products, modelling clay, toys) but a qualitative screening by use of this method can show the presence of substances.

The extraction is performed in the following way: a fibre which is coated with for instance PDMS (same type of coating as in general GC columns) collects substances in an aqueous solution or in the gas phase above a product after which the collected substances are desorbed thermally in the GC injector. It can be very sensitive to specific substances with a specific SPME fibre and will have different sensitivity to different groups of substances for the same fibre.

Apparently, many of the fragrances have several CAS numbers but most often it is a question of different CAS numbers for different stereoisomers. These isomers cannot be separated in an uncomplicated way as different stereoisomers of the same substance have the same molecular weight and thus they will coelute in a chromatogram, having identical retention time on usual GC-MS equipment (with non-chiral column).

As described in section 10.1 “Selection of substances”, 26 reference substances are purchased for the 29 different CAS numbers which are identified in Table 26 as possible to analyse. The 26 reference substances (and 29 different CAS numbers) cover in total 21 different fragrances. The three reference substances which are not purchased are thus other CAS numbers for the same substance (possibly an isomer). In addition to this, three reference mixtures with the 26 fragrances subject to declaration (Restek no. 33105) were purchased so that possible coincidences with the selected “other” fragrances could be determined.

11.1.1 Facts regarding the analytical method

Facts regarding the analytical method are as follows:

- SPME fibre DVB/PDMS (divinylbenzene/polydimethylsiloxane): 65 µm, 57293-U, Supelco, is used.
- Column: Zebron ZB.VAX 60 m x 0.25 mm x 0.25 µm.
- The samples are weighed in 10 ml headspace test tubes. Typical sample size 0.5 g. Only for the dolls with a very light material like fibre filling, there was only room for 40 mg or 170 mg for plush. Regarding the dolls, the filling material, different long plush, body and clothes were analysed separately as all parts had a scented smell.
- The fibre is pre-conditioned at 250 °C for 1 hour.
- The samples are heated to 60 °C for 20 minutes.
- Headspace-extraction: 20 minutes at 60 °C (sample).
- Fibre desorption at 220 °C in GC injector.
- Fibre conditioning at 250 °C for 2 minutes.

GC/MS conditions:

- Injector temperature 220 °C
- Flow: 1 ml/min.
- Injection: splitless mode 2 min. and then 50 ml/min.
- Temperature ion source and transfer line: 150 °C
- Oven: 45 °C, hold 2 min., with 15 °C/min. up to 230 °C, hold 16 min.
- MS scan: 39 – 450 m/z from 2 min till end.

The purchased references were dissolved individually in MTBE (50 mg to 5 ml). 10 µl of a solution was transferred to headspace test tubes and treated as samples so that the retention time of each individual substance and mass spectrum could be determined. Hereby, it was confirmed that the same substance with different CAS numbers had the same retention time and the same spectrum.

It turned out that hexadecanol acton, hexamethylindanopyran, 6-methyl coumarin, propylidene phthalide and vanillin had comparatively low sensitivity but could be seen.

Sclareol (CAS 515-03-7) could not be detected, neither at direct injection in the injector. This indicates that the substance probably breaks down and therefore it could not be detected contrary to expectations. At the same time, it is the fragrance with the highest molecular weight which may also be of importance.

Equally, 7 out of the 26 substances subject to declaration could not be collected on the chosen fibre. Thus, these substances: benzyl benzoate, benzyl cinnamate, benzyl salicylate, isoeugenol, cinnamyl alcohol, farnesol and hydroxyisohexyl 3-cyclohexene carboxaldehyde (lyral) cannot be detected or interfered in the analysis. Amyl cinnamal, hexyl cinnamal and butylphenyl methylpropional (lilial) are very weak but can be detected by use of another fibre (DVB, Carboxen. PDMS).

As an extra control, selected samples were analysed by use of another fibre (DVB, Carboxen. PDMS). This fibre turned out to have a larger sensitivity for vanillin and a number of other substances. The results stated below are thus the total results of the analyses executed by use of the two different fibres (for some of the samples).

11.2 Analytical results

The analytical results for which "other" fragrances, fragrances subject to declaration as well as other substances which are identified as evaporating from the analysed products are stated in Table 32 to Table 35 below. For other substances which were identified, a classification (harmonised or notified) from ECHA's C&L database of notified substances is stated. A possible harmonised classification is stated by a "*". The classification is exclusively stated regarding allergy. It has to be

noted that all these other interesting substances have solely been identified through the available NIST library. For these substances, no verification has thus been made, i.e. corresponding test of a reference substances to confirm the identity of these substances via retention time.

There are in total four tables with analytical results – two tables for the cosmetic products (CP), one table for modelling clay (MC) and one total table for slime (SL) and other toys (OT).

The used analytical method gives qualitative results, i.e. it is only stated whether the substances are proved to be evaporating from the product or not. However, it is marked with one, two or three “x” as qualitative specification of the concentration in headspace. How this corresponds to the amount in the product is unknown as it depends on many factors, including the affinity of the SPME fibre to the substance, the vapour pressure of the substance and the solubility of the substance in the product. However, it must be assumed that a large evaporation (i.e. three “x”) relates to a high concentration in the product. Still, the analytical method cannot indicate how high the concentration in the product is. On the other hand, a low evaporation (i.e. one “x”) does not mean that there is a low concentration of the substance in the product as we do not know anything about the degree of evaporation from the matrix.

From the 20 “other” fragrances, terpineol/alfa-terpineol, vanillin, benzaldehyde and camphor are found. Benzaldehyde and camphor coelute in the chromatogram and can thus interfere if they both are in the product – which, however, is not seen in the examined samples.

From the substances subject to declaration, alpha-isomethyl ionone, benzylalcohol, limonen, linalool, geraniol, citronellol, coumarin, hexyl cinnamal and butylphenyl methylpropional (lilial) are detected. As the method is not quantitative it cannot be determined whether the concentration in the product is so high that it has to be declared according to the regulation on cosmetic products.

The results of the “other” allergenic fragrances and the fragrances subject to declaration as well as other identified fragrances or allergenic substances are gathered in a summary table (Table 36).

Besides the fragrances, the largest tops and a few others are identified by means of their mass spectra and the NIST library. There are thus observed e.g. toluene and styrene in some samples, various preservatives (such as phenoxyethanol) and various antioxidants (such as BHT) as well as substances which may be added due to the odour. Heliotropine and ethyl vanillin have a smell similar to vanillin and are also observed in samples where a content of vanillin is found.

In the samples MO1 and MO9, a mineral oil fraction which covers the retention times 8 to 14 minutes was detected and therefore, it can hide potential fragrances.

Substances identified		Relevant classification (allergy)	CP1	CP2	CP3	CP4	CP5	CP6	CP7.1	CP7.2	CP7.3	CP7.4	CP8
Name of substance	CAS no.												
'Other' fragrances													
Terpineol (mix.)	8000-41-7		XX										
alpha-Terpineol	98-55-5		XX										
Vanillin	121-33-5												X
Fragrances subject to declaration													
Benzyl alcohol	100-51-6		X	X									
Alpha-isomethyl ionone	127-51-5			weak									
Limonene	5989-27-5						X	X					
Linalool	78-70-6						X	XX					
Other potentially allergenic substances													
Heliotropine (smell of vanilla)	120-57-0	Skin Sens. 1B (848). 'Likely contact allergen' according to SCCS.		X									
Ethylvanilin (smell of vanilla)	121-32-4	No relevant, but 'likely contact allergen' according to SCCS											X

TABLE 32
RESULTS OF THE ANALYSIS FOR COSMETIC PRODUCTS CP1 TO CP8.

Substances identified		Relevant classification (allergy)	CP	CP	CP	CP	CP	CP	CP	CP	CP	CP	CP	CP
Name of substance	CAS no.		9.1	9.2	9.3	9.4	9.5	10.1	10.2	10.3	10.4	11	12	13
'Other' fragrances														
Terpineol (mix.)	8000-41-7												XX	
Vanillin	121-33-5							X		X				
Benzaldehyde	100-52-7		X				X			X	X			
(+/-) Camphor	76-22-2								X	X	X			
Fragrances subject to declaration														
Alpha-isomethyl ionone	127-51-5				X	X							X	
Limonene	5989-27-5			X					X	X	X		XXX	XX
Linalool	78-70-6												XXX	
Geraniol	106-24-1												X	
Other potentially allergenic substances														
Heliotropine (smell of vanilla)	120-57-0	Skin Sens. 1B (848). 'Likely contact allergen' acc. to SCCS			X	X							X	X
Ethylvanillin (smell of vanilla)	121-32-4	No relevant, but' likely contact allergen' according to SCCS			X	X								

TABLE 33
RESULTS OF THE ANALYSIS FOR COSMETIC PRODUCTS CP₉ TIL CP₁₃

Substances identified		Relevant classification (allergy)	MO1	MO2	MO3	MO4	MO5	MO7	MO8	MO9	MO10	MO11
Name of substance	CAS no.											
'Other' fragrances												
Terpineol (mix.)	8000-41-7					X						
alpha-Terpineol	98-55-5										X	
Vanillin	121-33-5											X
Benzaldehyde	100-52-7			X	XX		X					X
Fragrances subject to declaration												
Benzyl alcohol	100-51-6										X	X
Limonene	5989-27-5										X	
Linalool	78-70-6					XXX					XX	
Geraniol	106-24-1					X					X	
Citronellol	106-22-9										X	
Other potentially allergenic substances												
Heliotropine (smell of vanilla)	120-57-0	Skin Sens. 1B (848). 'Likely contact allergen' according to SCCS.		X								
Pentanal	110-62-3	Skin Sens. 1 (755)		X								

Substances identified		Relevant classification (allergy)	MO1	MO2	MO3	MO4	MO5	MO7	MO8	MO9	MO10	MO11
Name of substance	CAS no.											
Octanal	124-13-0	Skin Sens. 1 (70)		x								
Chloroxylenol	88-04-0	Skin Sens. 1*				xx					xx	
2-pentylfuran	3777-69-3	Skin Sens. 1 (1)					x					x

TABLE 34

RESULT OF THE ANALYSIS OF MODELLING CLAYS MO1 TO MO11. PLEASE NOTICE THAT MO6 WAS NOT ANALYSED, AS THE PRODUCT DID NOT HAVE A SMELL OF PERFUME

* INDICATES THAT THE SUBSTANCE HAS A HARMONISED CLASSIFICATION

THE NUMBER IN BRACKETS INDICATES THE NUMBER OF NOTIFIED CLASSIFICATIONS WITH THE LISTED CLASSIFICATION.

Substances identified		Relevant classification (allergy)	SL1	SL2	SL3	SL4	SL5	SL6	SL7	OT1	OT2	OT3	OT4 ³
Name of substance	CAS no.												
'Other' fragrances													
alpha-Terpineol	98-55-5						x						
Vanillin	121-33-5									weak ¹	weak ¹		
Benzaldehyde	100-52-7											x	
Fragrances subject to declaration													
Benzyl alcohol	100-51-6						x						
Limonene	5989-27-5										x	xx	
Linalool	78-70-6			xx			x				x	x	
Coumarin	91-64-5			xx									
Hexylcinnamal	101-86-0			xxx									
Butylphenyl methylpropional (lilial)	80-54-6										x		
Other potentially allergenic substances													
Heliotropine (smell of vanilla)	120-57-0	Skin Sens. 1B (848). 'Likely contact allergen' according to SCCS.								x ²	x ²		

Substances identified		Relevant classification (allergy)	SL1	SL2	SL3	SL4	SL5	SL6	SL7	OT1	OT2	OT3	OT4 ³
Name of substance	CAS no.												
Ethylvanillin (smell of vanilla)	121-32-4	<i>No relevant, but 'likely contact allergen' according to SCCS</i>		x						x ²			
Raspberry ketone methyl ether (smell of raspberry)	104-20-1	<i>No relevant</i>											x
Butylated hydroxytoluen	128-37-0	Skin Sens. 1 (37)									x	xx	x

TABLE 35

RESULT OF THE ANALYSIS FOR SLIME (SL₁ TO SL₇) AND OTHER TOYS (OT₁ TO OT₄)

* INDICATES THAT THE SUBSTANCE HAS A HARMONISED CLASSIFICATION.

THE NUMBER IN BRACKETS INDICATES THE NUMBER OF NOTIFIED CLASSIFICATIONS WITH THE LISTED CLASSIFICATION.

1. VANILLIN WAS WEAKLY IDENTIFIED, BUT ONLY WITH ANOTHER FIBRE (DVB/CARB). IN AL₁ VANILLIN WAS DETECTED IN BOTH CAP AND BODY.

2. THE SUBSTANCE WAS WEAKLY IDENTIFIED, BUT ONLY WITH ANOTHER FIBRE (DVB/CARB). IN OT₁ THE SUBSTANCE WAS DETECTED IN THE CAP.

3. THE SUBSTANCE RASPBERRY KETONE METHYL ETHER (CAS 104-20-1) WAS IDENTIFIED FROM OT₄ (SMELL OF RASPBERRY), BUT THE SUBSTANCE HAS NO RELEVANT CLASSIFICATION CONCERNING ALLERGY.

Substances identified		Relevant classification (allergy)	Identified for the following products				
Name of substance	CAS no.		Cosmetic products	Modelling clay	Slime	Other toys	In total
'Other' allergenic fragrances							
Terpineol (mix.)	8000-41-7	Established contact allergen in humans according to SCCS	CP1, CP12	MO4			3
alpha-Terpineol	98-55-5		CP1	MO10	SL5		3
Vanillin	121-33-5		CP8, CP10.1, CP10.3	MO11		OT1, OT2	6
Benzaldehyde	100-52-7		CP9.1, CP9.5 CP10.3, CP10.4	MO2, MO3, MO5, MO11		OT3	9
(+/-) Camphor	76-22-2		CP10.2, CP10.3, CP10.4				3
Fragrances subject to declaration¹							
Alpha-isomethyl ionone	127-51-5	Established contact allergen in humans according to SCCS	CP2, CP9.3, CP9.4, CP12				4
Benzyl alcohol	100-51-6		CP1, CP2	MO10, MO11	SL5		5
Limonene	5989-27-5		CP5, CP6, CP9.2, CP10.2, CP10.3, CP10.4, CP12, CP13	MO10		OT2, OT3	11
Linalool	78-70-6		CP5, CP6, CP12	MO4, MO10	SL2, SL5	OT2, OT3	9
Coumarin	91-64-5				SL2		1

Substances identified		Relevant classification (allergy)	Identified for the following products				
Name of substance	CAS no.		Cosmetic products	Modelling clay	Slime	Other toys	In total
Geraniol	106-24-1	Established contact allergen in humans according to SCCS	CP12	MO4, MO10			3
Citronellol	106-22-9			MO10			1
Hexylcinnamal	101-86-0				SL2		1
Butylphenyl methylpropional (lilial)	80-54-6					OT2	1
Other potentially allergenic substances							
Heliotropine (smell of vanilla)	120-57-0	Skin Sens. 1B (848). 'Likely contact allergen' according to SCCS.	CP2, CP9.3, CP9.4, CP11, CP13	MO2		OT1, OT2	8
Ethylvanillin (smell of vanilla)	121-32-4	No relevant, but 'likely contact allergen' according to SCCS	CP8, CP9.3, CP9.4		SL2	OT1	5
Pentanal	110-62-3	Skin Sens. 1 (755)		MO2			1
Octanal	124-13-0	Skin Sens. 1 (70)		MO2			1
Chloroxylenol	88-04-0	Skin Sens. 1*		MO4, MO10			2
2-pentylfuran	3777-69-3	Skin Sens. 1 (1)		MO5, MO11			2

Substances identified		Relevant classification (allergy)	Identified for the following products				
Name of substance	CAS no.		Cosmetic products	Modelling clay	Slime	Other toys	In total
Butylated hydroxytoluene	128-37-0	Skin Sens. 1 (37)				OT2, OT3, OT4	3

TABLE 36

OVERVIEW OF THE IDENTIFIED 'OTHER' ALLERGENIC FRAGRANCES, FRAGRANCES SUBJECT TO DECLARATION AND OTHER POTENTIALLY ALLERGENIC SUBSTANCES IN THE 44 ANALYSED SUB-PRODUCTS.

* INDICATES THAT THE SUBSTANCE HAS A HARMONISED CLASSIFICATION.

THE NUMBER IN BRACKETS INDICATES THE NUMBER OF NOTIFIED CLASSIFICATIONS WITH THE LISTED CLASSIFICATION.

1. IT MUST BE NOTED THAT FOR THE FRAGRANCES SUBJECT TO DECLARATION, A NUMBER OF THE IDENTIFIED FRAGRANCES IS ALLOWED IN TOYS IN CONCENTRATIONS ABOVE 100 MG/KG, IF IT IS LABELLED ON THE PACKAGING OF THE TOYS. THESE ARE ALPHA-ISOMETHYL IONONE, LIMONENE, LINALOOL, CITRONELLOL, HEXYLCINNAMAL, BUTYLPHENYL METHYLPROPIONAL. ON THE OTHER HAND THE FRAGRANCES MARKED WITH GREEN BACKGROUND (BENZYL ALCOHOL, COUMARIN AND GERANIOL) ARE NOT ALLOWED IN TOYS IN CONCENTRATIONS ABOVE 100 MG/KG. AS NO QUANTITATIVE ANALYSIS IS CARRIED OUT IT CANNOT BE CLARIFIED WHETHER VIOLATIONS OF THE LIMIT VALUE OCCUR OR NOT.

11.3 Discussion of the analytical results

It is seen from the analytical results (the total overview in Table 36) that of the examined 20 “other” allergenic fragrances (28 CAS numbers), four are identified in the analysed products (terpineol (different isomers), vanillin, benzaldehyde and camphor). These “other” allergenic fragrances are found in 2-4 of the cosmetic products and in 1-4 modelling clays, in 1 slime and in 1-2 of the examined other pieces of toys. In total, one or several of these 4 “other” allergenic fragrances are identified for 19 of the examined 44 products. It means that a use of these fragrances in cosmetic products for children and toys on the Danish market takes place. These 4 “other” allergenic fragrances might be regarded as being reasonably widespread in cosmetic products (with perfume) and toys for children. However, it must be noted that only in total 22 products out of the 157 investigated products (14%) contained perfume. Hereof 15 products had a declared content of perfume but no declared content of the fragrances subject to declaration.

During the analyses, it was also noted if some of the fragrances subject to declaration were identified. The analytical results show that 9 out of the 19 fragrances subject to declaration which can be identified through the used method are identified in modelling clay, slime, other toys and even in cosmetic products even if the use is not declared. However, it must be noted it is not possible with the chosen analytical method (screening via headspace) to state anything about the concentration in the products even if the fragrances subject to declaration are identified in 12 out of the 23 analysed cosmetic sub-products. It might be that the concentration in the products is so low that they do not need to be declared on the products according to the regulation on cosmetic products. For leave-on cosmetic products applies that the fragrances subject to declaration must be declared if they are added in a concentration of above 0.001% (10 ppm) and the limit is 0.01% (100 ppm) for rinse-off cosmetic products. For toys, regulations on declaration of certain fragrances at 0.01% (100 ppm) apply. I.e. the concentration in these products (without declaration) may be so low (below 100 ppm) that they are added in concentrations below the general elicitation threshold for fragrances set by SCCS.

The fragrances subject to declaration are also identified in modelling clays (3 different), in slime (2 different) and in other toys (2 different). Limonene and linalool are the most frequently used of the fragrances subject to declaration which it was possible to identify with the used method. Some of the identified fragrances in the toys are not allowed in toys in concentrations above 100 ppm but as the exact content declaration is not known there might be no violation of the legislation.

Furthermore, a number of other substances are identified. These are classified as allergenic but they are not on the gross list of potentially allergenic substances. However, it must be mentioned that in some cases it is only a few companies which have notified the stated classifications.

Of other substances which have a notified or a harmonised classification as allergenic are (number of notifications are stated in brackets):

- Heliotropine (smells of vanilla) – notified classification as Skin Sens. 1B (848) and is stated by SCCS to be ‘likely contact allergen’ (SCCS no. 1459, 2012)
- Ethylvanillin (smells of vanilla) – no relevant classification but is stated by SCCS to be ‘likely contact allergen’ (SCCS no. 1459, 2012)
- Pentanal – notified classification as Skin Sens. 1 (755)
- Octanal – notified classification as Skin Sens. 1 (70)
- Chloroxyleneol – harmonised classification as Skin Sens. 1
- 2-pentylfuran – notified classification as Skin Sens. 1 (1)
- Butylated hydroxytoluen (BHT) – notified classification as Skin Sens. 1 (37)

These other potential allergenic substances were identified in 6 out of 13 cosmetic products, 5 out of 10 modelling clays, 1 out of 7 slimes and 4 out of 4 pieces of other toys.

From Table 32 to Table 35, it is evident that 12 out of the in total 34 analysed products are free from potential allergenic substances (based on the substances which it has been possible to identify).

These products are:

- CP3 – suntan lotion
- CP4 – suntan lotion
- CP7 – make-up set
- MO1 – modelling clay
- MO7 – modelling clay
- MO8 – soft modelling clay
- MO9 – formable sand
- SL1 – snot sucker with slime
- SL3 – toy figure which shoots with slime
- SL4 – slime in tub
- SL6 – skeleton head with slime
- SL7 – slime in tub

It must be noted that there is a difference in exposure (skin contact) for the examined products at use. For all cosmetic products applies that they are so-called leave-on products which are not rinsed off when used. Modelling clay, slime and the other toy are also in close skin contact during use but there is a difference in exposure time and the area of the skin which is exposed at use for the different products. For products, such as suntan lotion, body lotion and baby oil, the skin contact is much larger and for a longer time. For the slime substance which is added the water in the bath tub, the skin contact will be most of the body but not necessarily for a long time. Correspondingly, there may be prolonged skin contact but not on such a large area of skin for the make-up products and the toy (if the rubber bands are made to bracelets which are worn constantly and if the children carry their doll under the arm most of the day or hug the teddy bear in bed during the night). This survey does not indicate in how large concentrations the potentially allergenic substances are identified so it is unknown whether they are found in concentrations which can cause or develop allergy. For many of the allergenic substances, knowledge is missing with respect to the concentrations which may induce an allergy or trigger allergic symptoms in already sensitised persons.

However, it must be pointed out that the overall picture from the survey is that products without potentially allergenic substances are available on the market and that the part of the toy sector which answered the inquiry is aware of the problem and generally tries to avoid allergenic substances. The analysed products were intentionally selected because they could most probably contain potentially allergenic substances.

12. Discussion

In this project, the use of certain potentially allergenic substances in toys and leave-on cosmetic products for children was investigated. As many thousands of substances with a notified classification as allergenic exist, it was a choice in this project to focus on potentially allergenic substances among colourants, preservatives, UV filters and fragrances. These four groups of substances were selected as they are typically used in “chemical toys” and cosmetic products and as there is some knowledge on which substances that are allergenic. However, this choice means that there might be allergenic substances in both toys and cosmetic products for children which have not been in focus in this project.

In this project, the term “potentially allergenic substances” is used as in general, knowledge on allergenic substances is lacking and also at which levels of concentration they cause an allergenic reaction. For instance, for some substances, only a few cases of allergenic reactions are seen while for other substances, there is a far more frequent occurrence of allergy.

A survey of 157 cosmetic products for children was made. The survey showed that 127 out of the 157 investigated products were without a content of potentially allergenic substances (i.e. substances on the gross list of potentially allergenic substances which have been in focus in this project). It was possible for almost all the investigated product types (except the product types hair spray and perfume sets) to find products without potentially allergenic substances. However, it cannot be excluded that in these products, there might be found other potentially allergenic substances which have not been in focus in this project.

The survey of cosmetic products for children shows that primarily the following potentially allergenic substances seem to be used in cosmetic products for children:

- fragrances (mainly in products like suntan lotion, lip balm/lip gloss, face paint, make-up and perfume sets) and
- UV filters (mainly in products like suntan lotion and lip balm/lip gloss).

It has to be noted that many fragrances may have other functions in the cosmetic products than giving odour to the product. For instance, benzyl alcohol can also be used as a solvent and a preservative and limonene can also be used as a solvent. Both these substances are among the 26 fragrances subject to declaration. The identified potentially allergenic fragrances in the cosmetic products can thus be added due to other functions but this does not change the fact that they are still potentially allergenic.

However, it must be noted that in a more detailed hazard assessment (see chapter 8), the identified potentially allergenic UV filters turned out not to constitute a problem with regard to allergy. In an American study (Heurung et al., 2014), the incidence of allergy to UV filters is stated to be low and Professor Klaus Ejner Andersen from the Department of Dermatology and Allergy Centre at Odense University Hospital says that they have seen a few cases of allergenic reactions to UV filters but not to such a degree that it can be called a problem.

Furthermore, a survey of the use of allergenic substances in toys was made through contact to the Toy Sector and eight selected producers/dealers of toys. The survey of toys shows that out of the eight companies who have given information to the project, several of these set requirements for

allergenic substances. Among other things, the use of fragrances in chemical toys is unwanted by several companies and several companies require bans on the use of allergenic preservatives or work on a replacement of the allergenic preservatives in their chemical toy products. The contact to the companies shows that chemical toy products on the Danish market without use of potentially allergenic ingredients are available. However, it must be noted that during the project, contact was made to toy producers/dealers who did not deliver information to the project. It is unknown whether there is a larger use of the potentially allergenic substances, which have been in focus in this project, among the toy products of these companies – but it may be a possibility.

The survey of toys shows that primarily the following potentially allergenic substances seem to be used in chemical toys:

- fragrances (mainly in the cosmetic products such as face paint, make-up and perfume sets) and
- preservatives (mainly in finger paint, modelling clay, face paint and make-up as well as soap bubbles).

The fragrances are primarily used in the chemical toys to mask a chemical odour from the products and the preservatives have the function to avoid growth of micro-organisms in the products.

Generally, the survey shows for both cosmetic products targeted children and toys with a prolonged skin contact that there is a focus on avoiding potentially allergenic substances and that it is possible to find products without potentially allergenic substances (at least the substances which have been in focus in this survey).

As fragrances were identified in both cosmetic products and in toys, it was decided in the analytical phase to go into details with this group of potentially allergenic substances. In total 34 products for children were selected and purchased, distributed on 13 cosmetic products, 10 modelling clays, 7 slimes and 4 pieces of other toys which were analysed qualitatively for potentially allergenic fragrances.

Intentionally, it was a choice in the project to focus on other potentially allergenic fragrances than the 26 fragrances subject to declaration. SCCS has made an assessment of fragrances and states that in total 82 fragrances ought to be considered to be allergenic (26 of these are the fragrances subject to declaration). Therefore, at the beginning of the analytical phase, it was examined which of these “other potentially allergenic fragrances” it was possible to analyse for through a chemical analysis. As many fragrances are so-called natural extracts which consist of a mixture of several chemical substances it may complicate an identification through a chemical analysis. Furthermore, for several of these “other potentially allergenic fragrances”, it is not immediately possible to buy reference substances, which also makes an identification through a chemical analysis difficult. For these reasons, analyses for in total 21 of the remaining 56 (82-26) “other potentially allergenic fragrances” were made.

The performed qualitative analyses for the 21 “other potentially allergenic fragrances” on the 34 selected products for children in this project show that potentially allergenic fragrances in products for children on the Danish market are found. The 34 products were intentionally selected for analysis because they could most probably contain potentially allergenic fragrances. The cosmetic products were selected for analysis because they had a declared content of perfume (however, none of the fragrances subject to declaration in concentrations subject to declaration) and toys with odour or toys of the type modelling clay and slime were intentionally selected as they often are added fragrances to mask the more “chemical” odour of the products.

In total, 22 of the 34 analysed products (i.e. 65%) contained one or more potentially allergenic substances. These products were distributed on 10 of 13 cosmetic products, 6 of 10 modelling clays, 2 of 7 slimes and 4 of 4 pieces of other toys. The remaining approximately one third of the analysed

products was thus free from the potentially allergenic substances for which it was possible to analyse. Potentially, the products might have contained other potentially allergenic fragrances for which it was not possible to analyse through the selected analytical method.

It must be noted that during the survey the toy sector was exclusively asked about the use of the 26 fragrances subject to declaration and not fragrances in general. The reasons were: Firstly, not to make the inquiry to the companies in the toy sector too comprehensive and overwhelming, and secondly because the other fragrances than the fragrances subject to declaration did not come into focus in the project until *after* the completion of the survey. Thus it is unknown how large the use of the “other potentially allergenic fragrances” is within the toy sector. However, the analyses made in this project show that at least four of these “other potentially allergenic fragrances” are widespread among the examined products for children in this project (cosmetic products with a content of perfume for children, modelling clay, slime and other scented toys). Of the four “other potentially allergenic fragrances”:

- 4 were identified in 5 of the 13 scented cosmetic products for children
- 3 were identified in 6 of the 10 modelling clays
- 1 was identified in 1 of the 7 slimes
- 2 were identified in 3 of the 4 pieces of other scenting toys

In co-operation with the Danish EPA, it was decided that no risk assessment of the selected substances among the identified substances was to be made in this project. This is partly due to the limited knowledge on the elicitation and induction levels of the fragrances and partly that the analyses made in the project cannot indicate in how large concentrations the potentially allergenic substances are found. Therefore, it is unknown whether the substances are found in concentrations which can cause or develop allergy.

It must be noted that there is a difference in the exposure (at skin contact) for the examined products at use. For all cosmetic products applies that they are so-called leave-on products which are not rinsed off during use. Modelling clay, slimes and the other toy are also in close skin contact during use but there is a difference in the exposure time and the area of the skin which is exposed during use of the different products. One slime product is used to turn the bath tub water into slime and thus it gives a larger exposure than modelling clay and slime where only the hands are exposed. For teddy bears and dolls the exposure is again different. This survey is not able to state in how large concentrations the potentially allergenic substances occur so it is unknown if they are found in concentrations which can cause or develop allergy.

However, it is an interesting result that other potentially allergenic fragrances than the 26 fragrances subject to declaration seem to be used in cosmetic products and toys targeted children. As SCCS has assessed these other fragrances as allergenic, it is an area where there seems to be an increased need for focus in future. However, the possibility of declaring more than the 26 fragrances on cosmetics is already a subject of discussion in the EU today⁶.

However, it must be pointed out that the overall picture from the survey is that there are alternative products on the market without allergenic substances (at least the substances which have been in focus in this project) and that the part of the toy sector which answered the inquiry is aware of the problem and in general tries to avoid allergenic substances. The analysed products were intentionally selected because they could most probably contain potentially allergenic substances and therefore the results of the analyses show that a relatively large part of the analysed products may contain potentially allergenic fragrances.

⁶ http://ec.europa.eu/dgs/health_food-safety/dgs_consultations/ca/consultation_cosmetic-products_fragrance-allergens_201402_en.htm

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Appendix 1: Fragrances restricted in toys

This appendix contains an overview of allergenic fragrances which are restricted in toys according to the Danish statutory order regarding safety requirements for toys (BEK nr. 13, 2011).

In annex II named “Særlige sikkerhedskrav” (“special safety requirements” in English), it is listed in section III “Kemiske egenskaber” (“chemical properties” in English) (item no. 11 and 12) that:

- Toys shall not contain 55 specific allergenic fragrances (see Table 37).
- Traces of these fragrances are, however, allowed provided that such presence is technically unavoidable under good manufacturing practice and does not exceed 100 mg/kg.
- In addition, the names of 11 specific allergenic fragrances (see Table 38) must be listed on the toy, on an affixed label, on the packaging or in an accompanying leaflet if they are used in toys in concentrations exceeding 100 mg/kg or in toy components.
- However, the use of the fragrances listed as no. 41-55 (see Table 37) and the 11 fragrances (from Table 38) – corresponding to the 26 fragrances subject to declaration from the EU cosmetics regulation – are allowed in cosmetic kits provided that:
 - That these fragrances are clearly labelled on the packaging and that the packaging contains the following warning: “Contains fragrances that may cause allergies”.
 - That the resulting products made by the child in accordance with the instructions comply with the requirements of the cosmetics regulation.

No.	Name of the allergenic fragrance	CAS no.
1.	Alanroot oil (<i>Inula helenium</i>)	97676-35-2
2.	Allylisothiocyanate	57-06-7
3.	Benzyl cyanide	140-29-4
4.	4 tert-Butylphenol	98-54-4
5.	Chenopodium oil	8006-99-3
6.	Cyclamen alcohol	4756-19-8
7.	Diethyl maleate	141-05-9
8.	Dihydrocoumarin	119-84-6
9.	2,4-Dihydroxy-3-methylbenzaldehyde	6248-20-0
10.	3,7-Dimethyl-2-octen-1-ol (6,7-Dihydrogeraniol)	40607-48-5
11.	4,6-Dimethyl-8-tert-butyl-cumarin	17874-34-9
12.	Dimethyl citraconate	617-54-9
13.	7,11-Dimethyl-4,6,10-dodecatrien-3-one	26651-96-7
14.	6,10-Dimethyl-3,5,9-undecatrien-2-one	141-10-6
15.	Diphenylamine	122-39-4

No.	Name of the allergenic fragrance	CAS no.
16.	Ethyl acrylate	140-88-5
17.	Fig leaf, fresh and preparations	68916-52-9
18.	trans-2-Heptenal	18829-55-5
19.	trans-2-Hexenal diethyl acetal	67746-30-9
20.	trans-2-Hexenal dimethyl acetal	18318-83-7
21.	Hydroabietyl alcohol	13393-93-6
22.	4-Ethoxyphenol	622-62-8
23.	6-Isopropyl-2-decahydronaphthalenol	34131-99-2
24.	7-Methoxycoumarin	531-59-9
25.	4-Methoxyphenol	150-76-5
26.	4-(p-Methoxyphenyl)-3-buten-2-one	943-88-4
27.	1-(p-Methoxyphenyl)-1-penten-3-one	104-27-8
28.	Methyl trans-2-butenate	623-43-8
29.	6-Methyl coumarin	92-48-8
30.	7-Methyl coumarin	2445-83-2
31.	5-Methyl-2,3-hexanedion	13706-86-0
32.	Costus root oil (<i>Saussurea lappa</i> Clarke)	8023-88-9
33.	7-Ethoxy-4-methylcoumarin	87-05-8
34.	Hexahydrocoumarin	700-82-3
35.	Peru balsam, crude (Exudation of <i>Myroxylon pereirae</i> (Royle) Klotzsch)	8007-00-9
36.	2-Pentyliden-cyclohexanone	25677-40-1
37.	3,6,10-Trimethyl-3,5,9-undecatrien-2-one	1117-41-5
38.	Verbena oil (<i>Lippia citriodora</i> Kunth).	8024-12-2
39.	Musk ambrette (4-tert-Butyl-3-methoxy-2,6-dinitrotoluene)	83-66-9
40.	4-Phenylbut-3-en-2-one	122-57-6
41.	Amyl cinnamal	122-40-7

No.	Name of the allergenic fragrance	CAS no.
42.	Amylcinnamyl alcohol	101-85-9
43.	Benzyl alcohol	100-51-6
44.	Benzyl salicylate	118-58-1
45.	Cinnamyl alcohol	104-54-1
46.	Cinnamal	104-55-2
47.	Citral	5392-40-5
48.	Cumarin	91-64-5
49.	Eugenol	97-53-0
50.	Geraniol	106-24-1
51.	Hydroxycitronellal	107-75-5
52.	Hydroxy-methylpentylcyclohexencarboxaldehyde Hydroxyisohexyl 3-cyclohexene carboxaldehyde	31906-04-4
53.	Isoeugenol	97-54-1
54.	Oakmoss extracts Evernia prunastri extract	90028-68-5
55.	Treemoss extracts Evernia furfuracea extract	90028-67-4

TABLE 37

THE 55 ALLERGENIC FRAGRANCES THAT MUST NOT BE USED IN TOYS (BEK NR. 13, 2011).

FRAGRANCES NO. 41-55 ARE SUBJECT TO DECLARATION ACCORDING TO THE EU COSMETICS REGULATION.

No.	Name of the allergenic fragrance	CAS no.
1.	Anisyl alcohol	105-13-5
2.	Benzyl benzoate	120-51-4
3.	Benzyl cinnamate	103-41-3
4.	Citronellol	106-22-9
5.	Farnesol	4602-84-0
6.	Hexyl cinnamaldehyde Hexyl cinnamal	101-86-0
7.	Lilial Butylphenyl methylpropional	80-54-6
8.	d-Limonene	5989-27-5
9.	Linalool	78-70-6
10.	Methylheptincarbonate Methyl 2-octynoate	111-12-6
11.	3-methyl-4-(2,6,6-trimethyl-2-cyclohexen-1-yl)-3-buten-2-one alpha-Isomethyl ionone	127-51-5

TABLE 38

THE 11 ALLERGENIC FRAGRANCES THAT MAY BE USED IN TOYS IF THE CONTENT IS DECLARED ON THE PRODUCT (STAT.ORD. NO. 13, 2011).

ALL FRAGRANCES IN THIS TABLE ARE SUBJECT TO DECLARATION ACCORDING TO THE EU COSMETICS REGULATION.

Appendix 2: Gross list of potentially allergenic substances

This appendix contains the gross list of the in total 191 potentially allergenic substances which are identified through the approach that is described in chapter 3 “Gross list of potentially allergenic substances”. Of the 191 substances, 2 are colourants, 164 are fragrances, 19 are preservatives, 3 are UV filters and 3 can be applied as adhesives (binders) in cosmetics.

In the column “Allergenic potential”, the allergenic potential appears as described in an opinion from SCCS (Scientific Committee for Consumer Safety) if such an opinion exists and the allergenic potential is assessed. Otherwise, in this column, the reason for the substance being on the gross list of potentially allergenic substances is described, for instance that the substance releases allergenic formaldehyde (so-called formaldehyde releaser), that the substance is classified with a harmonised classification (harm. class.) as Skin Sens. 1 or that the substance is assessed to be allergenic according to Simonsen et al. (2013).

Type	CAS-no.	INCI-name or trade name	Covered by SCCS opinion	Allergy potential	Allergy potential fragrances (based on SCCS no. 1459, 2012)			Sensitisation rate (p value) Simonsen et al., 2013	Reference (except for SCCS opinion)
					Established human evidence Table 13-1	Animal evidence, EC 3 value (min; %) Table 13-2	SAR-evidence Table 13-3		
Colourant	1064-48-8	CI 20470	SCCS/1226/09 SCCS/1492/12	Moderate (EC 3 = 2.1%)					EU, Cosmetics Regulation Annex IV, 2009
Colourant	846-70-8	CI 10316	SCCP/1160/08	Extreme					EU, Cosmetics Regulation Annex IV, 2009
Preservative	50-00-0	FORMALDEHYDE	(SCCNFP/587/02) SCCS/1538/14	Strong Skin Sens 1 (harm. class.)				0.7 (0.95)	EU, Cosmetics Regulation Annex V, 2009; Simonsen et al., 2013; ECHA C&L Inventory, 2015
Preservative	30525-89-4	PARAFORMALDEHYD E	(SCCNFP/587/02)	Formaldehyde releaser					EU, Cosmetics Regulation Annex V, 2009; Danish Allergy Research Centre, 2015
Preservative	30007-47-7	5-BROMO-5-NITRO-1,3-DIOXANE	No	Formaldehyde releaser					EU, Cosmetics Regulation Annex V, 2009; Danish Allergy Research Centre, 2015
Preservative	52-51-7	2-BROMO-2-NITROPROPANE-1,3-DIOL	SCCNFP/0125/99	Formaldehyde releaser				0.2 (0.94)	EU, Cosmetics Regulation Annex V, 2009; Simonsen et al., 2013; Danish Allergy Research Centre, 2015

Type	CAS-no.	INCI-name or trade name	Covered by SCCS opinion	Allergy potential	Allergy potential fragrances (based on SCCS no. 1459, 2012)			Sensitisation rate (p value) Simonsen et al., 2013	Reference (except for SCCS opinion)
					Established human evidence Table 13-1	Animal evidence, EC 3 value (min; %) Table 13-2	SAR-evidence Table 13-3		
Preservative	59-50-7	P-CHLORO-M-CRESOL	SCCNFP/0125/99	Skin Sens 1 (harm. class.)					EU, Cosmetics Regulation Annex V, 2009; ECHA C&L Inventory, 2015
Preservative	88-04-0	4-chloro-3,5-dimethylphenol	SCCNFP/0125/99	Skin Sens 1 (harm. class.)					EU, Cosmetics Regulation Annex V, 2009; ECHA C&L Inventory, 2015
Preservative	1321-23-9	Chloroxylenol	SCCNFP/0125/99	Skin Sens 1 (harm. class.)					EU, Cosmetics Regulation Annex V, 2009; ECHA C&L Inventory, 2015
Preservative	39236-46-9	IMIDAZOLIDINYL UREA	SCCNFP/586/02	Formaldehyde releaser				0.3 (0.45)	EU, Cosmetics Regulation Annex V, 2009; Simonsen et al., 2013; Danish Allergy Research Centre, 2015
Preservative	32289-58-0	POLYAMINOPROPYL BIGUANIDE*	SCCS/1535/14	Moderate to strong sensitiser in animals					EU, Cosmetics Regulation Annex V, 2009
Preservative	100-97-0	METHENAMINE	SCHER's Risk Assessment Report on Methenamine	Skin Sens 1 (harm. class.) Formaldehyde releaser					EU, Cosmetics Regulation Annex V, 2009; ECHA C&L Inventory, 2015; Danish Allergy Research

Type	CAS-no.	INCI-name or trade name	Covered by SCCS opinion	Allergy potential	Allergy potential fragrances (based on SCCS no. 1459, 2012)			Sensitisation rate (p value) Simonsen et al., 2013	Reference (except for SCCS opinion)
					Established human evidence Table 13-1	Animal evidence, EC 3 value (min; %) Table 13-2	SAR-evidence Table 13-3		
									Centre, 2015
Preservative	4080-31-3	QUATERNIUM-15*	(SCCS/1344/10)	Formaldehyde releaser				0.2 (0.15)	EU, Cosmetics Regulation Annex V, 2009; Simonsen et al., 2013; Danish Allergy Research Centre, 2015
Preservative	51229-78-8	QUATERNIUM-15*	(SCCS/1344/10)	Formaldehyde releaser				0.2	EU, Cosmetics Regulation Annex V, 2009; Simonsen et al., 2013; Danish Allergy Research Centre, 2015
Preservative	6440-58-0	DMDM HYDANTOIN	No	Formaldehyde releaser					EU, Cosmetics Regulation Annex V, 2009; Danish Allergy Research Centre, 2015
Preservative	55965-84-9	Kathon	SCCS/1238/09	Skin Sens 1 (harm. class.) Extreme sensitizer				0.8 (0.94)	EU, Cosmetics Regulation Annex V, 2009; Simonsen et al., 2013; ECHA C&L Inventory, 2015
Preservative	26172-55-4	METHYLCHLOROISOT HIAZOLINONE	SCCS/1238/09	Potent allergen Mixture CMI/MI				0.8 (0.94)	EU, Cosmetics Regulation Annex V, 2009; Simonsen et al., 2013

Type	CAS-no.	INCI-name or trade name	Covered by SCCS opinion	Allergy potential	Allergy potential fragrances (based on SCCS no. 1459, 2012)			Sensitisation rate (p value) Simonsen et al., 2013	Reference (except for SCCS opinion)
					Established human evidence Table 13-1	Animal evidence, EC 3 value (min; %) Table 13-2	SAR-evidence Table 13-3		
				extreme sensitizer					
Preservative	2682-20-4	METHYLISOTHIAZOLI NONE	SCCS/1238/09 SCCS/1521/13 SCCS/1557/15	Sensitizing Increasing incidence of contact allergy				0.8 (0.94)	EU, Cosmetics Regulation Annex V, 2009; Danish Allergy Research Centre, 2015; Simonsen et al., 2013
Preservative	79-07-2	CHLOROACETAMIDE	SCCS/1360/10	Skin Sens 1 (harm. class.)					EU, Cosmetics Regulation Annex V, 2009; ECHA C&L Inventory, 2015
Preservative	78491-02-8	DIAZOLIDINYL UREA	SCCNFP/586/02	Formaldehyde releaser				0.3 (0.93)	EU, Cosmetics Regulation Annex V, 2009; Simonsen et al., 2013; Danish Allergy Research Centre, 2015
Preservative	111-30-8	GLUTARAL	No	Skin Sens 1 (harm. class.)					EU, Cosmetics Regulation Annex V, 2009; ECHA C&L Inventory, 2015
Preservative	70161-44-3	SODIUM HYDROXYMETHYLGL YCINATE	SCCNFP/586/02, final	Formaldehyde releaser					EU, Cosmetics Regulation Annex V, 2009; Danish Allergy Research Centre, 2015

Type	CAS-no.	INCI-name or trade name	Covered by SCCS opinion	Allergy potential	Allergy potential fragrances (based on SCCS no. 1459, 2012)			Sensitisation rate (p value) Simonsen et al., 2013	Reference (except for SCCS opinion)
					Established human evidence Table 13-1	Animal evidence, EC 3 value (min; %) Table 13-2	SAR-evidence Table 13-3		
Preservative	55406-53-6	IODOPROPYNYL BUTYLCARBAMATE	SCCNFP/0826/04	Skin Sens 1 (harm. class.)					EU, Cosmetics Regulation Annex V, 2009; ECHA C&L Inventory, 2015
Preservative		Paraben mix						0.5	Simonsen et al., 2013
Preservative	2634-33-5	BENZ-ISOTHIAZOLINONE	SCCS/1482/12	Moderate sensitizer					Poulsen & Nielsen, 2014
Adhesive	8050-09-7	Colophonium						2.4	Simonsen et al., 2013
Adhesive	25085-50-1	p-tert-Butyl formaldehyde resin						0.6	Simonsen et al., 2013
Adhesive		Epoxy resin						0.3	Simonsen et al., 2013
UV-filter	131-57-7	BENZOPHENONE-3	SCCP/1201/08	Can cause photo-allergic reactions					EU, Cosmetics Regulation Annex VI, 2009
UV-filter	6197-30-4	OCTOCRYLENE		Moderate sensitizer. Photo-contact allergen and a contact allergen					EU, Cosmetics Regulation Annex VI, 2009; Karlsson et al., 2011; Asthma-Allergy Denmark, 2015
UV-filter	155633-54-8	DROMETRIZOLE TRISILOXANE		Regularly responsible for					EU, Cosmetics Regulation Annex VI, 2009;

Type	CAS-no.	INCI-name or trade name	Covered by SCCS opinion	Allergy potential	Allergy potential fragrances (based on SCCS no. 1459, 2012)			Sensitisation rate (p value) Simonsen et al., 2013	Reference (except for SCCS opinion)
					Established human evidence Table 13-1	Animal evidence, EC 3 value (min; %) Table 13-2	SAR-evidence Table 13-3		
				cases of photo-allergy					Johansen et al., 2011
Fragrance	32388-55-9	ACETYLCEDRENE	SCCS/1459/11	Established contact allergen in humans	Human +				SCCS, 2011
Fragrance	122-40-7	AMYL CINNAMAL	SCCS/1459/11	Established contact allergen in humans	Human ++			2.5	SCCS, 2011; Simonsen et al., 2013 EU Cosmetics Regulation article 19,1 and Annex III (subject to declaration)
Fragrance	101-85-9	AMYL CINNAMYL ALCOHOL	SCCS/1459/11	Established contact allergen in humans	Human ++			2.5	SCCS, 2011; Simonsen et al., 2013 EU Cosmetics Regulation article 19,1 and Annex III (subject to declaration)
Fragrance	2050-08-0	AMYL SALICYLATE	SCCS/1459/11	Established contact allergen in humans	Human + (r.t.)				SCCS, 2011
Fragrance	4180-23-8	trans-ANETHOLE	SCCS/1459/11	Established contact allergen in humans	Human +				SCCS, 2011

Type	CAS-no.	INCI-name or trade name	Covered by SCCS opinion	Allergy potential	Allergy potential fragrances (based on SCCS no. 1459, 2012)			Sensitisation rate (p value) Simonsen et al., 2013	Reference (except for SCCS opinion)
					Established human evidence Table 13-1	Animal evidence, EC 3 value (min; %) Table 13-2	SAR-evidence Table 13-3		
Fragrance	105-13-5	ANISE ALCOHOL	SCCS/1459/11	Established contact allergen in humans	Human +				SCCS, 2011 EU Cosmetics Regulation article 19,1 and Annex III (subject to declaration)
Fragrance	100-52-7	BENZALDEHYDE	SCCS/1459/11	Established contact allergen in humans	Human +				SCCS, 2011
Fragrance	100-51-6	BENZYL ALCOHOL	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011 EU Cosmetics Regulation article 19,1 and Annex III (subject to declaration)
Fragrance	120-51-4	BENZYL BENZOATE	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011 EU Cosmetics Regulation article 19,1 and Annex III (subject to declaration)
Fragrance	103-41-3	BENZYL CINNAMATE	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011 EU Cosmetics Regulation article 19,1 and Annex III (subject to declaration)

Type	CAS-no.	INCI-name or trade name	Covered by SCCS opinion	Allergy potential	Allergy potential fragrances (based on SCCS no. 1459, 2012)			Sensitisation rate (p value) Simonsen et al., 2013	Reference (except for SCCS opinion)
					Established human evidence Table 13-1	Animal evidence, EC 3 value (min; %) Table 13-2	SAR-evidence Table 13-3		
Fragrance	118-58-1	BENZYL SALICYLAT	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011 EU Cosmetics Regulation article 19,1 and Annex III (subject to declaration)
Fragrance	80-54-6	BUTYLPHENYL METHYLPROPIONAL	SCCS/1459/11	Established contact allergen in humans	Human +				SCCS, 2011 EU Cosmetics Regulation article 19,1 and Annex III (subject to declaration)
Fragrance	76-22-2	CAMPHOR	SCCS/1459/11	Established contact allergen in humans	Human + (r.t.)				SCCS, 2011
Fragrance	464-49-3	CAMPHOR	SCCS/1459/11	Established contact allergen in humans	Human + (r.t.)				SCCS, 2011
Fragrance	87-44-5	beta-CARYOPHYLLENE	SCCS/1459/11	Established contact allergen in humans	Non-ox.: +, ox.:+				SCCS, 2011
Fragrance	99-49-0	CARVONE	SCCS/1459/11	Established contact allergen in humans	Human + (r.t.)				SCCS, 2011

Type	CAS-no.	INCI-name or trade name	Covered by SCCS opinion	Allergy potential	Allergy potential fragrances (based on SCCS no. 1459, 2012)			Sensitisation rate (p value) Simonsen et al., 2013	Reference (except for SCCS opinion)
					Established human evidence Table 13-1	Animal evidence, EC 3 value (min; %) Table 13-2	SAR-evidence Table 13-3		
Fragrance	6485-40-1	CARVONE	SCCS/1459/11	Established contact allergen in humans	Human + (r.t.)				SCCS, 2011
Fragrance	2244-16-8	CARVONE	SCCS/1459/11	Established contact allergen in humans	Human + (r.t.)				SCCS, 2011
Fragrance	104-55-2	CINNAMAL	SCCS/1459/11	Established contact allergen in humans	Human +++				SCCS, 2011 EU Cosmetics Regulation article 19,1 and Annex III (subject to declaration)
Fragrance	104-54-1	CINNAMYL ALCOHOL	SCCS/1459/11	Established contact allergen in humans	Human +++				SCCS, 2011 EU Cosmetics Regulation article 19,1 and Annex III (subject to declaration)
Fragrance	5392-40-5	CITRAL	SCCS/1459/11	Established contact allergen in humans	Human +++			2.4	SCCS, 2011; Simonsen et al., 2013 EU Cosmetics Regulation article 19,1 and Annex III (subject to declaration)

Type	CAS-no.	INCI-name or trade name	Covered by SCCS opinion	Allergy potential	Allergy potential fragrances (based on SCCS no. 1459, 2012)			Sensitisation rate (p value) Simonsen et al., 2013	Reference (except for SCCS opinion)
					Established human evidence Table 13-1	Animal evidence, EC 3 value (min; %) Table 13-2	SAR-evidence Table 13-3		
Fragrance	106-22-9	CITRONELLOL	SCCS/1459/11	Established contact allergen in humans	Human ++			2.4	SCCS, 2011; Simonsen et al., 2013 EU Cosmetics Regulation article 19,1 and Annex III (subject to declaration)
Fragrance	1117-61-9	CITRONELLOL	SCCS/1459/11	Established contact allergen in humans	Human ++			2.4	SCCS, 2011; Simonsen et al., 2013 EU Cosmetics Regulation article 19,1 and Annex III (subject to declaration)
Fragrance	7540-51-4	CITRONELLOL	SCCS/1459/11	Established contact allergen in humans	Human ++			2.4	SCCS, 2011; Simonsen et al., 2013 EU Cosmetics Regulation article 19,1 and Annex III (subject to declaration)
Fragrance	91-64-5	COUMARIN	SCCP/0935/05 SCCS/1459/11	Established contact allergen in humans	Human +++			2.4	SCCS, 2011; Simonsen et al., 2013 EU Cosmetics Regulation article 19,1 and Annex III (subject to declaration)

Type	CAS-no.	INCI-name or trade name	Covered by SCCS opinion	Allergy potential	Allergy potential fragrances (based on SCCS no. 1459, 2012)			Sensitisation rate (p value) Simonsen et al., 2013	Reference (except for SCCS opinion)
					Established human evidence Table 13-1	Animal evidence, EC 3 value (min; %) Table 13-2	SAR-evidence Table 13-3		
Fragrance	23696-85-7	ROSE KETONE-4	SCCS/1459/11	Established contact allergen in humans	Human + (r.t.)				SCCS, 2011
Fragrance	43052-87-5	alpha-DAMASCONE (TMCHB)	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	23726-94-5	alpha-DAMASCONE	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	23726-92-3	cis-beta-DAMASCONE	SCCS/1459/11	Established contact allergen in humans	Human +				SCCS, 2011
Fragrance	57378-68-4	delta-DAMASCONE	SCCS/1459/11	Established contact allergen in humans	Human +				SCCS, 2011
Fragrance	151-05-3	DIMETHYLBENZYL CARBINYL ACETATE	SCCS/1459/11	Established contact allergen in humans	Human +++				SCCS, 2011

Type	CAS-no.	INCI-name or trade name	Covered by SCCS opinion	Allergy potential	Allergy potential fragrances (based on SCCS no. 1459, 2012)			Sensitisation rate (p value) Simonsen et al., 2013	Reference (except for SCCS opinion)
					Established human evidence Table 13-1	Animal evidence, EC 3 value (min; %) Table 13-2	SAR-evidence Table 13-3		
Fragrance	97-53-0	EUGENOL	SCCS/1459/11	Established contact allergen in humans	Human +++			2.5	SCCS, 2011; Simonsen et al., 2013 EU Cosmetics Regulation article 19,1 and Annex III (subject to declaration)
Fragrance	4602-84-0	FARNESOL	SCCS/1459/11	Established contact allergen in humans	Human ++-+++			2.4	SCCS, 2011; Simonsen et al., 2013 EU Cosmetics Regulation article 19,1 and Annex III (subject to declaration)
Fragrance	106-24-1	GERANIOL	SCCS/1459/11	Established contact allergen in humans	Human +++			2.5	SCCS, 2011; Simonsen et al., 2013 EU Cosmetics Regulation article 19,1 and Annex III (subject to declaration)
Fragrance	109-29-5	HEXADECANOLACTONE	SCCS/1459/11	Established contact allergen in humans	Human + (r.t.)				SCCS, 2011
Fragrance	1222-05-5	HEXAMETHYLINDANOPYRAN	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011

Type	CAS-no.	INCI-name or trade name	Covered by SCCS opinion	Allergy potential	Allergy potential fragrances (based on SCCS no. 1459, 2012)			Sensitisation rate (p value) Simonsen et al., 2013	Reference (except for SCCS opinion)
					Established human evidence Table 13-1	Animal evidence, EC 3 value (min; %) Table 13-2	SAR-evidence Table 13-3		
Fragrance	101-86-0	HEXYL CINNAMAL	SCCS/1459/11	Established contact allergen in humans	Human ++			2.4	SCCS, 2011; Simonsen et al., 2013 EU Cosmetics Regulation article 19,1 and Annex III (subject to declaration)
Fragrance	31906-04-4	HYDROXYISOHEXYL 3-CYCLOHEXENE CARBOXALDEHYDE (HICC)	SCCS/1459/11	Established contact allergen in humans	Human +++++			2.4	SCCS, 2011; Simonsen et al., 2013 EU Cosmetics Regulation article 19,1 and Annex III (subject to declaration)
Fragrance	51414-25-6	HYDROXYISOHEXYL 3-CYCLOHEXENE CARBOXALDEHYDE (HICC)	SCCS/1459/11	Established contact allergen in humans	Human +++++			1.1	SCCS, 2011; Simonsen et al., 2013 EU Cosmetics Regulation article 19,1 and Annex III (subject to declaration)
Fragrance	107-75-5	HYDROXYCITRONELLAL	SCCS/1459/11	Established contact allergen in humans	Human +++			1.1	SCCS, 2011; Simonsen et al., 2013 EU Cosmetics Regulation article 19,1 and Annex III (subject to declaration)

Type	CAS-no.	INCI-name or trade name	Covered by SCCS opinion	Allergy potential	Allergy potential fragrances (based on SCCS no. 1459, 2012)			Sensitisation rate (p value) Simonsen et al., 2013	Reference (except for SCCS opinion)
					Established human evidence Table 13-1	Animal evidence, EC 3 value (min; %) Table 13-2	SAR-evidence Table 13-3		
Fragrance	97-54-1	ISOEUGENOL	SCCS/1459/11	Established contact allergen in humans	Human +++			2.5	SCCS, 2011; Simonsen et al., 2013 EU Cosmetics Regulation article 19,1 and Annex III (subject to declaration)
Fragrance	127-51-5	alpha-ISOMETHYL IONONE	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011 EU Cosmetics Regulation article 19,1 and Annex III (subject to declaration)
Fragrance	138-86-3	LIMONENE (DL-Limonene)	SCCS/1459/11	Established contact allergen in humans	Human ++ (non-ox.); +++ (ox.)				SCCS, 2011 EU Cosmetics Regulation article 19,1 and Annex III (subject to declaration)
Fragrance	5989-27-5	D-Limonene	SCCS/1459/11	Allergenic DL-Limonene is established contact allergen in humans					SCCS, 2011 EU Cosmetics Regulation article 19,1 and Annex III (subject to declaration)

Type	CAS-no.	INCI-name or trade name	Covered by SCCS opinion	Allergy potential	Allergy potential fragrances (based on SCCS no. 1459, 2012)			Sensitisation rate (p value) Simonsen et al., 2013	Reference (except for SCCS opinion)
					Established human evidence Table 13-1	Animal evidence, EC 3 value (min; %) Table 13-2	SAR-evidence Table 13-3		
Fragrance	78-70-6	LINALOOL	SCCS/1459/11	Established contact allergen in humans	Human ++ (non-ox.); +++ (ox.)				SCCS, 2011 EU Cosmetics Regulation article 19,1 and Annex III (subject to declaration)
Fragrance	115-95-7	LINALYL ACETATE	SCCS/1459/11	Established contact allergen in humans	Human + (non-ox.); ++ (ox.)				SCCS, 2011
Fragrance	1490-04-6	MENTHOL	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	89-78-1	MENTHOL	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	2216-51-5	MENTHOL	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	92-48-8	6-METHYL COUMARIN	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011

Type	CAS-no.	INCI-name or trade name	Covered by SCCS opinion	Allergy potential	Allergy potential fragrances (based on SCCS no. 1459, 2012)			Sensitisation rate (p value) Simonsen et al., 2013	Reference (except for SCCS opinion)
					Established human evidence Table 13-1	Animal evidence, EC 3 value (min; %) Table 13-2	SAR-evidence Table 13-3		
Fragrance	111-12-6	METHYL 2-OCTYNOATE	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011 EU Cosmetics Regulation article 19,1 and Annex III (subject to declaration)
Fragrance	119-36-8	METHYL SALICYLATE	SCCS/1459/11	Established contact allergen in humans	Human +				SCCS, 2011
Fragrance	67801-20-1	3-METHYL-5-(2,2,3-TRIMETHYL-3-CYCLOPENTENYL)PEN T-4-EN-2-OL	SCCS/1459/11	Established contact allergen in humans	Human ++ (r.t.)				SCCS, 2011
Fragrance	80-56-8	PINENE	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	127-91-3, resp	BETA-PINENES	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	17369-59-4	PROPYLIDENE PHTHALIDE	SCCS/1459/11	Established contact allergen in humans	Human + (r.t.)				SCCS, 2011

Type	CAS-no.	INCI-name or trade name	Covered by SCCS opinion	Allergy potential	Allergy potential fragrances (based on SCCS no. 1459, 2012)			Sensitisation rate (p value) Simonsen et al., 2013	Reference (except for SCCS opinion)
					Established human evidence Table 13-1	Animal evidence, EC 3 value (min; %) Table 13-2	SAR-evidence Table 13-3		
Fragrance	90-02-8	SALICYLALDEHYDE	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	115-71-9	ALPHA-SANTALOL	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	77-42-9	beta-SANTALOL	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	515-03-7	SCLAREOL	SCCS/1459/11	Established contact allergen in humans	Human +				SCCS, 2011
Fragrance	8000-41-7	TERPINEOL	SCCS/1459/11	Established contact allergen in humans	Human +				SCCS, 2011
Fragrance	10482-56-1	alpha-TERPINEOL	SCCS/1459/11	Established contact allergen in humans	Human +				SCCS, 2011
Fragrance	98-55-5	alpha-TERPINEOL	SCCS/1459/11	Established contact allergen in humans	Human +				SCCS, 2011

Type	CAS-no.	INCI-name or trade name	Covered by SCCS opinion	Allergy potential	Allergy potential fragrances (based on SCCS no. 1459, 2012)			Sensitisation rate (p value) Simonsen et al., 2013	Reference (except for SCCS opinion)
					Established human evidence Table 13-1	Animal evidence, EC 3 value (min; %) Table 13-2	SAR-evidence Table 13-3		
Fragrance	586-62-9	Terpinolene	SCCS/1459/11	Established contact allergen in humans	Human +				SCCS, 2011
Fragrance	54464-57-2	TETRAMETHYL ACETYLOCTAHYDRON APHTHALENES	SCCS/1459/11	Established contact allergen in humans	Human +				SCCS, 2011
Fragrance	54464-59-4	TETRAMETHYL ACETYLOCTAHYDRON APHTHALENES	SCCS/1459/11	Established contact allergen in humans	Human +				SCCS, 2011
Fragrance	68155-66-8	TETRAMETHYL ACETYLOCTAHYDRON APHTHALENES	SCCS/1459/11	Established contact allergen in humans	Human +				SCCS, 2011
Fragrance	68155-67-9	TETRAMETHYL ACETYLOCTAHYDRON APHTHALENES	SCCS/1459/11	Established contact allergen in humans	Human +				SCCS, 2011
Fragrance	103694-68-4	TRIMETHYL-BENZENEPROPANOL	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	121-33-5	VANILLIN	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011

Type	CAS-no.	INCI-name or trade name	Covered by SCCS opinion	Allergy potential	Allergy potential fragrances (based on SCCS no. 1459, 2012)			Sensitisation rate (p value) Simonsen et al., 2013	Reference (except for SCCS opinion)
					Established human evidence Table 13-1	Animal evidence, EC 3 value (min; %) Table 13-2	SAR-evidence Table 13-3		
Fragrance	83863-30-3	CANANGA ODORATA FLOWER OIL	SCCS/1459/11	Established contact allergen in humans	Human +++				SCCS, 2011
Fragrance	8006-81-3	CANANGA ODORATA LEAF OIL	SCCS/1459/11	Established contact allergen in humans	Human +++				SCCS, 2011
Fragrance	92201-55-3	CEDRUS ATLANTICA BARK OIL	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	8000-27-9	CEDRUS ATLANTICA BARK OIL	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	8007-80-5	CINNAMOMUM CASSIA LEAF OIL	SCCS/1459/11	Established contact allergen in humans	Human ++ (r.t.)				SCCS, 2011
Fragrance	84649-98-9	CINNAMOMUM CASSIA BARK OIL	SCCS/1459/11	Established contact allergen in humans	Human ++ (r.t.)				SCCS, 2011
Fragrance	72968-50-4	CITRUS AURANTIUM AMARA FLOWER OIL	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011

Type	CAS-no.	INCI-name or trade name	Covered by SCCS opinion	Allergy potential	Allergy potential fragrances (based on SCCS no. 1459, 2012)			Sensitisation rate (p value) Simonsen et al., 2013	Reference (except for SCCS opinion)
					Established human evidence Table 13-1	Animal evidence, EC 3 value (min; %) Table 13-2	SAR-evidence Table 13-3		
Fragrance	8016-38-4	CITRUS AURANTIUM AMARA PEEL OIL	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	89957-91-5	CITRUS BERGAMIA PEEL OIL EXPRESSED	SCCS/1459/11	Established contact allergen in humans	Human + (r.t.)				SCCS, 2011
Fragrance	84929-31-7	CITRUS LIMONUM PEEL OIL EXPRESSED	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	97766-30-8	CITRUS SINENSIS PEEL OIL EXPRESSED	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	8028-48-6	CITRUS SINENSIS PEEL EXTRACT	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	89998-14-1	CYMBOPOGON CITRATUS LEAF OIL	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	8007-02-1	CYMBOPOGON CITRATUS LEAF	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011

Type	CAS-no.	INCI-name or trade name	Covered by SCCS opinion	Allergy potential	Allergy potential fragrances (based on SCCS no. 1459, 2012)			Sensitisation rate (p value) Simonsen et al., 2013	Reference (except for SCCS opinion)
					Established human evidence Table 13-1	Animal evidence, EC 3 value (min; %) Table 13-2	SAR-evidence Table 13-3		
Fragrance	89998-16-3	CYMBOPOGON SCHOENANTHUS OIL	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	92502-70-0	EUCALYPTUS SPECIES LEAF OIL	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	8000-48-4	EUCALYPTUS SPECIES LEAF EXTRACT	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	8000-34-8	EUGENIA CARYOPHYLLUS FLOWER OIL	SCCS/1459/11	Established contact allergen in humans	Human +++				SCCS, 2011
Fragrance	90028-67-4	EVERNIA FURFURACEA EXTRACT (Tree moss)	SCCS/1459/11	Established contact allergen in humans	Human +++				SCCS, 2011 EU Cosmetics Regulation article 19,1 and Annex III (subject to declaration)
Fragrance	90028-68-5	EVERNIA PRUNASTRI EXTRACT (Oak moss)	SCCS/1459/11	Established contact allergen in humans	Human +++			2.5	SCCS, 2011; Simonsen et al., 2013 EU Cosmetics Regulation article 19,1 and Annex III (subject to declaration)

Type	CAS-no.	INCI-name or trade name	Covered by SCCS opinion	Allergy potential	Allergy potential fragrances (based on SCCS no. 1459, 2012)			Sensitisation rate (p value) Simonsen et al., 2013	Reference (except for SCCS opinion)
					Established human evidence Table 13-1	Animal evidence, EC 3 value (min; %) Table 13-2	SAR-evidence Table 13-3		
Fragrance	84776-64-7	JASMINUM GRANDIFLORUM FLOWER EXTRACT	SCCS/1459/11	Established contact allergen in humans	Human +++				SCCS, 2011
Fragrance	90045-94-6	JASMINUM OFFICINALE FLOWER OIL	SCCS/1459/11	Established contact allergen in humans	Human +++				SCCS, 2011
Fragrance	8022-96-6	JASMINUM OFFICINALE OIL	SCCS/1459/11	Established contact allergen in humans	Human +++				SCCS, 2011
Fragrance	8000-27-9	JUNIPERUS VIRGINIANA	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	85085-41-2	JUNIPERUS VIRGINIANA	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	8002-41-3	LAURUS NOBILIS	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	8007-48-5	LAURUS NOBILIS	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011

Type	CAS-no.	INCI-name or trade name	Covered by SCCS opinion	Allergy potential	Allergy potential fragrances (based on SCCS no. 1459, 2012)			Sensitisation rate (p value) Simonsen et al., 2013	Reference (except for SCCS opinion)
					Established human evidence Table 13-1	Animal evidence, EC 3 value (min; %) Table 13-2	SAR-evidence Table 13-3		
Fragrance	84603-73-6	LAURUS NOBILIS	SCCS/1459/11	Established contact allergen in humans	Human + (r.t.)				SCCS, 2011
Fragrance	91722-69-9	LAVANDULA HYBRIDA	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	84776-65-8	LAVANDULA OFFICINALIS	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	8006-90-4	MENTHA PIPERITA	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	84082-70-2	MENTHA PIPERITA	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	84696-51-5	MENTHA SPICATA	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	8007-00-9	MYROXYLON PEREIRAE	SCCS/1459/11	Established contact allergen in humans	Human ++++			1.0	SCCS, 2011; Simonsen et al., 2013

Type	CAS-no.	INCI-name or trade name	Covered by SCCS opinion	Allergy potential	Allergy potential fragrances (based on SCCS no. 1459, 2012)			Sensitisation rate (p value) Simonsen et al., 2013	Reference (except for SCCS opinion)
					Established human evidence Table 13-1	Animal evidence, EC 3 value (min; %) Table 13-2	SAR-evidence Table 13-3		
Fragrance	diverse	NARCISSUS SPP.	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	90082-51-2	PELARGONIUM GRAVEOLENS	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	8000-46-2	PELARGONIUM GRAVEOLENS	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	90082-72-7	PINUS MUGO/PUMILA	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	97676-05-6	PINUS MUGO/PUMILA	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	8014-09-3	POGOSTEMON CABLIN	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	84238-39-1	POGOSTEMON CABLIN	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011

Type	CAS-no.	INCI-name or trade name	Covered by SCCS opinion	Allergy potential	Allergy potential fragrances (based on SCCS no. 1459, 2012)			Sensitisation rate (p value) Simonsen et al., 2013	Reference (except for SCCS opinion)
					Established human evidence Table 13-1	Animal evidence, EC 3 value (min; %) Table 13-2	SAR-evidence Table 13-3		
Fragrance	diverse	ROSE FLOWER OIL	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011
Fragrance	84787-70-2	SANTALUM ALBUM	SCCS/1459/11	Established contact allergen in humans	Human +++				SCCS, 2011
Fragrance	8006-87-9	SANTALUM ALBUM	SCCS/1459/11	Established contact allergen in humans	Human +++				SCCS, 2011
Fragrance	8006-64-2	TURPENTINE	SCCS/1459/11	Established contact allergen in humans	Human ++++				SCCS, 2011
Fragrance	9005-90-7	TURPENTINE (oil)	SCCS/1459/11	Established contact allergen in humans	Human ++++				SCCS, 2011
Fragrance	8052-14-0	TURPENTINE (oil)	SCCS/1459/11	Established contact allergen in humans	Human ++++				SCCS, 2011
Fragrance	8024-12-2	VERBENA ABSOLUTE	SCCS/1459/11	Established contact allergen in humans	Human ++				SCCS, 2011

Type	CAS-no.	INCI-name or trade name	Covered by SCCS opinion	Allergy potential	Allergy potential fragrances (based on SCCS no. 1459, 2012)			Sensitisation rate (p value) Simonsen et al., 2013	Reference (except for SCCS opinion)
					Established human evidence Table 13-1	Animal evidence, EC 3 value (min; %) Table 13-2	SAR-evidence Table 13-3		
Fragrance	7493-74-5	Allyl phenoxyacetate	SCCS/1459/11	Established contact allergen in animals	None	3.1			SCCS, 2011
Fragrance	18127-01-0	4-TERT-BUTYLDIHYDROCINNAMALDEHYDE	SCCS/1459/11	Established contact allergen in animals	None	4.3			SCCS, 2011
Fragrance	103-95-7	CYCLAMEN ALDEHYDE	SCCS/1459/11	Established contact allergen in animals	None	22			SCCS, 2011
Fragrance	103-50-4	Dibenzyl ether	SCCS/1459/11	Established contact allergen in animals	None	6.3			SCCS, 2011
Fragrance	116-26-7	2,3-DIHYDRO-2,2,6-TRIMETHYLBENZALDEHYDE	SCCS/1459/11	Established contact allergen in animals	Limited	7.5			SCCS, 2011
Fragrance	6728-26-3	trans-2-Hexenal	SCCS/1459/11	Established contact allergen in animals	None	2.6			SCCS, 2011
Fragrance	17373-89-6	2-Hexylidene cyclopentanone	SCCS/1459/11	Established contact allergen in animals	None	2.4			SCCS, 2011

Type	CAS-no.	INCI-name or trade name	Covered by SCCS opinion	Allergy potential	Allergy potential fragrances (based on SCCS no. 1459, 2012)			Sensitisation rate (p value) Simonsen et al., 2013	Reference (except for SCCS opinion)
					Established human evidence Table 13-1	Animal evidence, EC 3 value (min; %) Table 13-2	SAR-evidence Table 13-3		
Fragrance	6259-76-3	HEXYL SALICYLATE	SCCS/1459/11	Established contact allergen in animals	Negative	0.18			SCCS, 2011
Fragrance	6658-48-6	3-(P-CUMENYL)-2-METHYLPROPIONALD EHYDE	SCCS/1459/11	Established contact allergen in animals	None	9.5			SCCS, 2011
Fragrance	1335-66-6	Isocyclocitra	SCCS/1459/11	Established contact allergen in animals	None	7.3			SCCS, 2011
Fragrance	101-39-3	METHYLCINNAMIC ALDEHYDE	SCCS/1459/11	Established contact allergen in animals	None	4.5			SCCS, 2011
Fragrance	1205-17-0	METHYLENEDIOXYPH ENYL METHYLPROPANAL	SCCS/1459/11	Established contact allergen in animals	None	16.4			SCCS, 2011
Fragrance	110-41-8	METHYLUNDECANAL	SCCS/1459/11	Established contact allergen in animals	None	10			SCCS, 2011
Fragrance	93-51-6	2-Methoxy-4-methylphenol	SCCS/1459/11	Established contact allergen in animals	None	5.8			SCCS, 2011

Type	CAS-no.	INCI-name or trade name	Covered by SCCS opinion	Allergy potential	Allergy potential fragrances (based on SCCS no. 1459, 2012)			Sensitisation rate (p value) Simonsen et al., 2013	Reference (except for SCCS opinion)
					Established human evidence Table 13-1	Animal evidence, EC 3 value (min; %) Table 13-2	SAR-evidence Table 13-3		
Fragrance	5462-06-6	METHOXYHYDRATROPALDEHYDE	SCCS/1459/11	Established contact allergen in animals	None	23.6			SCCS, 2011
Fragrance	111-80-8	METHYLOCTINE CARBONATE	SCCS/1459/11	Established contact allergen in animals	Limited	2.5			SCCS, 2011
Fragrance	2111-75-3	PERILLALDEHYDE	SCCS/1459/11	Established contact allergen in animals	None	8.1			SCCS, 2011
Fragrance	122-78-1	PHENYLACETALDEHYDE	SCCS/1459/11	Established contact allergen in animals	Limited	3			SCCS, 2011
Fragrance	91770-14-8	JASMINUM SAMBAC FLOWER EXTRACT	SCCS/1459/11	Established contact allergen in animals	None	35.4			SCCS, 2011
Fragrance	7779-50-2	AMBRETTOLIDE	SCCS/1459/11	Likely contact allergen	Limited	None	SAR +		SCCS, 2011
Fragrance	499-75-2	CARVACROL	SCCS/1459/11	Likely contact allergen	Limited	None	SAR +		SCCS, 2011
Fragrance	8016-20-4	CITRUS PARADISI JUICE	SCCS/1459/11	Likely contact allergen	None	R43	n.a.		SCCS, 2011

Type	CAS-no.	INCI-name or trade name	Covered by SCCS opinion	Allergy potential	Allergy potential fragrances (based on SCCS no. 1459, 2012)			Sensitisation rate (p value) Simonsen et al., 2013	Reference (except for SCCS opinion)
					Established human evidence Table 13-1	Animal evidence, EC 3 value (min; %) Table 13-2	SAR-evidence Table 13-3		
Fragrance	122-03-2	CUMINALDEHYDE	SCCS/1459/11	Likely contact allergen	Limited	None	SAR +		SCCS, 2011
Fragrance	502-72-7	CYCLOPENTADECANONE	SCCS/1459/11	Likely contact allergen	Limited	None	SAR +		SCCS, 2011
Fragrance	71048-82-3	TRANS-ROSE KETONE-3	SCCS/1459/11	Likely contact allergen	None	R43	SAR +		SCCS, 2011
Fragrance	68039-49-6	2,4-DIMETHYL-3-CYCLOHEXENE CARBOXALDEHYDE	SCCS/1459/11	Likely contact allergen	Limited	None	SAR +		SCCS, 2011
Fragrance	68737-61-1	DIMETHYLTETRAHYDRO BENZALDEHYDE	SCCS/1459/11	Likely contact allergen	Limited	None	SAR +		SCCS, 2011
Fragrance	121-32-4	ETHYL VANILLIN	SCCS/1459/11	Likely contact allergen	Limited	None	SAR +		SCCS, 2011
Fragrance	120-57-0	HELIOTROPINE	SCCS/1459/11	Likely contact allergen	Limited	None	SAR ++		SCCS, 2011
Fragrance	87-20-7	ISOAMYL SALICYLATE	SCCS/1459/11	Likely contact allergen	Limited	None	SAR +		SCCS, 2011
Fragrance	33407-62-4	ISOLONGIFOLENEKETONE	SCCS/1459/11	Likely contact allergen	Limited	None	SAR +		SCCS, 2011

Type	CAS-no.	INCI-name or trade name	Covered by SCCS opinion	Allergy potential	Allergy potential fragrances (based on SCCS no. 1459, 2012)			Sensitisation rate (p value) Simonsen et al., 2013	Reference (except for SCCS opinion)
					Established human evidence Table 13-1	Animal evidence, EC 3 value (min; %) Table 13-2	SAR-evidence Table 13-3		
Fragrance	475-20-7	LONGIFOLENE	SCCS/1459/11	Likely contact allergen	None	R43	SAR +		SCCS, 2011
Fragrance	68917-18-0	MENTHA ARVENSIS LEAF OIL	SCCS/1459/11	Likely contact allergen	None	R43	SAR +		SCCS, 2011
Fragrance	3613-30-7	METHOXYCITRONELLAL	SCCS/1459/11	Likely contact allergen	Limited	None	SAR +		SCCS, 2011
Fragrance	103-26-4	METHYL CINNAMATE	SCCS/1459/11	Likely contact allergen	Limited	None	SAR ++		SCCS, 2011
Fragrance	55599-63-8	METHYLIONANTHEM E	SCCS/1459/11	Likely contact allergen	Limited	None	SAR +		SCCS, 2011
Fragrance	79-69-6	5-METHYL-alpha-IONONE	SCCS/1459/11	Likely contact allergen	Limited	None	SAR +		SCCS, 2011
Fragrance	123-35-3	MYRCENE	SCCS/1459/11	Likely contact allergen	Limited	None	SAR ++		SCCS, 2011
Fragrance	515-00-4	MYRTENOL	SCCS/1459/11	Likely contact allergen	Limited	None	SAR +		SCCS, 2011
Fragrance	106-25-2	NEROL	SCCS/1459/11	Likely contact allergen	Limited	None	SAR ++		SCCS, 2011
Fragrance	7212-44-4	Nerolidol ISOMERS	SCCS/1459/11	Likely contact allergen	Limited	None	SAR ++		SCCS, 2011

Type	CAS-no.	INCI-name or trade name	Covered by SCCS opinion	Allergy potential	Allergy potential fragrances (based on SCCS no. 1459, 2012)			Sensitisation rate (p value) Simonsen et al., 2013	Reference (except for SCCS opinion)
					Established human evidence Table 13-1	Animal evidence, EC 3 value (min; %) Table 13-2	SAR-evidence Table 13-3		
Fragrance	128-51-8	NOPYL ACETATE	SCCS/1459/11	Likely contact allergen	Limited	None	SAR +		SCCS, 2011
Fragrance	150-86-7	PHYTOL	SCCS/1459/11	Likely contact allergen	Limited	None	SAR +		SCCS, 2011
Fragrance	6812-78-8	RHODINOL	SCCS/1459/11	Likely contact allergen	Limited	None	SAR +		SCCS, 2011
Fragrance	39872-57-6	trans-ROSE KETONE-5	SCCS/1459/11	Likely contact allergen	Limited	None	SAR ++		SCCS, 2011
Fragrance		Sorbitan sesquioleate						2.5	Simonsen et al., 2013

TABLE 39

GROSS LIST OF POTENTIALLY ALLERGENIC SUBSTANCES WHICH IS USED AS A STARTING POINT FOR THE SURVEY IN THIS PROJECT

“OX.” = OXIDISED; “NON-OX.” = NON-OXIDISED; “R.T.” = RARELY TESTED, += UP TO 10 POSITIVE TEST REACTIONS REPORTED, ++= 11 TO 100, +++= 101-1000, ++++= >1000 ACCORDING TO SCCS NO. 1459/11 (2012).

“HARM. CLASS.” = HARMONISED CLASSIFICATION.

* THESE PRESERVATIVES ARE NO LONGER ALLOWED IN COSMETIC PRODUCTS, BUT ARE ALLOWED FOR USE IN TOYS.

REGARDING THE SAR CATORIES: NOT SENSITISING (o); POSSIBLE SENTISISER (+); PREDICTED SENSITISER (++); NOT PREDICTABLE (N.P.) ACCORDING TO SCCS NO. 1459/11 (2012).

Appendix 3: Identified colourants, preservatives, fragrances and UV filters in the cosmetic products

In this appendix, the colourants, preservatives, fragrances and UV filters which are identified in the survey of the 157 cosmetic products are presented. In total, 4 different tables for each group of substances are thus presented and it is stated which of these that are considered to be potentially allergenic (i.e. included in the gross list). In total the following are identified:

- 55 different colourants
- 15 different preservatives
- 31 different fragrances, hereof one entry is the generic term "perfume" and 21 substances which are listed with the function "perfuming" in the CosIng database
- 14 different UV filters

Colourants	Identified in number of products	Potentially allergenic*
Aluminium hydroxide	1	
Barium sulfate	1	
Calcium stearate	1	
CI 10316	2	
CI 12085	2	
CI 12490	6	
CI 14700	2	
CI 14720	1	
CI 15850	55	
CI 15850:1	2	
CI 15880	4	
CI 15985	12	
CI 16035	10	
CI 16255	1	
CI 17200	4	
CI 18035	1	
CI 19140	40	
CI 19410	1	

Colourants	Identified in number of products	Potentially allergenic*
CI 42051	4	
CI 42090	48	
CI 42090:2	1	
CI 45380	1	
CI 45410	28	
CI 45410:1	2	
CI 45410:2	1	
CI 45430:1	2	
CI 47005	10	
CI 47005:1	1	
CI 60725	1	
CI 73360	6	
CI 74160	6	
CI 75470	9	
CI 77000	18	
CI 77007	26	
CI 77019	3	
CI 77163	5	
CI 77266	5	
CI 77268:1	4	
CI 77288	8	
CI 77289	2	
CI 77400	1	
CI 77442	1	
CI 77491	31	

Colourants	Identified in number of products	Potentially allergenic*
CI 77492	38	
CI 77499	47	
CI 77510	12	
CI 77742	14	
CI 77891	48	
Kaolin	2	
Magnesium stearate	10	
Pigment	1	
Titanium dioxide	52	
Zinc oxide	4	
Zinc stearate	4	

TABLE 40

USED COLOURANTS IN THE 157 COSMETIC PRODUCTS FROM THE SURVEY. IF THE COLOURANT IS POTENTIALLY ALLERGENIC, IT MEANS THAT THE SUBSTANCE IS INCLUDED IN THE GROSS LIST OF POTENTIALLY ALLERGENIC SUBSTANCES.

* A BLANK FIELD MEANS EITHER THAT THE SUBSTANCE IS NOT ALLERGENIC OR THAT NO INFORMATION ON THE ALLERGENIC PROPERTIES OF THE SUBSTANCE WAS FOUND.

Preservatives	Identified in number of products	Potentially allergenic*
Benzoic acid	22	
Benzyl alcohol	1	Yes
Chlorhexidine digluconate	2	
Chlorophenesin	1	
Dehydroacetic acid	19	
Ethylparaben	2	
Imidazolidinyl urea	1	Yes
Methylparaben	5	
Phenoxyethanol	103	
Polyaminopropyl biguanide	3	Yes
Potassium sorbate	15	
Propylparaben	18	
Sodium benzoate	40	
Sodium dehydroacetate	1	
Sorbic acid	5	
Benzoic acid	22	

TABLE 41

USED PRESERVATIVES IN THE 157 COSMETIC PRODUCTS FROM THE SURVEY. IF THE PRESERVATIVE IS POTENTIALLY ALLERGENIC, IT MEANS THAT THE SUBSTANCE IS INCLUDED IN THE GROSS LIST OF POTENTIALLY ALLERGENIC SUBSTANCES.

* A BLANK FIELD MEANS EITHER THAT THE SUBSTANCE IS NOT ALLERGENIC OR THAT NO INFORMATION ON THE ALLERGENIC PROPERTIES OF THE SUBSTANCE WAS FOUND.

Fragrances	Identified in number of products	Potentially allergenic*
Acetyl tributyl citrate	9	
Aroma	3	
Benzyl alcohol	1	Yes
Calendula officinali flower extract	1	
Caprylic/capric triglyceride	4	
Cera alba	19	
Citral	1	Yes
Citronellol	1	Yes
Cocos nucifera oil	2	
Coumarin	1	Yes
Ethyl ricinoleate	1	
Eethylhexyl palmitate	2	
Eugenol	1	Yes
Euphorbia Cerifera Cera	2	
Geraniol	2	Yes
Glyceryl oleate	1	
Glycine soja oil	1	
Hexyl benzoate	1	
Hydrogenated polydecene	3	
Isopropyl alcohol	1	
Isopropyl myristate	2	
Isopropyl palmitate	3	
Limonene	3	Yes
Linalool	2	Yes
Linum usitassimum seed oil	1	

Fragrances	Identified in number of products	Potentially allergenic*
N-butyl alcohol	1	
Octyldodecanol	6	
Olea europaea fruit oil	4	
Olea europaea leaf extract	2	
Parfum	22	(perhaps)
Ricinus communis seed oil	13	

TABLE 42

USED FRAGRANCES IN THE 157 COSMETIC PRODUCTS FROM THE SURVEY. IF THE FRAGRANCE IS POTENTIALLY ALLERGENIC, IT MEANS THAT THE SUBSTANCE IS INCLUDED IN THE GROSS LIST OF POTENTIALLY ALLERGENIC SUBSTANCES.

* A BLANK FIELD MEANS EITHER THAT THE SUBSTANCE IS NOT ALLERGENIC OR THAT NO INFORMATION ON THE ALLERGENIC PROPERTIES OF THE SUBSTANCE WAS FOUND.

UV filters	Identified in number of products	Potentially allergenic*
Benzophenone-3	2	Yes
Bis-ethylhexyloxyphenol methoxyphenyl triazine	17	
Butyl methoxydibenzoylmethane	15	
Diethylamino hydroxybenzoyl hexyl benzoate	14	
Diethylhexyl butamido triazone	17	
Drometrizole trisulfoxane	6	Yes
Ethylhexyl methoxycinnamate	1	
Ethylhexyl salicylate	10	
Ethylhexyl triazone	18	
Homosalate	3	
Methylene bis-benzotriazolyl tetramethylbutylphenol	2	
Ocotrylene	9	Yes
Phenylbenzimidazole sulfonic acid	3	
Polysilicone-15	1	
Sodium phenylbenzimidazole sulfonate	1	
Terephthalylidene dicamphor sulfonic acid	6	
Titanium dioxide	52	

TABLE 43

USED UV FILTERS IN THE 157 COSMETIC PRODUCTS FROM THE SURVEY. IF THE UV FILTER IS POTENTIALLY ALLERGENIC, IT MEANS THAT THE SUBSTANCE IS INCLUDED IN THE GROSS LIST OF POTENTIALLY ALLERGENIC SUBSTANCES.

* A BLANK FIELD MEANS EITHER THAT THE SUBSTANCE IS NOT ALLERGENIC OR THAT NO INFORMATION ON THE ALLERGENIC PROPERTIES OF THE SUBSTANCE WAS FOUND.

Appendix 4: Screening for analytical methods for ‘other’ fragrances

In an opinion on fragrances in cosmetics (SCCS no. 1459, 2012), SCCS (Scientific Committee for Consumer Safety) has prepared a list of 82 established contact allergens in humans (Table 13-1 from SCCS no. 1459, 2012). The list of the 82 established contact allergens covers 54 individual chemicals and 28 natural extracts. SCCS has assessed these 82 fragrances to be established contact allergens as human cases of contact allergy to these substances have been published for all these fragrances. Among these 82 fragrances, the 26 fragrances subject to declaration are also included and they are distributed as 24 individual chemicals and 2 natural extracts.

As fragrances in the form of natural extracts can consist of a large number of different chemicals, it was in advance decided to exclude these substances due to analytical reasons as an analysis is complicated when it is not pure substances. Therefore, it was decided that focus was to be on the 54 individual fragrances deducted the 24 fragrances subject to declaration. For these in total 30 fragrances (which cover in total 42 different CAS numbers), a screening for possible analytical methods has been made as no standard analyses for these “other” fragrances exist. The screening was undertaken through a search on the internet and the following is described for each individual substance (CAS number):

- Synonyms
- Chemical structure for the substance
- Molecular weight/molecular formula (the reference here is ChemIDPlus (Toxnet), if nothing else is stated)
- Analytical methods
- Matrix
- Accessibility of the reference substance as well as a price for this, if any

In this appendix, the information which was identified for these “other” fragrances is reported. Data is presented in a table for each CAS number. Please note that more CAS numbers for the same substance name exist for more of the fragrances.

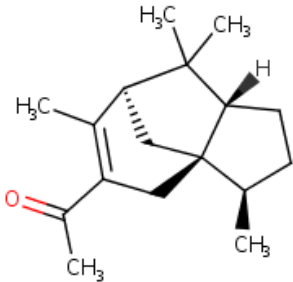
CAS no. 32388-55-9	ACETYLCEDRENE	
Synonyms	Methyl cedryl ketone	
Molecular weight	246.39 g/mol (C ₁₇ H ₂₆ O)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC-MS specific method ⁷		The substance is listed as peak no. 12 in the chromatogram
GC-MS ⁸		Is available in the NIST library
GC ⁹		Specific data regarding column, temperature etc. is described.
Availability and prices		
Price reference substance	Comments	
	No prices or possibilities to buy the substance as a reference substance, which has been identified.	

TABLE 44
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

⁷ <http://www.agilent.com/cs/library/chromatograms/425D.jpg>

⁸ <http://webbook.nist.gov/cgi/cbook.cgi?ID=C80449587&Mask=2000%20-%20Gas-Chrom>

⁹ <http://www.sigmaaldrich.com/catalog/search?term=methyl+cedryl+ketone&interface=All&N=0+220003051&mode=partialmax&lang=en®ion=DK&focus=analytical>

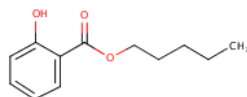
CAS no. 2050-08-0	AMYL SALICYLATE	
Synonyms	n-Pentyl-2-hydroxybenzoate, Pentyl Salicylate, Pentyl 2-hydroxybenzoate, 3-methylbutyl 2-hydroxybenzoate, pentyl 2-hydroxybenzoate	
Molecular weight	208.26 g/mol (C ₁₂ H ₁₆ O ₃)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC-MS ¹⁰	Cosmetics?	It is not clear whether amyl salicylate is comprised by the method (not a free article)
GC-MS ¹¹	Bark	Amyl salicylate is not directly mentioned, but 'similar' substances are
GC-MS ¹²		Is available in the NIST library
HS-SPME-GC-MS ¹³		Description of HeadSpace Solid Phase MicroExtraction GC-MS method, but amyl salicylate is not mentioned directly.
		Is mentioned in Danish EPA survey no. 92, but the analytical methods are not described ¹⁴ .
Availability and prices		
Price reference substance	Comments	
Not available	Sigma-Aldrich ¹⁵ - was not available at the time of search.	

TABLE 45
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

¹⁰ <http://onlinelibrary.wiley.com/doi/10.1034/j.1600-0536.2002.470606.x/abstract;jsessionid=1A9Fo4BEA235692A5CFF2053A75B1A7D.f02t02?userIsAuthenticated=false&deniedAccessCustomisedMessage>

¹¹ <http://www.ncbi.nlm.nih.gov/pubmed/12112739>

¹² <http://webbook.nist.gov/cgi/cbook.cgi?ID=C2050080&Units=SI&Mask=2000%20-%20Gas-Chrom>

¹³ http://www.researchgate.net/publication/49808767_Determination_of_volatile_organic_compounds_in_recycled_polyethylene_terephthalate_and_high-density_polyethylene_by_headspace_solid_phase_microextraction_gas_chromatography_mass_spectrometry_to_evaluate_the_efficiency_of_recycling_processes

¹⁴ <http://www2.mst.dk/udgiv/publikationer/2008/978-87-7052-742-2/pdf/978-87-7052-743-9.pdf>

¹⁵ <http://www.sigmaaldrich.com/catalog/search?term=2050-08-o&interface=CAS%20No.&N=O&mode=partialmax&lang=en®ion=DK&focus=product>

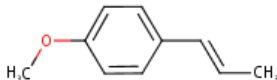
CAS no. 4180-23-8	Trans-ANETHOLE	
Synonyms	1-(4-METHOXYPHENYL)-1-PROPENE 1-METHOXY-4-(1-PROPENYL)BENZENE PARA METHOXY ALPHA PHENYL PROPENE P-METHOXYPROPENYLBENZENE P-PROPENYLANISOLE P-PROPENYLPHENYL METHYL ETHER	
Molecular weight	148.20 g/mol (C ₁₀ H ₁₂ O)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC-MC ¹⁶		Is available in the NIST library
GC-FID detektor ¹⁷ GC-MS	Dried plants	(E)-anethole is identified by the listed methods
GC-MS ¹⁸	Essential oils	The method is used in the Danish EPA survey no. 92 concerning essential oils. Extraction with dichloromethane.
Availability and prices		
Price reference substance	Comments	
210 DKK / 1 ml	Sigma-Aldrich ¹⁹ . The price is for an 'analytical standard'.	

TABLE 46
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

¹⁶ <http://webbook.nist.gov/cgi/cbook.cgi?ID=C4180238&Units=SI&Mask=2000%20-%20Gas-Chrom>

¹⁷ <http://www.sciencedirect.com/science/article/pii/S0308814605004450>

¹⁸ <http://www2.mst.dk/common/Udgivramme/Frame.asp?http://www2.mst.dk/udgiv/publikationer/2008/978-87-7052-742-2/html/helepubl.htm>

¹⁹ <http://www.sigmaaldrich.com/catalog/search?term=4180-23-8&interface=CAS%20No.&N=O&mode=partialmax&lang=en®ion=DK&focus=product>

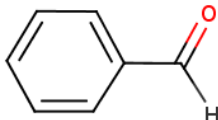
CAS no. 100-52-7	BENZALDEHYDE	
Synonyms	Benzene carbaldehyde Benzoic aldehyde	
Molecular weight	106.12 g/mol (C ₇ H ₆ O)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC-MS ²⁰	Aquatic acidic solution	The entire article is not available (not a free article)
GC-MS ²¹	Mushrooms	The entire article is not available (not a free article)
HP-GLC GLC-MS ²²	Gas phase over broccoli?	The entire article is not available (not a free article)
Availability and prices		
Price reference substance	Comments	
474 DKK / 5 ml	Sigma-Aldrich ²³ . The price is for an 'analytical standard'.	

TABLE 47
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

²⁰ <http://pubs.acs.org/doi/abs/10.1021/jf960079k>

²¹ <http://pubs.acs.org/doi/abs/10.1021/jf00047a034>

²² <http://pubs.acs.org/doi/abs/10.1021/jf00017a029>

²³ <http://www.sigmaaldrich.com/catalog/search?term=100-52-7&interface=CAS%20No.&N=0&mode=partialmax&lang=en®ion=DK&focus=product>

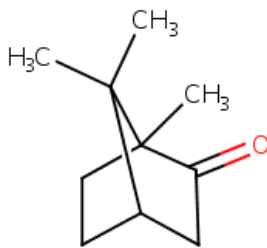
CAS no. 76-22-2	CAMPHOR (DL)	
Synonyms	1,7,7-Trimethylbicyclo[2.2.1]heptan-2-one Bornan-2-one	
Molecular weight	152.24 g/mol (C ₁₀ H ₁₆ O)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC-MS ²⁴		Is available in the NIST library
Not listed		ALS environmental describes camphor and can probably carry out a chemical analysis of the substances, but no analytical method is described ²⁵ .
GC-MS ²⁶	Essential oils	The method is used in the Danish EPA survey no. 92 concerning essential oils. Extraction with dichloromethane.
Availability and prices		
Price reference substance	Comments	
135 DKK / 50 g	Sigma-Aldrich ²⁷ . The price is for > 95% purity (GC).	

TABLE 48
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

²⁴ <http://webbook.nist.gov/cgi/cbook.cgi?ID=C76222&Mask=2000%20-%20Gas-Chrom#Gas-Chrom>

²⁵ http://www.caslab.com/Camphor_CAS_76-22-2/

²⁶ <http://www2.mst.dk/common/Udgivramme/Frame.asp?http://www2.mst.dk/udgiv/publikationer/2008/978-87-7052-742-2/html/lelepubl.htm>

²⁷ <http://www.sigmaaldrich.com/catalog/search?term=76-22-2&interface=CAS%20No.&N=O&mode=partialmax&lang=en®ion=DK&focus=product>

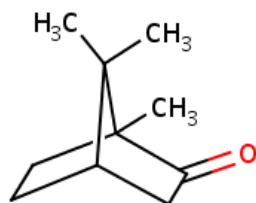
CAS no. 464-49-3	CAMPHOR (D-Camphor)	
Synonyms	2-Bornanone 2-Camphanone	
Molecular weight	152.24 g/mol (C ₁₀ H ₁₆ O)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC-MS ²⁸		Is available in the NIST library
SFE extraction + GC-MS Headspace SPME + GC-MS Hydrodistillation ²⁹		SFE (supercritical fluid extraction) and headspace SPME (solid phase micro-extraction) followed by GC-MS compared with hydrodistillation. By use of hydrodistillation it is not possible to detect the very volatile fragrances. Only abstract available.
GC-MS ³⁰	Essential oils	Possibly the same method as for DL-camphor, i.e. the method is used in the Danish EPA survey no. 92 concerning essential oils. Extraction with dichloromethane.
Availability and prices		
Price reference substance	Comments	
313 DKK / 100 mg	Sigma-Aldrich ³¹ . The price is for an 'analytical standard'.	

TABLE 49
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

²⁸ <http://webbook.nist.gov/cgi/cbook.cgi?ID=C464493&Mask=2000%20-%20Gas-Chrom>

²⁹ <http://link.springer.com/article/10.1365%2Fs10337-008-0921-y>

³⁰ <http://www2.mst.dk/common/Udgivramme/Frame.asp?http://www2.mst.dk/udgiv/publikationer/2008/978-87-7052-742-2/html/helepubl.htm>

³¹ <http://www.sigmaaldrich.com/catalog/search?term=464-49-3&interface=CAS%20No.&N=O+&mode=partialmax&lang=en®ion=DK&focus=product>

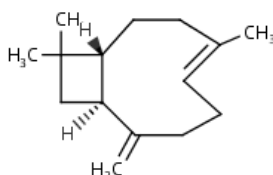
CAS no. 87-44-5	Beta-CARYOPHYLLENE (ox.)	
Synonyms	(-)-trans-Caryophyllene trans-(1R,9S)-8-Methylene-4,11,11-trimethylbicyclo[7.2.0]undec-4-ene CARYOPHYLLENE, ALPHA + BETA MIXT.	
Molecular weight	204.36 g/mol (C ₁₅ H ₂₄)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
Headspace SPME + GC ³²	Nanoemulsion	The best condition for extraction of betacaryphyllene was at 45 °C and 20 minutes sampling time. Only abstract available.
GC-MS ³³		The precise analytical methods are not mentioned in the abstract. Only abstract available.
Availability and prices		
Price reference substance	Comments	
Not available	Sigma-Aldrich ³⁴ . The substance was not available at the time of the search.	
7 \$ / 100 g	Cgherbals.com ³⁵	
540 DKK / 1 kg	Different suppliers and prices are available through this website ³⁶	

TABLE 50
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

³² <http://www.sciencedirect.com/science/article/pii/S0003267012002115>

³³ <http://www.sciencedirect.com/science/article/pii/S0278691505002863>

³⁴ <http://www.sigmaaldrich.com/catalog/search?term=87-44-5&interface=CAS%20No.&N=o+&mode=partialmax&lang=en®ion=DK&focus=product>

³⁵ http://cgherbals.com/aromatic-isolates/caryophyllene-98/p-7814780-10672932508-cat.html%20-%20variant_id=7814780-64192502345

³⁶ <http://www.thegoodscentscompany.com/data/rw1060851.html>

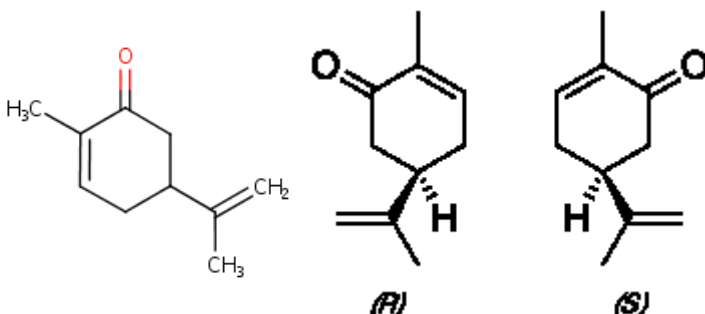
CAS no. 90-49-0	CARVONE	
Synonyms	2-Methyl-5-(1-methylethenyl)-2-cyclohexenone 2-Methyl-5-(prop-1-en-2-yl)cyclohex-2-enone	
Molecular weight	150.22 g/mol (C ₁₀ H ₁₄ O)	
Chemical structure	 <p>The image shows three chemical structures of Carvone. On the left is the general structure: a cyclohexenone ring with a methyl group at position 2 and an isopropenyl group at position 5. To the right are the two enantiomers, labeled (R) and (S), showing the stereochemistry at the chiral center (C5) with a hydrogen atom and an isopropenyl group.</p>	
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC ³⁷	Essential oils	By use of a Chiral column in order to distinguish between L- and D-carvone.
Availability and prices		
Price reference substance	Comments	
Not available	Not available at Sigma-Aldrich on this CAS no. (However, the R and S structures are)	
350 \$ / 1 gram	Ark Pharm Inc. ³⁸	
Price is not listed	LGC ³⁹	

TABLE 51
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

³⁷ <http://www.sigmaaldrich.com/technical-documents/articles/analytical/food-beverage/chiral-gc-carvone.html>

³⁸ <http://www.arkpharminc.com/web/products-detail.html?catalogno=AK111292>

³⁹ <http://www.lgcstandards.com/GB/en/Carvone/p/DRE-C11052000>

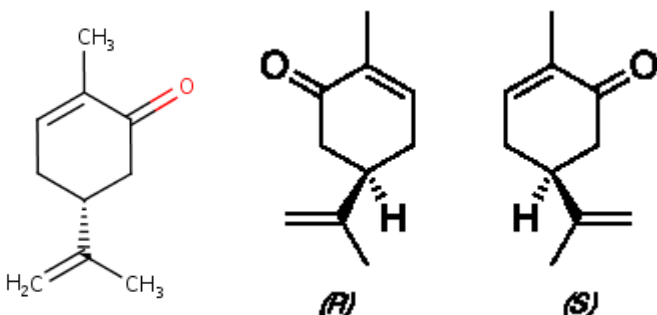
CAS no. 6485-40-1	(R) CARVONE	
Synonyms	(R)-5-Isopropenyl-2-methyl-2-cyclohexenone (-)-Carvone Carvol L-Carvone	
Molecular weight	150.22 g/mol (C ₁₀ H ₁₄ O)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC ⁴⁰	Essential oils	By use of a Chiral column in order to distinguish between L- and D-carvone.
Availability and prices		
Price reference substance	Comments	
635 DKK / 5 ml	Sigma-Aldrich ⁴¹ . The price is for an 'analytical standard'.	

TABLE 52
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

⁴⁰ <http://www.sigmaaldrich.com/technical-documents/articles/analytical/food-beverage/chiral-gc-carvone.html>

⁴¹ <https://www.sigmaaldrich.com/catalog/product/sial/22060?lang=en®ion=DK>

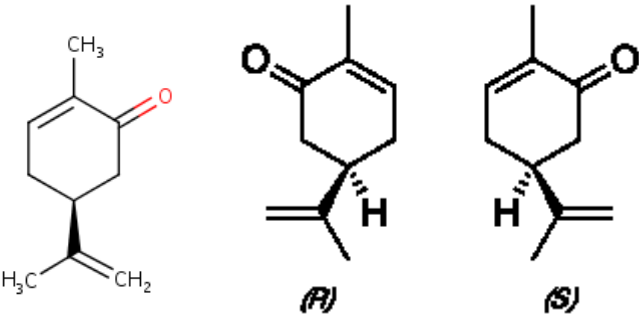
CAS no. 2244-16-8	(S) CARVONE	
Synonyms	(+) -Carvone (S)-5-Isopropenyl-2-methyl-2-cyclohexenone p-Mentha-6,8-dien-2-one D-Carvone	
Molecular weight	150.22 g/mol (C ₁₀ H ₁₄ O)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC ⁴²	Essential oils	By use of a Chiral column in order to distinguish between L- and D-carvone.
Availability and prices		
Price reference substance	Comments	
372 DKK / 25 ml 155 DKK / 1 ml	Sigma-Aldrich ⁴³ . The price is for an 'analytical standard'.	

TABLE 53
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

⁴² <http://www.sigmaaldrich.com/technical-documents/articles/analytical/food-beverage/chiral-gc-carvone.html>

⁴³ <https://www.sigmaaldrich.com/catalog/product/sial/22070?lang=en®ion=DK>

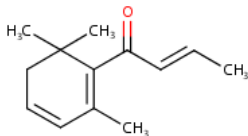
CAS no. 23696-85-7	ROSE KETONE-4 (DAMASCENONE)	
Synonyms	1-(2,6,6-Trimethyl-1,3-cyclohexadien-1-yl)-2-buten-1-one Damascenone 2-Buten-1-one, 1-(2,6,6-trimethyl-1,3-cyclohexadien-1-yl)- β-Damascenone	
Molecular weight	190.28 g/mol (C ₁₃ H ₁₈ O)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC ⁴⁴	Food	Only abstract available – description of method is not clear.
GC/MS/MS ⁴⁵	Essential oils (rose oil)	As the mixture consists of several terpenes and terpenoides with similar volatility and polarity, there is a need for more than just ordinary GC/MS for a better distinction between the substances. It is listed that MS/MS can give a better identification than MS. A long column of 30 metres is used.
Availability and prices		
Price reference substance	Comments	
626 DKK / 25 g	Sigma-Aldrich ⁴⁶	

TABLE 54
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

⁴⁴ <http://pubs.acs.org/doi/abs/10.1021/jf00004a028>

⁴⁵ <https://www.agilent.com/cs/library/applications/A01697.pdf>

⁴⁶ http://www.sigmaaldrich.com/catalog/product/aldrich/w342017?lang=en®ion=DK&gclid=CKTEoLi_xsgCFcXhcgodN5oA5A

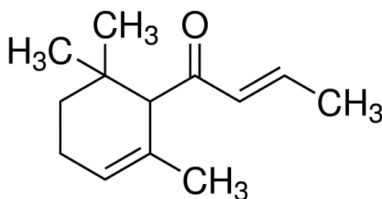
CAS no. 43052-87-5	alpha-DAMASCONE (TMCHB)	
Synonyms	1-(2,6,6-Trimethyl-2-cyclohexen-1-yl)-2-butenone 2-Buten-1-one, 1-(2,6,6-trimethyl-2-cyclohexen-1-yl)- α-Damascone 2,6,6-Trimethyl-1-crotonyl-2-cyclohexene	
Molecular weight	192.3 g/mol (C ₁₃ H ₂₀ O)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
Headspace SPME + GC-ITMS ⁴⁷	Red wine	The method stated is for β-Damascone.
Method not stated ⁴⁸		Not a free article. It is not possible to see which method is used, however, analysis of (R)-(+)- and (S)-(-)-.alpha.-damascone is described.
Availability and prices		
Price reference substance	Comments	
208 DKK / 1 ml	Sigma-Aldrich ⁴⁹ . The price is for an 'analytical standard'.	

TABLE 55
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

⁴⁷ <http://www.sciencedirect.com/science/article/pii/S030881460900466X>

⁴⁸ <http://pubs.acs.org/doi/abs/10.1021/ja00228a064>

⁴⁹ <http://www.sigmaaldrich.com/catalog/search?term=43052-87-5&interface=CAS%20No.&N=O+&mode=partialmax&lang=en®ion=DK&focus=product>

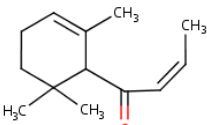
CAS no. 23726-94-5	alpha-DAMASCONE (TMCHB)	
Synonyms	1-(2,6,6-Trimethyl-2-cyclohexen-1-yl)-2-butenone 2-Buten-1-one, 1-(2,6,6-trimethyl-2-cyclohexen-1-yl)- α-Damascone (Z)-1-(2,6,6-trimethyl-2-cyclohexen-1-yl)-2-buten-1-one (Z)- α-Damascone	
Molecular weight	192.3 g/mol (C ₁₃ H ₂₀ O)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
Not identified		No analytical methods are identified for this CAS number.
Availability and prices		
Price reference substance	Comments	
Not identified	This CAS no. is not available at Sigma-Aldrich, but the previous CAS no. for alpha-Damascone is.	

TABLE 56
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

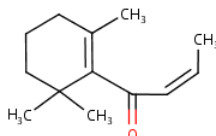
CAS no. 23726-92-3	cis-beta-DAMASCONE	
Synonyms	(Z)-β-Damascone 4-(2,6,6-Trimethylcyclohex-1-enyl)but-2-en-4-one cis-2-Buten-1-one, 1-(2,6,6-trimethyl-1-cyclohexen-1-yl)- (Z)-1-(2,6,6-Trimethyl-1-cyclohexen-1-yl)-2-buten-1-one	
Molecular weight	192.3 g/mol (C ₁₃ H ₂₀ O)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
Headspace SPME + GC-ITMS ⁵⁰	Red wine	The analytical method listed is for β-Damascone.
GC-MS ⁵¹	Apples	The analytical method listed is for β-Damascone.
Availability and prices		
Price reference substance	Comments	
705 DKK / 100 mg	Sigma-Aldrich ⁵² . The price is for an 'analytical standard'.	

TABLE 57
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

⁵⁰ <http://www.sciencedirect.com/science/article/pii/S030881460900466X>

⁵¹ <http://pubs.acs.org/doi/abs/10.1021/jfo0038a021>

⁵² <http://www.sigmaaldrich.com/catalog/product/sial/12301?lang=en®ion=DK>

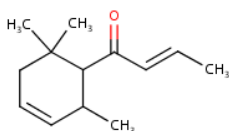
CAS no. 57378-68-4	delta-DAMASCONE	
Synonyms	1-(2,6,6-Trimethyl-3-cyclohexen-1-yl)-2-buten-1-one 2-Buten-1-one, 1-(2,6,6-trimethyl-3-cyclohexen-1-yl)- δ-Damascone	
Molecular weight	192.3 g/mol (C ₁₃ H ₂₀ O)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
Not identified		No analytical methods are identified for this CAS number.
Availability and prices		
Price reference substance	Comments	
230 DKK /1 ml	Sigma-Aldrich ⁵³ . The price is for an 'analytical standard'.	

TABLE 58
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

⁵³ <http://www.sigmaaldrich.com/catalog/search?term=57378-68-4&interface=CAS%20No.&N=O&mode=match%20partialmax&lang=en®ion=DK&focus=product>

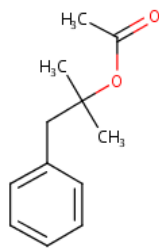
CAS no. 151-05-3	DIMETHYLBENZYL CARBINYL ACETATE (DMBCA)	
Synonyms	2-Benzyl-2-propyl acetate Benzylpropyl acetate α,α-Dimethylphenethyl acetate	
Molecular weight	192.26 g/mol (C ₁₂ H ₁₆ O)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC-MS ⁵⁴		Is available in the NIST library
Availability and prices		
Price reference substance	Comments	
446 DKK / 1 kg	Sigma-Aldrich ⁵⁵	

TABLE 59
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

⁵⁴ <http://webbook.nist.gov/cgi/cbook.cgi?ID=C151053&Units=SI&Mask=2000%20-%20Gas-Chrom>

⁵⁵ <http://www.sigmaaldrich.com/catalog/search?term=151-05-3&interface=CAS%20No.&N=O+&mode=partialmax&lang=en®ion=DK&focus=product>

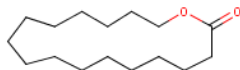
CAS no. 109-29-5	HEXADECANOLACTONE	
Synonyms	1,16-Hexadecalactone 16-Hydroxyhexadecanoic acid lactone Oxacycloheptadecan-2-one 16-Hexadecanolide Cyclohexadecanolideoxacycloheptadecan-2- Hexadecanoic-16-lactone Juniperic acid lactone	
Molecular weight	254.41 g/mol (C ₁₆ H ₃₀ O ₂)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC-MS ⁵⁶		Is available in the NIST library
GC-MS and GC ⁵⁷	Plant material (oils)	Analysis was carried out by GC-MS and GC. Two columns with different polarity (DB-Wax and HP-5) were used for a better separation of the substances.
GC-MS ⁵⁸		Retention times and NIST spectra are listed for the substance.
Availability and prices		
Price reference substance	Comments	
337 DKK / 100 mg	Sigma-Aldrich ⁵⁹	

TABLE 6o
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

⁵⁶ <http://webbook.nist.gov/cgi/cbook.cgi?ID=C109295&Units=SI&Mask=2000%20-%20Gas-Chrom>

⁵⁷ <http://onlinelibrary.wiley.com/doi/10.1002/cbdv.200490144/abstract>

⁵⁸ <http://www.chemspider.com/Chemical-Structure.7695.html>

⁵⁹ <http://www.sigmaaldrich.com/catalog/substance/16hexadecanolide2544110929511?lang=en®ion=DK>

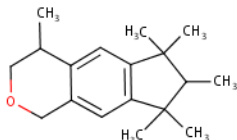
CAS no. 1222-05-5	HEXAMETHYLINDANOPYRAN	
Synonyms	Galaxolide 1,3,4,6,7,8-Hexahydro-4,6,6,7,8,8-hexamethyl-cyclopenta-gamma-2-benzopyran Hexahydrohexamethyl cyclopentabenzopyran (HHCB)	
Molecular weight	258.40 g/mol (C ₁₈ H ₂₆ O)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC-MS ⁶⁰	Fish	
MA-HS-SPME + GC-MS ⁶¹	Sediment	MA-HS-SPME (microwave-assisted headspace solid-phase microextraction) followed by GC-MS.
Availability and prices		
Price reference substance	Comments	
418 DKK / 10 mg	Sigma-Aldrich ⁶² . The price is for an 'analytical standard'.	

TABLE 61
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

⁶⁰ <http://www.ncbi.nlm.nih.gov/pubmed/9718694>

⁶¹ <http://www.ncbi.nlm.nih.gov/pubmed/20303495>

⁶² <http://www.sigmaaldrich.com/catalog/search?term=1222-05-5&interface=CAS%20No.&N=0&mode=match%20partialmax&lang=en®ion=DK&focus=product>

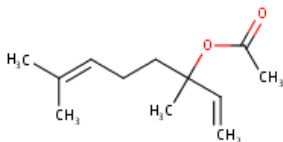
CAS no. 115-95-7	LINALYL ACETATE	
Synonyms	1,6-Octadien-3-ol, 3,7-dimethyl-, acetate 3,7-Dimethyl-1,6-octadien-3-ol acetate Bergamot mint oil	
Molecular weight	196.29 g/mol (C ₁₂ H ₂₀ O ₂)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC-MS ⁶³	Essential oils	
LC/ESI-MS/MS ⁶⁴	Cosmetics	A C3 column is used. It is described that the method demands further validation in order to be used for routine sampling.
Availability and prices		
Price reference substance	Comments	
221 DKK / 100 mg	Sigma-Aldrich ⁶⁵ . The price is for an 'analytical standard'.	

TABLE 62
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

⁶³ <http://www.ncbi.nlm.nih.gov/pubmed/25786161>

⁶⁴ <http://www.ncbi.nlm.nih.gov/pubmed/23404959>

⁶⁵ <http://www.sigmaaldrich.com/catalog/search?term=115-95-7&interface=CAS%20No.&N=o&mode=match%20partialmax&lang=en®ion=DK&focus=product>

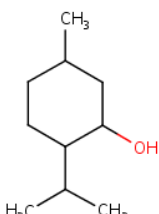
CAS no. 1490-04-6	MENTHOL	
Synonyms	2-Isopropyl-5-methylcyclohexanol 5-Methyl-2-(1-methylethyl)cyclohexanol DL-Menthol Hexahydrothymol	
Molecular weight	156.27 g/mol (C ₁₀ H ₂₀ O)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
HS SPME +GC-MS ⁶⁶	Cosmetics	Headspace SPME (solid-phase microextraction) is used
HPLC ⁶⁷	Medicine	
Availability and prices		
Price reference substance	Comments	
857 DKK	Sigma-Aldrich ⁶⁸ . The size and purity of the sample are not described.	

TABLE 63
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

⁶⁶ <http://www.ncbi.nlm.nih.gov/pubmed/16246353>

⁶⁷ <http://www.ncbi.nlm.nih.gov/pubmed/21180473>

⁶⁸ <http://www.sigmaaldrich.com/catalog/search?term=1490-04-6&interface=CAS%20No.&N=O&mode=match%20partialmax&lang=en®ion=DK&focus=product>

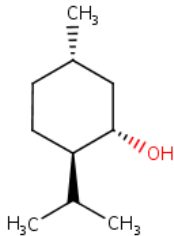
CAS no. 89-78-1	MENTHOL	
Synonyms	(+-)-Menthol DL-menthol (1R,2S,5R)-Menthol 5-Methyl-2-(1-methylethyl)cyclohexanol, (1alpha,2beta,5alpha)- Menthol racemic p-Menthan-3-ol 2-isopropyl-5-methylcyclohexanol	
Molecular weight	156.27 g/mol (C ₁₀ H ₂₀ O)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
HS SPME +GC-MS ⁶⁹	Cosmetics	Headspace SPME (solid-phase microextraction) is used
HPLC ⁷⁰	Medicine	
Availability and prices		
Price reference substance	Comments	
221 DKK / 100 mg	Sigma-Aldrich ⁷¹ . The price is for an 'analytical standard'.	

TABLE 64
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

⁶⁹ <http://www.ncbi.nlm.nih.gov/pubmed/16246353>

⁷⁰ <http://www.ncbi.nlm.nih.gov/pubmed/21180473>

⁷¹ <http://www.sigmaaldrich.com/catalog/search?term=89-78-1&interface=CAS%20No.&N=o&mode=match%20partialmax&lang=en®ion=DK&focus=product>

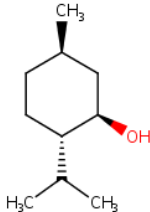
CAS no. 2216-51-5	MENTHOL	
Synonyms	Levomenthol (-)-Menthol (1R)-(-)-Menthol L-Menthol (-)-(1R,3R,4S)-Menthol (1R-(1- α ,2- β ,5- α))-5-Methyl-2-(1-methylethyl)cyclohexanol	
Molecular weight	156.27 g/mol (C ₁₀ H ₂₀ O)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
HS SPME +GC-MS ⁷²	Cosmetics	Headspace SPME (solid-phase microextraction) is used
HPLC ⁷³	Medicine	
Availability and prices		
Price reference substance	Comments	
533 DKK / 1 kg	Sigma-Aldrich ⁷⁴ . The price is for a purity of >99%.	

TABLE 65
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

⁷² <http://www.ncbi.nlm.nih.gov/pubmed/16246353>

⁷³ <http://www.ncbi.nlm.nih.gov/pubmed/21180473>

⁷⁴ <http://www.sigmaaldrich.com/catalog/search?term=2216-51-5&interface=CAS%20No.&N=0&mode=match%20partialmax&lang=en®ion=DK&focus=product>

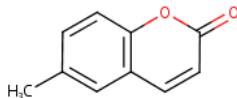
CAS no. 92-48-8	6-METHYL COUMARIN	
Synonyms	Methyl coumarin 2H-1-Benzopyran-2-one, 6-methyl- 5-Methyl-2-hydroxyphenylpropenoic acid lactone 6-Methyl-2H-chromen-2-one	
Molecular weight	160.17 g/mol (C ₁₀ H ₈ O ₂)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC-MS ⁷⁵	Cosmetics	
HPLC ⁷⁶	Cosmetics	
Availability and prices		
Price reference substance	Comments	
410 DKK / 100 g	Sigma-Aldrich ⁷⁷ . The price is for a purity of >99%.	

TABLE 66
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

⁷⁵ <http://wprim.whooc.org.cn/local/detail.jsp?channelid=75002&searchword=WPRIMID%3D492870>

⁷⁶ <http://www.sciencedirect.com/science/article/pii/S0731708583800326>

⁷⁷ <http://www.sigmaaldrich.com/catalog/search?term=92-48-8&interface=CAS%20No.&N=o&mode=match%20partialmax&lang=en®ion=DK&focus=product>

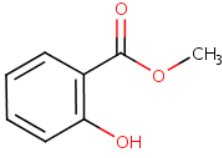
CAS no. 119-36-8	METHYL SALICYLATE	
Synonyms	Benzoic acid, 2-hydroxy-, methyl ester 2-Hydroxybenzoic acid, methyl ester 2-Carbomethoxyphenol Methyl 2-hydroxybenzoate Betula oil Wintergreen oil	
Molecular weight	152.15 g/mol (C ₈ H ₈ O ₃)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC-MS ⁷⁸	Extraction from leaves	
HPLC ⁷⁹	Extraction from leaves	Use of high-performance liquid chromatographic analysis (HPLC)
Availability and prices		
Price reference substance	Comments	
214 DKK / 1 ml	Sigma-Aldrich ⁸⁰ . The price is for an 'analytical standard'.	

TABLE 67
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

⁷⁸ <http://www.ncbi.nlm.nih.gov/pubmed/26457083>

⁷⁹ <http://jat.oxfordjournals.org/content/28/3/214.full.pdf>

⁸⁰ <http://www.sigmaaldrich.com/catalog/search?term=119-36-8&interface=CAS%20No.&N=O&mode=match%20partialmax&lang=en®ion=DK&focus=product>

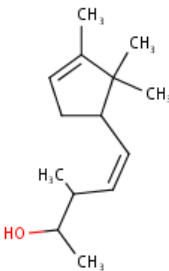
CAS no. 67801-20-1	3-METHYL-5-(2,2,3-TRIMETHYL-3-CYCLOPENTENYL)PENT-4-EN-2-OL	
Synonyms	3-Methyl-5-(2,2,3-trimethyl-3-cyclopenten-1-yl)-4-penten-2-ol 4-Penten-2-ol, 3-methyl-5-(2,2,3-trimethyl-3-cyclopenten-1-yl)-Ebanol	
Molecular weight	208.34 g/mol (C ₁₄ H ₂₄ O)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC-MS ⁸¹	Essential oils	GC-MS and two-dimensional GC (GC x GC) are used. GC x GC appears to give a better resolution for the peaks.
Availability and prices		
Price reference substance	Comments	
273 DKK / 250 mg	Sigma-Aldrich ⁸² . The price is for an 'analytical standard'.	

TABLE 68
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

⁸¹ <http://www.ncbi.nlm.nih.gov/pubmed/15516281>

⁸² <http://www.sigmaaldrich.com/catalog/search?term=67801-20-1&interface=CAS%20No.&N=o&mode=match%20partialmax&lang=en®ion=DK&focus=product>

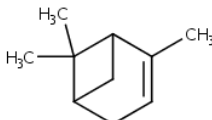
CAS no. 80-56-8	CYCLOPENTENYL)PENT-4-EN-2-OL alpha-PINENE	
Synonyms	2,6,6-Trimethylbicyclo(3.1.1)-2-hept-2-ene α-Pinene 4,6,6-Trimethylbicyklo(3,1,1)hept-3-en Bicyclo(3.1.1)hept-2-ene, 2,6,6-trimethyl-	
Molecular weight	136.24 g/mol (C ₁₀ H ₁₆)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC-MS ⁸³	Essential oils	
GC-FID + GC-MS ⁸⁴	Plant materials	
Headspace SPME + GC-MS ⁸⁵	Aquatic solutions (baby bath water)	A good precision was displayed for all compounds.
Availability and prices		
Price reference substance	Comments	
1213 DKK / 100 mg	Sigma-Aldrich ⁸⁶ . The price is for a pharmaceutical reference standard.	

TABLE 69
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

⁸³ <http://www.ncbi.nlm.nih.gov/pubmed/26411037>

⁸⁴ <http://www.ncbi.nlm.nih.gov/pubmed/26299522>

⁸⁵ <http://link.springer.com/article/10.1007/s00216-009-2829-2?no-access=true>

⁸⁶ <http://www.sigmaaldrich.com/catalog/search?term=80-56-8&interface=CAS%20No.&N=O&mode=match%20partialmax&lang=en®ion=DK&focus=product>

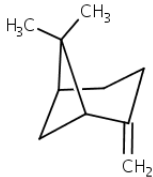
CAS no. 127-91-3	CYCLOPENTENYL)PENT-4-EN-2-OL beta-PINENE	
Synonyms	B-Pinene 2,2,6-Trimethylbicyclo(3.1.1)hept-2-ene (1)-6,6-Dimethyl-2-methylenebicyclo(3.1.1)heptane	
Molecular weight	136.24 g/mol (C ₁₀ H ₁₆)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC-FID + GC-MS ⁸⁷	Essential oils	
Availability and prices		
Price reference substance	Comments	
960 USD / 1 g	SBT (USA) ⁸⁸	

TABLE 70
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

⁸⁷ <http://www.ncbi.nlm.nih.gov/pubmed/26299522>

⁸⁸ <http://www.scbt.com/datasheet-397893-casnumber-127-91-3.html>

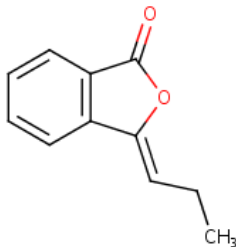
CAS no. 17369-59-4	PROPYLIDENE PHTHALIDE	
Synonyms	3-Propylenephthalide 1(3H)-Isobenzofuranone, 3-propylidene-	
Molecular weight	174,20 g/mol (C ₁₁ H ₁₀ O ₂)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
		No analytical methods are identified
Availability and prices		
Price reference substance	Comments	
266 DKK / 1 ml	Sigma-Aldrich ⁸⁹ . The price is for an 'analytical standard', but is a mixture of isomers (racemic mixture).	

TABLE 71
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

⁸⁹ <http://www.sigmaaldrich.com/catalog/search?term=17369-59-4&interface=CAS%20No.&N=O&mode=match%20partialmax&lang=en®ion=DK&focus=product>

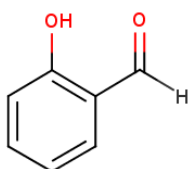
CAS no. 90-02-8	SALICYLALDEHYDE	
Synonyms	2-Formylphenol 2-hydroxy-benzaldehyde	
Molecular weight	122.12 g/mol (C ₇ H ₆ O ₂)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC-MS ⁹⁰	Plant extraction	
HPLC ⁹¹	Plant extraction	
Availability and prices		
Price reference substance	Comments	
200 DKK / 1 ml	Sigma-Aldrich ⁹² . The price is for an 'analytical standard'.	

TABLE 72
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

⁹⁰ <http://www.ncbi.nlm.nih.gov/pubmed/22757696>

⁹¹ <http://www.revistafarmacia.ro/2011/art12%20-%20toiu%20106-112.pdf>

⁹² <http://www.sigmaaldrich.com/catalog/search?term=90-02-8&interface=CAS%20No.&N=O&mode=match%20partialmax&lang=en®ion=DK&focus=product>

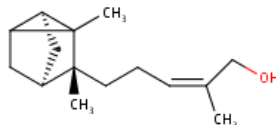
CAS no. 115-71-9	alpha-SANTALOL	
Synonyms	(Z)-alpha-Santalol d-alpha-Santalol 5-(2,3-Dimethyltricyclo(2.2.1.0(2,6))hept-3-yl)-2-methyl-2-penten-1-ol 2-Penten-1-ol, 5-((1R,3R,6S)-2,3-dimethyltricyclo(2.2.1.0(2,6))hept-3-yl)-2-methyl-, (2Z)-	
Molecular weight	220.35 g/mol (C ₁₅ H ₂₄ O)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC-MS ⁹³	Essential oils	
HPLC ⁹⁴	Human plasma	The method is applicable specifically for α- and β-santalol in human plasma.
Availability and prices		
Price reference substance	Comments	
440 USD / 1 g	SPT (USA) ⁹⁵ . It is assumed that the price covers a mixture of α- and β-santalol.	

TABLE 73
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

⁹³ <http://www.ncbi.nlm.nih.gov/pubmed/25918813>

⁹⁴ <http://abstracts.aaps.org/Verify/AAPS2014/PosterSubmissions/W5238.pdf>

⁹⁵ <http://www.scbt.com/datasheet-482737-casnumber-11031-45-1.html>

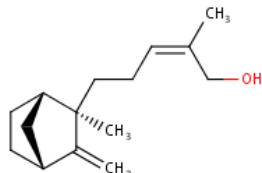
CAS no. 77-42-9	beta-SANTALOL	
Synonyms	2-Methyl-5-(2-methyl-3-methylene-2-norbornyl)-2-penten-1-ol (1S-(1alpha,2alpha(Z),4alpha))-2-Methyl-5-(2-methyl-3-methylenebicyclo(2.2.1)hept-2-yl)-2-penten-1-ol	
Molecular weight	220.35 g/mol (C ₁₅ H ₂₄ O)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC-MS ⁹⁶	Essential oils	
HPLC ⁹⁷	Human plasma	The method is applicable specifically for α- and β-santalol in human plasma.
Availability and prices		
Price reference substance	Comments	
440 USD / 1 g	SPT (USA) ⁹⁸ . It is assumed that the price covers a mixture of α- and β-santalol.	

TABLE 74
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

⁹⁶ <http://www.ncbi.nlm.nih.gov/pubmed/25918813>

⁹⁷ <http://abstracts.aaps.org/Verify/AAPS2014/PosterSubmissions/W5238.pdf>

⁹⁸ <http://www.scbt.com/datasheet-482737-casnumber-11031-45-1.html>

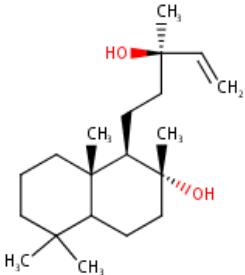
CAS no. 515-03-7	SCLAREOL	
Synonyms	(13R)-Labd-14-ene-8,13-diol 1-Naphthalenepropanol, alpha-ethenyldecahydro-2-hydroxy-alpha,2,5,5,8a-pentamethyl-, (1theta-(1alpha(theta),2beta,4abeta,8aalpha))- (1R,2R,8aS)-Decahydro-1-(3-hydroxy-3-methyl-4-pentenyl)-2,5,5,8a-tetramethyl-2-naphthol	
Molecular weight	308.50 g/mol (C ₂₀ H ₃₆ O ₂)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC and GC-MS ⁹⁹		
Availability and prices		
Price reference substance	Comments	
337 DKK / 100 mg	Sigma-Aldrich ¹⁰⁰ . The price is for an 'analytical standard'.	

TABLE 75
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

⁹⁹ <http://www.ncbi.nlm.nih.gov/pubmed/24929006>

¹⁰⁰ <http://www.sigmaaldrich.com/catalog/search?term=515-03-7&interface=CAS%20No.&N=0&mode=match%20partialmax&lang=en®ion=DK&focus=product>

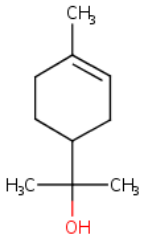
CAS no. 8000-41-7	TERPINEOL (mixture of isomers)	
Synonyms	Terpineols	
Molecular weight	154.25 g/mol (C ₁₀ H ₁₈ O)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC-MS ¹⁰¹	Essential oils	
Availability and prices		
Price reference substance	Comments	
228 DKK / 1 ml	Sigma-Aldrich ¹⁰² . The price is for an 'analytical standard' and for a mixture of isomers.	

TABLE 76
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

¹⁰¹ <http://www.ncbi.nlm.nih.gov/pubmed/26197558>

¹⁰² <http://www.sigmaaldrich.com/catalog/search?term=8000-41-7&interface=CAS%20No.&N=O&mode=match%20partialmax&lang=en®ion=DK&focus=product>

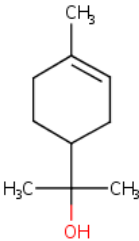
CAS no. 10482-56-1	alpha-TERPINEOL	
Synonyms	(L)-alpha-Terpineol 3-Cyclohexene-1-methanol, alpha,alpha,4-trimethyl-, (S)-	
Molecular weight	154.25 g/mol (C ₁₀ H ₁₈ O)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC-MS ¹⁰³	Essential oils	The same method is listed for the mixture of isomers.
Availability and prices		
Price reference substance	Comments	
252 DKK / 100 mg	Sigma-Aldrich ¹⁰⁴ . The price is for an 'analytical standard'.	

TABLE 77
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

¹⁰³ <http://www.ncbi.nlm.nih.gov/pubmed/26197558>

¹⁰⁴ <http://www.sigmaaldrich.com/catalog/search?term=10482-56-1&interface=CAS%20No.&N=o&mode=match%20partialmax&lang=en®ion=DK&focus=product>

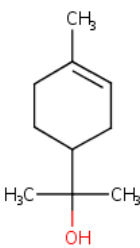
CAS no. 98-55-5	alpha-TERPINEOL	
Synonyms	1-Menthene-8-ol 1-Methyl-4-isopropyl-1-cyclohexen-8-ol alpha,alpha,4-Trimethyl-3-cyclohexene-1-methanol	
Molecular weight	154.25 g/mol (C ₁₀ H ₁₈ O)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC-MS ¹⁰⁵	Essential oils	The same method is listed for the mixture of isomers.
Availability and prices		
Price reference substance	Comments	
252 DKK / 100 mg	Sigma-Aldrich ¹⁰⁶ . The price is for an 'analytical standard'.	

TABLE 78
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

¹⁰⁵ <http://www.ncbi.nlm.nih.gov/pubmed/26197558>

¹⁰⁶ <http://www.sigmaaldrich.com/catalog/search?term=10482-56-1&interface=CAS%20No.&N=O&mode=match%20partialmax&lang=en®ion=DK&focus=product>

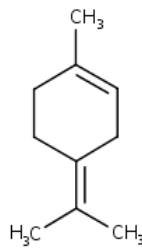
CAS no. 586-62-9	Terpinolene	
Synonyms	1,4(8)-p-Menthadiene <i>p</i> -Menth-1,4(8)-diene <i>p</i> -Meth-1-en-8-yl-formate Cyclohexene, 1-methyl-4-(1-methylethylidene)- 1-Methyl-4-(1-methylethylidene)cyclohexene 4-Isopropylidene-1-methylcyclohexene	
Molecular weight	136.24 g/mol (C ₁₀ H ₁₆)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC-MS ¹⁰⁷	Essential oils	The same method is listed for the mixture of isomers.
Availability and prices		
Price reference substance	Comments	
418 DKK / 1 kg	Sigma-Aldrich ¹⁰⁸ . The price is for a purity of >90%.	

TABLE 79
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

¹⁰⁷ <http://www.ncbi.nlm.nih.gov/pubmed/26197558>

¹⁰⁸ <http://www.sigmaaldrich.com/catalog/search?term=586-62-9&interface=CAS%20No.&N=O&mode=match%20partialmax&lang=en®ion=DK&focus=product>

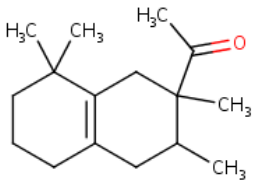
CAS no. 54464-57-2	TETRAMETHYL ACETYLOCTAHYDRONAPHTHALENES	
Synonyms	Isocyclemone E 1',2',3',4',5',6',7',8'-Octahydro-2',3',8',8'-tetramethyl-2'-acetonaphthone 1-(1,2,3,4,5,6,7,8-Octahydro-2,3,8,8-tetramethyl-2-naphthyl)ethan-1-one 2-Acetyloctahydro-2,3,8,8-tetramethylnaphthalene Boisvelone Iso-E super OTNE	
Molecular weight	234.38 g/mol (C ₁₆ H ₂₆ O)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC-GC ¹⁰⁹	Water, sediment and air	The same method as for the other CAS numbers
GC-MS ¹¹⁰	House dust	The same method as for the other CAS numbers
Availability and prices		
Price reference substance	Comments	
48 USD / 500 ml	Perfumers Apprentice (USA). The substance is not available pure, only as part of a perfume raw material.	

TABLE 8o
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

¹⁰⁹ <http://www.ncbi.nlm.nih.gov/pubmed/18786673>

¹¹⁰ <http://www.ncbi.nlm.nih.gov/pubmed/22684881>

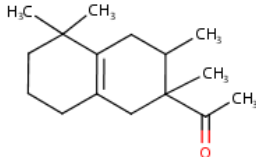
CAS no. 54464-59-4	TETRAMETHYL ACETYLOCTAHYDRONAPHTHALENES	
Synonyms	Ethanone, 1-(1,2,3,4,5,6,7,8-octahydro-2,3,5,5-tetramethyl-2-naphthalenyl)- 1-(1,2,3,4,5,6,7,8-Octahydro-2,3,5,5-tetramethyl-2-naphthyl)ethan-1-one	
Molecular weight	234.38 g/mol (C ₁₆ H ₂₆ O)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC-GC ¹¹¹	Water, sediment and air	The same method as for the other CAS numbers
GC-MS ¹¹²	House dust	The same method as for the other CAS numbers
Availability and prices		
Price reference substance	Comments	
-	No price was identified for this CAS number	
	The suppliers can apparently not distinguish between the four different CAS numbers for the substance (68155-66-8, 68155-67-9, 54464-59-4 and 54464-57-2)	

TABLE 81
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

¹¹¹ <http://www.ncbi.nlm.nih.gov/pubmed/18786673>

¹¹² <http://www.ncbi.nlm.nih.gov/pubmed/22684881>

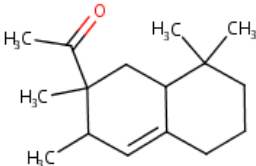
CAS no. 68155-66-8	TETRAMETHYL ACETYLOCTAHYDRONAPHTHALENES	
Synonyms	1-(2,3,8,8-Tetramethyl-1,2,3,5,6,7,8,8a-octahydronaphthalen-2-yl)ethanone 1-(1,2,3,5,6,7,8,8a-Octahydro-2,3,8,8-tetramethyl-2-naphthyl)ethan-1-one	
Molecular weight	234.38 g/mol (C ₁₆ H ₂₆ O)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC-GC ¹¹³	Water, sediment and air	The same method as for the other CAS numbers
GC-MS ¹¹⁴	House dust	The same method as for the other CAS numbers
Availability and prices		
Price reference substance	Comments	
195 USD / 1 kg	CreatingPerfume ¹¹⁵ . Is a mixture of several CAS numbers. The purity is unknown.	
	The suppliers can apparently not distinguish between the four different CAS numbers for the substance (68155-66-8, 68155-67-9, 54464-59-4 and 54464-57-2)	

TABLE 82
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

¹¹³ <http://www.ncbi.nlm.nih.gov/pubmed/18786673>

¹¹⁴ <http://www.ncbi.nlm.nih.gov/pubmed/22684881>

¹¹⁵ <http://www.creatingperfume.com/isoesuper.aspx>

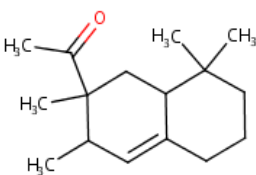
CAS no. 68155-67-9	TETRAMETHYL ACETYLOCTAHYDRONAPHTHALENES	
Synonyms	1-(2,3,8,8-Tetramethyl-1,2,3,4,6,7,8,8a-octahydronaphthalen-2-yl)ethanone 1-(1,2,3,4,6,7,8,8a-Octahydro-2,3,8,8-tetramethyl-2-naphthyl)ethan-1-one Iso-E super IFF	
Molecular weight	234.38 g/mol (C ₁₆ H ₂₆ O)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC-GC ¹¹⁶	Water, sediment and air	The same method as for the other CAS numbers
GC-MS ¹¹⁷	House dust	The same method as for the other CAS numbers
Availability and prices		
Price reference substance	Comments	
195 USD / 1 kg	CreatingPerfume ¹¹⁸ . Is a mixture of several CAS numbers. The purity is unknown.	
	The suppliers can apparently not distinguish between the four different CAS numbers for the substance (68155-66-8, 68155-67-9, 54464-59-4 and 54464-57-2)	

TABLE 83
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

¹¹⁶ <http://www.ncbi.nlm.nih.gov/pubmed/18786673>

¹¹⁷ <http://www.ncbi.nlm.nih.gov/pubmed/22684881>

¹¹⁸ <http://www.creatingperfume.com/isoesuper.aspx>

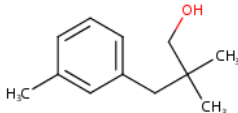
CAS no. 103694-68-4	TRIMETHYL-BENZENEPROPANOL (Majantol)	
Synonyms	2,2-Dimethyl-3-(3-methylphenyl)propanol 3-(2,2-Dimethyl-3-hydroxypropyl)toluene Benzenepropanol, beta,beta,3-trimethyl- Majantol	
Molecular weight	178.27 g/mol (C ₁₂ H ₁₈ O)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC-MS ¹¹⁹	Cosmetics	Extraction with TBME and subsequent GC-MS
GC x GC–TOF MS ¹²⁰	Cosmetics	Two-dimensional gas chromatography with TOF MS (time-of-flight mass spectrometry)
Availability and prices		
Price reference substance	Comments	
238 DKK /250 mg	Sigma-Aldrich ¹²¹ . The price is for an 'analytical standard'.	

TABLE 84
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

¹¹⁹ <http://www.oekotest.de/cgi/index.cgi?artnr=104368&action=Z&bernr=>

¹²⁰ <http://www.azom.com/article.aspx?ArticleID=11440>

¹²¹ <http://www.sigmaaldrich.com/catalog/search?term=103694-68-4&interface=CAS%20No.&N=O&mode=match%20partialmax&lang=en®ion=DK&focus=product>

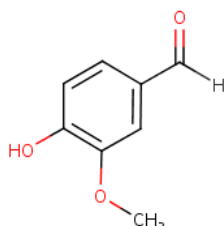
CAS no. 121-33-5	VANILLIN	
Synonyms	4-Hydroxy-3-methoxybenzaldehyde 2-Methoxy-4-formylphenol Benzaldehyde, 4-hydroxy-3-methoxy- 3-Methoxy-4-hydroxybenzaldehyde	
Molecular weight	152.15 g/mol (C ₈ H ₈ O ₃)	
Chemical structure		
Identified analytical methods		
Analytical methods	Possible matrix	Comments
GC-MS ¹²²		Is available in the NIST library
HPLC ¹²³		ChemicalBook states that HPLC can be used as a method for detection. No other data is listed.
GC-MS ¹²⁴		The precise analytical method is not stated, but vanillin can be detected together with other fragrances (some of the fragrances subject to declaration)
Headspace? ¹²⁵	Wine	The precise analytical method is not stated
Availability and prices		
Price reference substance	Comments	
168 DKK / 2 g	Sigma-Aldrich ¹²⁶ . The price is for an 'analytical standard'.	

TABLE 85
INFORMATION REGARDING THE ANALYTICAL METHODS IDENTIFIED VIA AN INTERNET SEARCH

¹²² <http://webbook.nist.gov/cgi/cbook.cgi?ID=121-33-5>

¹²³ http://www.chemicalbook.com/CASEN_121-33-5.htm

¹²⁴ <http://www.agilent.com/cs/library/chromatograms/383b.pdf>

¹²⁵ <http://www.sciencedirect.com/science/article/pii/S0003267009014512>

¹²⁶ <http://www.sigmaaldrich.com/catalog/search?term=121-33-5&interface=CAS%20No.&N=0&mode=match%20partialmax&lang=en®ion=DK&focus=product>

Survey of allergenic substances in products targeted children – toys and cosmetic products

The purpose of the project was to investigate whether toys and cosmetic products addressed to children and in prolonged contact with the skin contain allergenic substances and if corresponding products without allergenic substances can be found. Lists of ingredients from in total 157 cosmetic products for children were examined for contents of 191 potentially allergenic substances, and the Danish Toy Sector was requested about the use of chosen potential allergenic substances in toys. Of the 157 cosmetic products, 30 products contained between one and eight potentially allergenic substances. A content of many potentially allergenic substances was typically due to a content of many different fragrances. 15 out of the in total 157 investigated products had a declared content of fragrance but no content of the 26 fragrances subject to declaration in concentrations subject to declaration. Therefore, it was decided that focus on substances for possible chemical analyses had to be changed to "other" potentially allergenic fragrances, i.e. fragrances which SCCS assesses as allergenic in humans but which are not a part of the 26 fragrances subject to declaration. 13 cosmetics products consisting of in total 23 sub-products and 21 pieces of toys with fragrances were analyzed for content of fragrances. Four fragrances were identified in 19 of the analyzed products. Furthermore, several of the fragrances subject to declaration (in cosmetics) were identified. An essential conclusion from the survey is that it is possible to find cosmetic products for children in the Danish shops without potentially allergenic substances (based on the list of potentially allergenic substances established in the project). It is possible for nearly all the investigated product types (except for the product types hair spray and perfume set) to find products without potentially allergenic substances (from the established in the project). Fragrances turned out to be the group of substances which could constitute the biggest problem with regards to allergy.



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