Ministry of Environment and Food
The Danish Environmental Protection Agency

Survey and health and environmental assessment of preservatives in cosmetic products

Survey of chemical substances in consumer products No. 138, 2015

Title:

Survey and health and environmental assessment of preservatives in cosmetic products

Editing:

Dorthe Nørgaard Andersen, Tina Slothuus, Torben Wilde Schou, Anne Rathmann Petersen, Dorte Rasmussen og Ann Detmer, DHI
Pia Brunn Poulsen og Maria Strandesen, FORCE Technology

Publisher:

The Danish Environmental Protection Agency
Strandgade 29
1401 Copenhagen K
Denmark
www.mst.dk/english

Year:

2015

ISBN no.

978-87-93352-19-3

Contents

Foreword **6**

Summary and Conclusion **7**

1. Introduction **11**
1.1 Background 11
1.2 Definition of preservatives 11
1.3 Objective 11
1.4 Definition of product types 11
1.5 Definition of preservatives/substances 12
1.6 Ensuring product durability 12
1.7 Distribution of cosmetic products on the Danish market 13
1.8 Previous studies of cosmetic products 15
1.8.1 The most commonly used preservatives according to Cosmetics Europe 16

2. Legislation and Environmental labelling **17**
2.1 Legislation 17
2.1.1 The Cosmetics Regulation (Regulation No. 1223, 2009) 17
2.1.2 Statutory Order prohibiting the use of certain parabens (Statutory Order 166, 2011 and Statutory Order 1217, 2013) 18
2.2 Swan labelling of cosmetic products 19
2.2.1 Criteria for Swan labelling of cosmetic products 19

3. Survey of the market **20**
3.1 Objective of the survey 20
3.2 Procedure for the survey 20
3.2.1 Definition of types of cosmetic products 20
3.2.2 Search on the web for the lists of ingredients of cosmetic products 21
3.2.3 Study of lists of ingredients of cosmetic products in shops 21
3.3 Preparation of a list of cosmetic products 22
3.4 Survey results 23
3.4.1 Results of contact with the industry 23
3.4.2 Information received from manufacturers of preservatives 27
3.4.3 General comments from the contacted companies 28
3.4.4 Results of study on lists of ingredients 28
3.5 Conclusions from the survey 41

4. Survey of the use as a biocidal active substance **43**

5. Prioritising the preservatives **50**
5.1 Screening – environmental impacts 56
5.2 Screening – health impacts 64

6. Analyses **78**
6.1 Analytical method – quantitative analysis of phenoxyethanol 78
6.2 Analytical results – quantitative analysis of phenoxyethanol 79

7. Hazard identification **86**
7.1 DMDM Hydantoin 86
7.1.1 Chemical identity 86

7.1.2 Acute toxicity ... 86
7.1.3 Irritation ... 87
7.1.4 Skin sensitisation ... 87
7.1.5 Dermal absorption ... 87
7.1.6 Repeated toxicity ... 87
7.1.7 Reproduction toxicity ... 88
7.1.8 Mutagenicity / genotoxicity ... 88
7.1.9 Carcinogenicity ... 88
7.1.10 Toxicokinetics ... **Fejl! Bogmærke er ikke defineret.**
7.1.11 Photo-induced toxicity ... 88
7.1.12 Human data ... 89
7.1.13 Special studies ... 89
7.1.14 Conclusion ... 89
7.2 Imidazolidinyl urea ... 90
7.2.1 Chemical identity ... 90
7.2.2 Acute toxicity ... 90
7.2.3 Irritation ... 90
7.2.4 Skin sensitisation ... 91
7.2.5 Dermal absorption ... 91
7.2.6 Repeated toxicity ... 91
7.2.7 Reproduction toxicity ... 91
7.2.8 Mutagenicity / genotoxicity ... 91
7.2.9 Carcinogenicity ... 92
7.2.10 Toxicokinetics ... **Fejl! Bogmærke er ikke defineret.**
7.2.11 Photo-induced toxicity ... 92
7.2.12 Human data ... 92
7.2.13 Special studies ... 92
7.2.14 Conclusion ... 93
7.3 Thimerosal ... 93
7.3.1 Chemical identity ... 93
7.3.2 Acute toxicity ... 93
7.3.3 Irritation ... 94
7.3.4 Skin sensitisation ... 94
7.3.5 Dermal absorption ... 94
7.3.6 Repeated toxicity ... 94
7.3.7 Reproduction toxicity ... 94
7.3.8 Mutagenicity / genotoxicity ... 94
7.3.9 Carcinogenicity ... 95
7.3.10 Toxicokinetics ... 95
7.3.11 Photo-induced toxicity ... 95
7.3.12 Human data ... 95
7.3.13 Special studies ... 96
7.3.14 Conclusion ... 96
7.4 Zinc pyrithione ... 96
7.4.1 Chemical identity ... 96
7.4.2 Acute toxicity ... 96
7.4.3 Irritation ... 97
7.4.4 Skin sensibilisation ... 97
7.4.5 Dermal absorption ... 97
7.4.6 Repeated toxicity ... 97
7.4.7 Reproduction toxicity ... 98
7.4.8 Mutagenicity / genotoxicity ... 98
7.4.9 Carcinogenicity ... 98

7.4.10 Toxicokinetics ... 98
7.4.11 Photo-induced toxicity ... 98
7.4.12 Human data ... 99
7.4.13 Special studies ... 99
7.4.14 Conclusion ... 99

8. Exposure assessment ... 100
8.1 Method for assessment of exposure calculation ... 102
8.1.1 Method for calculation of total exposure ... 103
8.2 Exposure scenarios ... 103
8.3 Data used in the exposure calculations ... 103
8.4 Results – exposure calculations ... 108
8.4.1 Results – DMDM Hydantoin ... 110
8.4.2 Results – Imidazolidinyl urea ... 110
8.4.3 Results – Phenoxyethanol ... 112
8.4.4 Results – exposure of the diaper areas of babies ... 116
8.4.5 Results – Thimerosal ... 117
8.4.6 Results – Zinc pyrithione ... 117

9. Risk assessment ... 118
9.1 Method for calculation of risk ... 118
9.1.1 Method for calculation of overall risk ... 118
9.2 Used NOAEL values ... 119
9.3 Results – risk assessment ... 119
9.3.1 Results – DMDM Hydantoin ... 120
9.3.2 Results – Imidazolidinyl urea ... 120
9.3.3 Results – Phenoxyethanol ... 121
9.3.4 Results – Thimerosal ... 126
9.3.5 Results – Zinc pyrithione ... 127
9.4 Discussion ... 127
9.4.1 Other effects besides allergies ... 127
9.4.2 Contact allergy ... 129

10. Conclusion ... 131
Appendix 1: List of preservatives permitted in cosmetic products (Annex V of the Cosmetics Regulation) ... 138
Appendix 2: Extract from Statistics Denmark on the imports and exports of cosmetic products ... 170
Appendix 3: Previous surveys of cosmetic products ... 173
Appendix 4: Indicative list of products considered to be cosmetic products ... 181
Appendix 5: Number of products for each of the 55 product types ... 182
Appendix 6: Preservatives used in different groups of cosmetic products ... 186
Appendix 7: Classification of biocidal product types ... 193

Foreword

This project on preservatives in cosmetic products was carried out from July 2013 to August 2014.

This report describes the results of the project, including a survey of the market and the results of the survey, and a risk assessment of selected preservatives.

The project was conducted by DHI and FORCE Technology.

The project participants:

- Dorthe Nørgaard Andersen (project manager), DHI
- Ann Detmer, DHI
- Torben Wilde Schou, DHI
- Anne Rathmann Petersen, DHI
- Tina Slothuus, DHI
- Pia Brunn Poulsen, FORCE Technology
- Maria Strandesen, FORCE Technology

The project was followed by a reference group consisting of Jette Rud Larsen Heltved (took over the project management from Louise in October 2013), Lærke Ambo Nielsen, Bettina Ørsnes Andersen and Louise Fredsbo Karlsson from the Environmental Protection Agency.

The project was funded by the Environmental Protection Agency.

Summary and Conclusion

The overall objective of this project is to assess whether there may be a risk associated with the use of preservatives in cosmetic products. This issue was sought answered by examining the following sub-objectives:

1. To identify the preservatives used in practice in cosmetic products on the Danish market today, and to identify the permitted preservatives that are most frequently used in cosmetic products on the Danish market today.
2. To make an environmental and health assessment (screening) of the selected permitted preservatives, as well as a hazard and risk assessment of the selected permitted preservatives.

Survey of the Danish market
A total of 639 different cosmetic products has been identified divided into groups ranging from sunscreens to powder to wet wipes. The survey identified a total of 53 preservatives used in cosmetic products on the Danish market. These 53 preservatives include a total of 31 of the 55 reference numbers for preservatives in Annex V of the cosmetics legislation. Of the total of 639 identified products, 31 % did not contain preservatives, which may be because of the product's packaging and/or composition making preservation unnecessary.
The survey shows that the use of preservatives in various types of products is basically identical in rinse-off products compared with leave-on products. Furthermore, it was observed that typically far fewer preservatives were used in products for children and in Swan labelled products. In these products, Phenoxyethanol, Sodium benzoate, Benzoic acid, Dehydroacetic acid and Potassium sorbate in various combinations are mainly used. Phenoxyethanol is generally the most commonly used preservative - either alone or in combination with other preservatives, which is also seen in previous studies.
By comparison with previous studies of cosmetic products, it is seen that the use of parabens is decreasing, which is also confirmed by the manufacturers who have supplied information for this survey. In a previous study of cosmetic products for children, parabens were the most commonly used preservatives, whereas this survey shows that parabens are virtually no longer used in products for children.
It should be pointed out that in this study parabens were only observed to be used in 3 out of 36 products for children and that these parabens were either methylparaben or ethylparaben. All tested products therefore meet the temporary Danish statutory order prohibiting the use of certain parabens in cosmetic products for children under the age of 3.

Environmental and health screening and selection of substances for hazard and risk assessment
An environmental and health screening of 25 of the permitted preservatives was made on the basis of information from the survey, information on the individual substances' classification, the EU Scientific Committee on Consumer Safety (SCCS)'s assessments of the preservatives individually or in groups, knowledge of their use as biocidal active substances, and an assessment in relation to their impact on the environment.

Generally, it is found that the published data for the selected preservatives are limited. Many of the available data are older (back from the 80s - 90s), and literature studies show that only very few new data have been published for the substances. SCCS may have received new data for the

preservatives, but these have not been available in this project. Regarding the use of preservatives that are permitted in cosmetic products, and at the same time used in biocidal products, and thus by this use may be subject to the Biocides Regulation, the re-evaluation of the biocidal active substances has not come so far that it has been possible to get access to assessment reports for approval as biocidal active substances.

The environmental screening showed that seven of the substances or the substance groups meet the criteria for either being persistent (P) or toxic (T) to aquatic organisms. These substances are Formaldehyde (T), Sulfites, see reference number 9 in Annex V (expected P), Climbazole (P), mixture of 5-Chloro-2-methyl-isothiazol-3 (2H)-one and 2-Methylisothiazole-3 (2H)-one with Magnesium chloride and Magnesium nitrate (expected P), Chlorhexidine (P), Methylisothiazolinone (expected P) and Zinc pyrithione (T). None of the substances meet the criteria for being bioaccumulative (B). Only the substance Phenyl mercuric acetate meets the criteria for being both persistent and toxic (P, T). This substance is not seen in the 639 cosmetic products on the Danish market identified in this project, but is typically used in mascaras and cleansing products for eye makeup.
From the screening for human health effects of the selected 25 preservatives, it was assessed that for many of the substances it will not be possible to identify more recent data than those already available in the form of opinions from the SCCS. Some of the substances were discarded in the further analysis, because they are already under evaluation in the EU. This applies to the highly publicised substance MI, which is assessed to be strongly allergenic. Formaldehyde was also discarded because the substance in December 2013 (effective from 26 September 2015) was reclassified as carcinogenic category 1B and mutagenic (Muta2), which eventually may lead to complete prohibition of the substance in cosmetic products. Based on the screening, the following preservatives were assessed to be assessed in more detail: Formaldehyde releasers, Mercury-containing preservatives, Phenoxyethanol and Zinc pyrithione. The formaldehyde releasing substances (Diazolidinyl urea, DMDM Hydantoin, Imidazolidinyl urea, 2-Bromo-2-nitropropane-1,3-diol) should be included in the further investigation, mainly because of their sensitising potential, and because of Formaldehyde's classification as mutagenic and carcinogenic.
In Denmark, there is focus on the consumption of mercury, and the two substances containing mercury (Thimerosal and Phenyl mercuric acetate) were assessed to be relevant for further investigation. However, the two substances were not found in cosmetic products on the Danish market in the survey of 639 products in this project.
France in 2012 assessed Phenoxyethanol to have a low margin of safety in terms of health effects, and not to be safe for use in children under the age of 3. The substance was therefore selected for further assessment, mainly based on the widespread use and because Phenoxyethanol in many cases probably replaces parabens and therefore may have an even larger prevalence. At the Commission's request, SCCS initiated a reassessment of Phenoxyethanol and the maximum permitted concentration for use in cosmetic products. This assessment is expected to be completed in 2015.
Zinc pyrithione was also selected for further investigation, partly because the substance may have harmful effects on the environment, partly because of its relatively low threshold for causing health effects. The substance is used as a remedy for dandruff and apparently rarely as a preservative.

Hazard and risk assessment of five substances and analysis of Phenoxyethanol
A hazard assessment and subsequently a risk assessment were made for the Formaldehyde releasing substances DMDM Hydantoin and Imidazolidinyl urea, and the substances Zinc pyrithione and Thimerosal. Phenoxyethanol is included in the group of substances for which a risk assessment is made. In this project, an actual hazard assessment of Phenoxyethanol has not been made, but the hazard assessment in the French study from 2012 forms the basis of the risk assessment of Phenoxyethanol. Furthermore, a more recent NOAEL (No observed adverse effect level) from a REACH dossier is used in the risk assessment. According to information from the trade association SPT, more recent studies exist that may be relevant, but it is not known whether

these studies were performed according to the official guidelines. Thus, as a worst-case is used the lowest stated NOAEL for the risk calculation of Phenoxyethanol.

The risk assessments of Phenoxyethanol, DMDM Hydantoin, Imidazolidinyl urea, Zinc pyrithione and Thimerosal show that disregarding the sensitising risk by use of the substances, a product is safe to use even when the preservatives are added to the product in the maximum permitted amount. It generally applies to the study, that no cosmetic product in itself constitutes a risk as all calculated margins of safety (MoS) are above 100, which is usually the lowest value for MoS at safe use. The hypothetical worst case scenario - that the substances were found in all cosmetic products used by adults and children in one day - showed no risk for DMDM Hydantoin, but showed a risk for Imidazolidinyl urea. But as Imidazolidinyl urea is used relatively rarely in cosmetics, the substance is not expected to pose a risk when used in the currently maximum permitted concentration of 0.6 % compared to other health effects besides allergies.
Zinc pyrithione and Thimerosal are only permitted in a few product types, and therefore a risk calculation using several products on the same day has not been conducted for these two substances.
Concerning the risk assessment of Phenoxyethanol, 30 cosmetic products have been selected for content analyses of Phenoxyethanol in cooperation with the Environmental Protection Agency. The purpose of this is to get more knowledge about the specific content of this substance in various types of cosmetic products. The measured concentrations of the substance were subsequently used in the risk assessment of Phenoxyethanol in various cosmetic products. All the analysed products comply with the permitted amount of Phenoxyethanol of max 1 % (w/w). The identified concentrations are between 0.10 % and 0.89 %.
Regarding the risk assessment of Phenoxyethanol, there is an uncertainty about the value for skin absorption and the NOAEL value to be used in the calculations. The applied skin absorption of 80 % originates from *in vitro* studies with the substance, and it is debatable whether it is realistic for skin absorption in humans. A study in few humans showed absorption that was somewhat lower (between 8.5 and 48 %). The applied NOAEL of 164 mg/kg bw/day used in the worst case risk calculation for Phenoxyethanol originates from a study from 1996. Different parties have argued for the use of a NOAEL for Phenoxyethanol of 697 mg/kg bw/day, which was found in a recent study, or to use NOAELs from other recent studies in the risk assessment. The following describes the calculations with the different values.
The calculations (NOAEL 164 mg/kg bw/day and skin absorption of 80 %) that were made show that no cosmetic product containing Phenoxyethanol in itself constitutes a risk. By exposure of babies' diaper areas with wet wipes containing Phenoxyethanol, calculations of MoS also showed that there was no risk by using the products.
When calculating the total daily exposure to the 14 mostly used everyday cosmetic products, it gives a MoS of above 100, calculated from the sum of the measured concentrations of Phenoxyethanol in this study. If sunscreen is used in the recommended amount of 36 g/day, it gives a MoS just below 100, but the more realistic amount of sunscreen of 18 g/day gives a MoS of 100 indicating no risk.
If the underlying basis is the maximum permitted concentration of Phenoxyethanol in all 14 products, it can be calculated that there is a risk associated with daily use of the 14 everyday products both with and without the use of sunscreen and using a NOAEL of 164 mg/kg bw/day and a skin absorption of 80 %.
Using a skin absorption of 48 % and a NOAEL of 164 mg/kg bw/day, MoS for use of several products on the same day is above 100, also at concurrent use of sunscreen in the recommended amount of 36 g/day. For the calculation of the lower skin absorption of 48 %, the use may therefore be considered safe.
Using the higher NOAEL, MoS for all exposure scenarios is above 100, and thus there is no risk in the daily use of 14 everyday products.
Thus, it is seen that the values for skin absorption and NOAEL may change the risk calculations significantly. The selection of NOAEL for health effects of Phenoxyethanol should be made based on the quality of the data presented in the studies, ie the most reliable study. It has not been possible to

make a robust risk assessment with the available data for this project. Based on a mandate from 22 April 2014 prepared by the Commission, the SCCS is currenly assessing the safe use of Phenoxyethanol in cosmetic products. The mandate requests SCCS to assess whether a concentration of 1 % is safe for all age groups (SCCS, 2013b). In connection with the assessment of Phenoxyethanol, the trade association Cosmetics Europe has submitted a safety dossier to defend the use of Phenoxyethanol in up to 1 % in cosmetic products.

Contact allergy to preservatives is well described in the literature, and is one of the major causes of contact allergy to cosmetic products. For the selected preservatives in this project, the critical effect is also assessed to be allergy for several of them. The available data are insufficient to determine a threshold value and thus calculate a risk by the permitted concentration of the substance and the number of products in which they are typically found. Generally, patch tests in humans show incidence of allergy to formaldehyde releasing substances at levels of about 1-2 %, and for Thimerosal, allergy incidence of up to 4.7 % is seen.

It can thus be concluded that there is a risk of allergy by using cosmetic products containing 3 of the 5 preservatives investigated in this project. It is remarkable that the incidence of allergy to Thimerosal is relatively high, bearing in mind that it is only permitted in eye cosmetics. However, Thimerosal is used in vaccines as well, and it can not be excluded that this use may cause allergy problems. The phased out use of parabens may lead to the use of other, from an allergy perspective, more problematic preservatives. Especially the use of formaldehyde releasing preservatives is assessed to pose a risk regarding allergies, and the release of formaldehyde from these substances and the consequent reflections on CMR (carcinogenic, mutagenic and reproduction toxic effects) should also be included in the overall assessment of the substances. An approved analytical method for measuring the released formaldehyde has not yet been developed, and therefore it has not been possible in this study to analyse on the actual levels of released formaldehyde from the selected formaldehyde releasing preservatives. Formaldehyde's classification as carcinogen 1B (effective from 26 September 2015) may eventually lead to a possible restriction of formaldehyde releasers in cosmetic products, and is expected in the near future to trigger a reassessment of the formaldehyde releasing preservatives.

Most formaldehyde releasers can release formaldehyde under the right circumstances, which may result in allergic contact dermatitis. If allergic to Formaldehyde, leave-on cosmetics preserved with the formaldehyde releasers Quaternium-15, Diazolidinyl urea, DMDM Hydantoin or Imidazolidinyl urea should be avoided, although in some cases the products might have been tolerated anyway.

1. Introduction

1.1 Background

Preservatives are added to cosmetic products as needed to prevent the growth of fungi and bacteria in the products and to ensure a good durable quality, and ensure that consumers are protected from harmful influence of microorganismens in the product. Some of the preservatives have been shown to cause allergy while others are suspected of being endocrine disruptors or to provide resistance to some bacteria. The Environmental Protection Agency therefore launched this project to increase the level of knowledge regarding the use of preservatives in cosmetic products on the Danish market.

1.2 Definition of preservatives

This report defines preservatives as specified in the Cosmetics Regulation (Regulation No 1223, 2009). That is, preservatives are "substances which are exclusively or mainly intended to prevent the development of microorganisms in the cosmetic product" (Article 2 section. 1 l, Regulation No. 1223, 2009). Preservatives permitted for use in cosmetic products are listed in Annex V of the Cosmetics Regulations. Annex V contains a total of 58 reference numbers of preservatives comprising a total of approx. 140 different preservatives (CAS-numbers). Some of these preservatives may be used for other purposes than preservation and are also regulated in Annex III of the regulation, which is a list of substances that may be used in cosmetic products with restrictions. The list of permitted preservatives is presented in Appendix 1 to this report. When the concept of preservatives is used in this report, reference is therefore made to the permitted preservatives in Annex V of the Cosmetics Regulation.

1.3 Objective

The overall objective of this project is to assess whether there may be a risk associated with the use of preservatives in cosmetic products. This question has been sought answered by examining the following sub-objectives:

- To identify the preservatives used in practice in cosmetic products on the Danish market:
  - Which of the permitted preservatives are used most frequently in cosmetic products on the Danish market today? That is, are some preservatives more frequently used than others?
  - Is there a difference between the uses of preservatives for different product types?
  - Are there types of cosmetic products on the market not containing preservatives?
- To investigate whether there are preservatives permitted in cosmetic products, but not permitted under the Biocides Regulation - especially if this lack of permission is justified by health concerns.
- To make environmental assessments (screening) of selected permitted preservatives.
- To make health assessments and risk assessments of selected permitted preservatives.

1.4 Definition of product types

Initially, the definition of the project was discussed with the EPA. Cosmetic products cover many different types of products ranging from wet wipes to lipstick. A preliminary assumption was that products not containing water (such as powder, eye shadow, oils of various kinds) do not contain preservatives, as they should not need to be preserved (due to the lack of water content). Similarly,

a preliminary assumption was that products with a high content of alcohol (such as eau de parfum, eau de toilette, skin tonic and similar products) do not contain preservatives, since alcohol in itself is preserving. The initial studies for declarations of contents on various cosmetic products showed, however, that products without water can contain preservatives. Previous studies of cosmetic products have also shown (see Section 1.8 "Previous studies of cosmetic products") that products without water can contain preservatives. In addition, it appeared from the information from the industry that in some cases preservatives are added to products not containing water to protect them from external microorganisms. For these reasons, it was decided not to exclude certain types of cosmetic products in advance, and a definition of the project has not been made with regard to types of cosmetic products.

It was initially decided in cooperation with the EPA that the content of preservatives should be examined for approx. 10 products within each product type.

1.5 Definition of preservatives/substances

The project was defined exclusively to investigate the products for presence of one or more of the 58 reference numbers containing approx. 140 preservatives listed in the Cosmetics Regulation Annex V. Other substances may also have preserving properties, but then typically they have another primary function - such as alcohol that is primarily used as a solvent, but also has preserving properties. These other substances with multiple functions have not been studied in the project (see Section 1.6 on multi-functional ingredients).

1.6 Ensuring product durability

Cosmetic product durability can be improved in many ways - the use of preservatives is just one of them; eg. manufacture under sterile conditions (GLP - Good Laboratory Practice and/or GMP - Good Manufacturing Practice) may help to promote cosmetic product durability, but will not prevent a possible contamination of the product with microorganisms at the consumers place. Product packaging is also of vital importance to the need for preservatives. For example, the packaging for fluid products can be designed with a metering pump that prevents the decline of air to the container and thereby also ensures that the product is not contaminated by contact with the user's fingers (Varvaresou *et al*, 2009).

The production and formulation of the products also provide opportunities to reduce the need for preservatives, for example by adjusting the pH value and the water activity (ie. the presence of water). The growth rate of microorganisms is contingent on the presence of water and is generally favoured around a neutral pH value. The possibilities to adjust the pH is limited by the fact that a too alkaline or acidic pH could degrade the preservative, and could also irritate the skin. Finally, multi-functional ingredients are used, which are ingredients with multiple functions in the cosmetic product, ie. antibacterial activity or to support the effect of other preservatives, which can then be used in minor amounts. The multi-functional ingredients do not appear from Annex V of the Cosmetics Regulation, as the preserving properties are not their main function.

Some examples of the use of multi-functional ingredients are caprylyl glycol (which may essentially increase the antimicrobial activity for certain preservatives), caprylic acid, glyceryl caprate, and ethylhexyl glycerin (reduce the surface tension of microbial cell membranes, thereby increasing the contact surface to the preservative), citric acid and EDTA (may increase the permeability of the cell membranes, making them more sensitive to preservatives), and various essential oils may also have antibacterial properties. This is detailed in the EPA report on non-preserved cosmetics (Poulsen & Strandesen, 2011).

The survey (described in Chapter 3) confirms the use of multi-functional ingredients. As can be seen from the survey, many of the above multi-functional ingredients are used as boosters, ie. as "help"

or "support" to increase the functions of the applied preservatives. Contact with suppliers during the survey revealed that multi-functional ingredients are widely used.

1.7 Distribution of cosmetic products on the Danish market

According to the trade association SPT[1], cosmetic products for nearly 8 billion DKK were sold in Denmark. The Danish cosmetics market is divided as shown in Figure 1 below. Hair care and skin care products accounted for the largest market (by value) by 29 % and 24 % of the total sales in 2011. Sales are stated in Danish kroner.

Via Statistics Denmark (Statistics Bank) it is possible to draw more detailed statistics on cosmetic products, namely a list in which cosmetic products are divided into 29 different product codes. The Statistics Bank gives data for turnover in Danish kroner and in quantities (kilograms). In Appendix 2 "Extract from Statistics Denmark for import and export of cosmetic products", imports are specified (in kilograms) for the 29 product codes for 2012. These 29 product codes have in the following Figure 2 been distributed to the five groups of cosmetic products used by the SPT (ie. perfumes and fragrances, decorative cosmetics, skin care, hair care, and toiletries). The grouping is based on an estimate of which product code belongs to which of the five groups of cosmetic products. In some instances, however, a product code covers both decorative cosmetics and skin care products, so the division cannot be made in full compliance with the 5 groups.

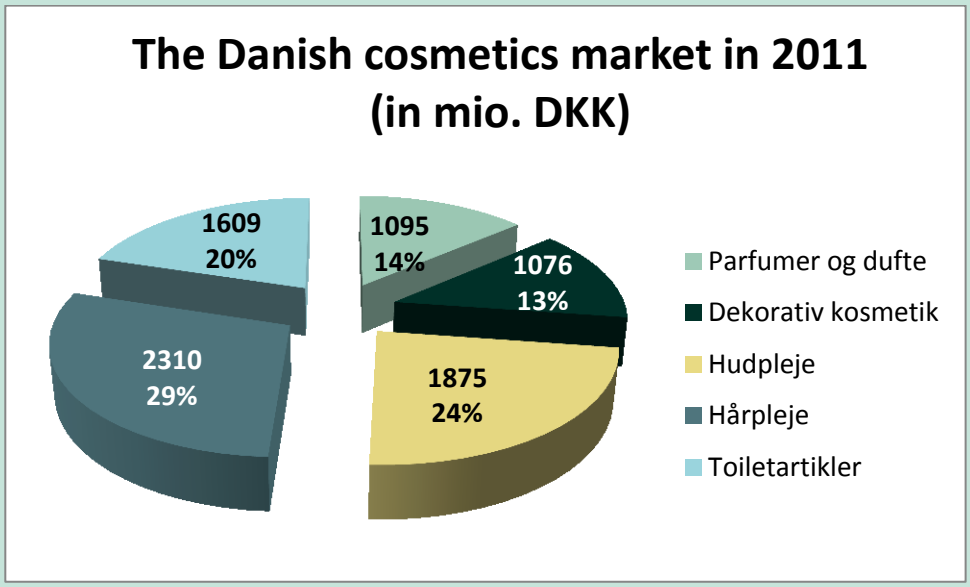

FIGURE 1
THE DANISH COSMETICS MARKET IN 2011 ACC. TO SPT'S WEBSITE. SALES OF COSMETICS IN PHARMACIES ARE INCLUDED. THE FIGURES ARE STATED IN MILLION DKK RSP (RETAIL SAILS PRICES). STATISTICS CONTAIN BOTH CONCRETE REPORTED FIGURES AND ESTIMATES. FIGURES ARE EXCLUSIVE OF TAX-FREE SALES AND SALES TO GREENLAND AND THE FAROE ISLANDS (SOURCE: WWW.SPT.DK).

[1] SPT is a broad-based trade organisation for manufacturers and suppliers of detergents, cosmetics and personal care products.

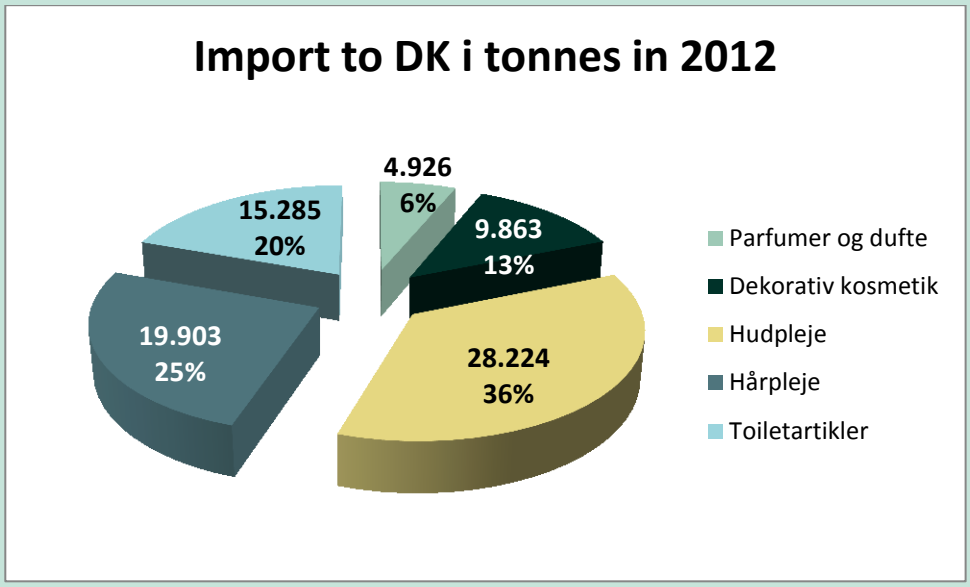

FIGURE 2
EXTRACT FROM STATISTICS DENMARK – IMPORT TO DENMARK IN TONS IN 2012. THE EXTRACT ARISES FROM 29 DIFFERENT PRODUCT CODES, WHICH ACC. TO ESTIMATE ARE LOCATED IN THE SAME FIVE GROUPS OF COSMETIC PRODUCTS USED BY SPT ABOVE (FIGURE 1). (SOURCE: STATISTICS BANK).

Although Figure 1 and Figure 2 cover different years (2011 and 2012, respectively), and the figures illustrate different units (Danish kroner and tonnes, respectively), the distribution between the individual groups of cosmetic products is relatively similar in the two figures. Perfumes and fragrances account for a smaller percentage measured in volume than in price, which is related to the fact that this category covers expensive products (ie. low weight but high price). Skin care and hair care cover the largest groups of cosmetics and in 2012 accounted for 61.5 % of the total imports of cosmetics in terms of volume (tonnes). Toiletries (such as soap, toothpaste, etc.) accounted for 20 % of the total imports of cosmetics in 2012.

Significant information from Appendix 2 "Extract from Statistics Denmark for imports and exports of cosmetic products" includes the fact that of the total of approx. 78 tonnes imported in 2012 (sum of the total of 29 product codes), the following groups of cosmetic products are the most significant:

- Soap in various forms: approx. 25 000 tonnes
- Hair care products: approx. 10 100 tonnes
- Dental care products (including products for dentists): approx. 9800 tonnes
- Shampoos: approx. 8300 tonnes
- Beauty care products for make-up and preparations for skin care: approx. 8300 tonnes

Thus soaps, hair care products, shampoos, dental care products, beauty care products, and skin care products were the main cosmetic products imported to the Danish market in 2012. It should be noted that there are significant differences in the breakdown of the different types of cosmetic products in Statistics Denmark and SPT's information. Product codes from Statistics Denmark in some cases cover both decorative cosmetics and skin care products."Beauty care products and preparations for skin care" (about 8300 tonnes), for example, are grouped under decorative cosmetics in Figure 2.

1.8 Previous studies of cosmetic products

The EPA has made a number of previous surveys concerning cosmetic products:

- Hair dyes (365 products, 2011)
- Non-preserved cosmetics (89 products, 2009) - use of a few preservatives was seen here, as a group of "naturally" preserved products were also included in the study
- Sunscreen lotions and creams for children in the project on exposure of 2-year old children to chemical substances (60 products, 2008)
- Cosmetic products for children (208 products, 2007)
- Hair styling products (328 products, 2001)

The use of preservatives in these types of products from the previous studies is presented in Appendix 3 "Previous studies of cosmetic products". It should be noted that cosmetic products are frequently reformulated, and therefore these studies, all of which are several years old, can be used only as a snapshot of the time they were made. The information from these previous studies is therefore used only as historical background, and to provide a picture of the fact that certain types of cosmetic products are probably not preserved.

The survey of hair dyes showed that sodium sulfite and sodium metabisulfite are almost exclusively used as preservatives in hair dyes (in 54 % and 38 % of the investigated products). This picture is clearly different from other types of cosmetic products. In total, approx. 67 % of the hair dyes were preserved (Poulsen & Strandesen, 2013).

The survey of non-preserved cosmetics also included products that were marketed as "naturally preserved". These few products contained preservatives, of which sodium benzoate, potassium sorbate and phenoxyethanol were the most common (Poulsen & Strandesen, 2011).

The survey of sunscreens and creams for children showed that phenoxyethanol was the most commonly used preservative in both sunscreens (61 %) and creams (50 %) for children. After this, the most commonly used preservatives are sodium benzoate and parabens used in both product types. A total of 59 % of the creams and 68 % of the sunscreens were preserved (Tønning et al, 2009).

In the survey of cosmetic products for children, the parabens were overall the most commonly used preservatives. The parabens were used in the following percentages of the examined products: methylparaben 38 %, ethylparaben 22 %, propylparaben 34 %, butylparaben 23 %, isobutylparaben 19 %, and isopropylparaben 2 %. Phenoxyethanol was used in approx. 24 % of the examined products. In total, 63 % of the products was preserved (Poulsen and Schmidt, 2007).

In the survey of hair styling products, methylparaben (23 %) and phenoxyethanol (18 %) were the most commonly used preservatives. A total of 49 % of the hair styling products contained preservatives (Poulsen et al, 2002).

The previous studies show that very few product types do not contain preservatives. Bath oils seem to be the only product type, in which no preservatives were identified (and where the group of examined products has been more than 1-2 products). For some product types only a small proportion has been found to contain preservatives. This applies to eg. hairspray (20 %), perfume/eau de toilette (11 %), and solid soap (9 %). This picture is not expected to have changed, although the oldest of the studies is more than 10 years old.

The previous studies also show that many cosmetic products typically contain preservatives, but definitely not all. For example, 59 % and 68 % of creams and sunscreens, respectively, were preserved.

The previous studies also show that the following preservatives have been most commonly used:

- Phenoxyethanol (most commonly used in all previous studies)
- Sodium benzoate (used relatively frequently in all the previous studies)

- Parabens (methylparaben and propylparaben are the most commonly used parabens – this applies to most of the previous studies)

The use of parabens may be in a smaller scale today because of new knowledge about their endocrine disrupting potential and thus large press coverage. Furthermore, the use of propyl, isopropyl, butyl and isobutylparaben has been temporarily banned nationally in products for children under the age of 3 since 2011 (Statutory Order 166, 2011).

In Chapter 3, the results from these previous studies are compared with the results from the survey of the market in this project (2013). The previous studies cover a segment of the cosmetics market as it appeared at the time.

1.8.1 The most commonly used preservatives according to Cosmetics Europe

Cosmetics Europe refers on their website to a US study on the use of preservatives, where the FDA in 2010 conducted a survey of the use of preservatives in the United States and Canada. The survey was voluntary and is thus based on responses received from the industry in the United States and Canada. This study showed that the following preservatives were the most commonly used in the US and Canada at the time (Steinberg, 2010):

1. Parabens (all forms of parabens)
2. Phenoxyethanol
3. Methylisothiazolinone / Methylchloroisothiazolinone
4. Formaldehyd releasers, such as DMDM Hydantoin, Diazolidinyl urea, Imidazolidinyl urea and Quaternium-15
5. Sorbic acid / Potassium sorbate
6. Benzoic acid / Sodium benzoate
7. Dehydroacetic acid / Sodium dehydroacetate
8. Chlorphenesin
9. Chlorhexidine digluconate
10. Benzyl alcohol

Cosmetics Europe assesses that the picture is not expected to be very different in the EU, but that there may be a different order among the preservatives in the EU, particularly in light of the publicity and assessment of the parabens in the EU. Therefore, parabens are not expected to be the most commonly used preservatives in the EU.

2. Legislation and Environmental labelling

This chapter describes the legislation on cosmetic products, as well as the criteria for the Swan labelled cosmetic products, as it is mainly the Swan ecolabel that occurs on cosmetic products on the Danish market[2].

2.1 Legislation

In 2009, EU adopted a new regulation on cosmetic products (the "Cosmetics Regulation", Regulation No. 1223, 2009). This regulation applied from July 11, 2013 with the exception of a few provisions in force already from 1 December 2010 and 11 January 2013. Some of the cosmetic products examined in this project were on the market before 11 July 2013, which means that they are not necessarily comprised by the regulation.

The Cosmetics Regulation is further described below with focus is on the aspects relevant to this project, ie. the rules for the lists of ingredients, safety assessments and preservatives.

Furthermore, the Danish prohibition of the use of certain parabens in cosmetic products for children under the age of 3 is described.

2.1.1 The Cosmetics Regulation (Regulation No. 1223, 2009)

The Cosmetics Regulation includes a number of provisions concerning the content of chemicals in cosmetic products and labelling of the products. According to Article 3 of the Cosmetics Regulation, a cosmetic product made available on the EU market must be safe for human health when applied under normal or reasonably foreseeable conditions. The Cosmetics Regulation also contains a number of restrictions related to various chemicals, eg. only certain preservatives are allowed to be used.

2.1.1.1 List of ingredients

According to the Cosmetics Regulation, cosmetic products must be labelled with full ingredients lists (Art. 19). Therefore, it is possible to see the preservatives used in the product on the product packaging. In the lists of ingredients, the ingredients must be stated by their INCI names. INCI is short for "International Nomenclature of Cosmetic Ingredients" and is a common nomenclature to be used in the declaration of the contents in cosmetic products in the EU. An INCI name may cover several different chemicals. The list of INCI names is indicative, meaning that it is not a list of approved ingredients in cosmetic products (Article 33). If an INCI name for an ingredient does not exist, the chemical name of the substance must be used (Article 19).

[2] According to Ecolabelling Denmark, per March 2014 there is more than 2,200 Swan labelled cosmetic products on the Danish market, whereas the figure for Flower labelled cosmetic products is 28.

2.1.1.2 Safety assessment

A safety assessment of the cosmetic products must be made (Article 10).
The safety assessment is described in a safety report. One of the requirements for safety assessment is that the microbiological quality must be assessed, as lack of preservation may constitute a health problem, but on the other hand the amount of preservative in the specific assessment must be safe for human health.

2.1.1.3 Preservatives

In the Cosmetics Regulation, preservatives are defined as "substances which are exclusively or mainly intended to prevent development of microorganisms in cosmetic products" (Article 2 section. 1 l).

According to the Cosmetics Regulation, it is not allowed to use preservatives other than those listed in Annex V. In addition, the preservatives must be used in accordance with the conditions specified in Annex V (typically the maximum permitted concentration or that the preservative must not be used in oral care products, for example).

Annex V to the Cosmetics Regulation contains a total of 58 reference numbers for preservatives, which totally cover approx. 140 different CAS numbers. The list of permitted preservatives is given in Appendix 1 to this report.

According to Annex V, the labels of all finished products, containing formaldehyde or substances in Annex V, which may release formaldehyde, must be provided with the text “Contains formaldehyde”, if the concentration of formaldehyde in the finished product exceeds 0.05 %, except for nail hardening products in which a concentration of 5 % is allowed according to Annex III.

The safety by use of the preservatives is assessed by the EU Scientific Committee on Consumer Safety (SCCS), who publishes an opinion describing the safe use (ie. for product type, concentration, etc.) before the substances may be used. Inclusion of preservatives in Annex V to the Cosmetics Regulation is effected by vote of the Member States.

Some preservatives can be used for purposes other than preservation and are regulated in the regulation’s Annex III, which is a list of substances that may be used in cosmetic products with limitations.

2.1.2 Statutory Order prohibiting the use of certain parabens (Statutory Order 166, 2011 and Statutory Order 1217, 2013)

Statutory Order no. 1217 (2013) and the previous Statutory Order no. 166 (2011) prohibiting import, sale and use of certain parabens in cosmetic products for children under the age of 3 prohibit the use of the following parabens and their salts:

- Propylparaben
- Butylparaben
- Isopropylparaben
- Isobutylparaben

The prohibition is valid only for these parabens and solely for cosmetic products intended for children under the age of 3, ie. baby products or other products that may be intended for children under the age of 3. The statutory order came into force in March 2011.

The parabens methylparaben and ethylparaben are still permitted for use in cosmetic products for children under the age of 3, because they are considered safe to use by the SCCS.

2.2 Swan labelling of cosmetic products

Ecolabelling Denmark has been contacted during this survey[3]. Ecolabelling Denmark informed that they do not operate with a positive list of preservatives permitted for use in Swan labelled cosmetic products. In each case, it is considered whether the preservatives can meet the demands of the criteria document. Ecolabelling Denmark informed that it is often the requirement for bioaccumulation and the requirement for content of sensitising substances that can not be met by the preservatives.

2.2.1 Criteria for Swan labelling of cosmetic products

According to the criteria document for Swan labelling of cosmetic products (Nordic Ecolabelling, 2010), the following criteria apply for the use of 'ingoing substances', including preservatives:

- The preservative's chemical name, trade name, INCI-name, any CAS-no., and ingoing amount (including and excluding water) must be disclosed.
- The preservative must not be classified (in practise, this applies to both harmonised classification or self-classificaton) as sensitising by skin contact or inhalation, carcinogenic (all categories), mutagenic (all categories) or harmful to reproduction (all categories).
- If the preservative is classified as environmentally hazardous under Statutory Order 1272/2008/EEC (as of 1 December 2010) or Directive 67/548/EEC (until 1 December 2010 and during the transition period from 2010 to 2015), limitations are set for the concentration in the product.
- Recommendations by EU's Scientific Committee on Consumer Safety (SCCS)[4] must always be followed. This means that if the SCCS has recommended that a preservative is only safe when used in a concentration of less than permitted by the cosmetics legislation, the recommendations from the SCCS must be followed, although this recommendation has not (yet) been incorporated in the regulation.
- Triclosan and parabens (4-hydroxybenzoic acid and its salts and esters) and other substances considered to be potential endocrine disruptors are not allowed in the product (Annex 2 of the criteria document on definition elaborating that it concerns substances listed on the EU list of potential endocrine disruptors).
- If the preservative is assessed by the EU to be PBT or vPvB, it must not be present in the product.
- For products that are rinsed off with water immediately after use (rinse-off products such as shampoos), it applies that the content of organic substances (including preservatives) that is not readily biodegradable, must not exceed certain established exposure limits for aNBO (Aerobic Non-biodegradable Organics) and anNBO (Anaerobic Non-biodegradable Organics).
- For other cosmetic products (ie. leave-on products), requirements for the degradation and aquatic toxicity of the ingoing organic substances are established.
- The preservative must not be bioaccumulative.
- The use of preservatives for other purposes than preservation of the product itself is not allowed, unless the preservative is included in Annex III of the Cosmetics Regulation.
- In addition, it applies that for the product types toothpaste, lip products, and oral care products, the used preservatives must be approved as food additives.

It should be noted that the requirements do not apply to 'contaminations' below 0.01 % (100 ppm) in products, which are rinsed off immediately after use (rinse-off products), and for leave-on products, the limit is 0.001 % (10 ppm), unless the substances have been intentionally added to the products in these concentrations with a specific purpose. Known degradation products must also comply with the requirements.

[3] Telephone conversation with Trine Pedersen, senior consultant, Ecolabelling Denmark, July 2013
[4] EU's Scientific Committee on Consumer Safety (SCCS)

3. Survey of the market

In the summer of 2013, a survey was carried out on the use of preservatives in cosmetic products on the Danish market. Methods and results etc. of this survey are described below and form the basis for the rest of the project.

3.1 Objective of the survey

The objective of the survey is to investigate the kind of preservatives mainly used in cosmetic products on the Danish market. The Cosmetics Regulation (No. 1223, 2009) includes Annex V: "List of preservatives permitted in cosmetic products". It is thus not permitted to use other than the 58 reference numbers for preservatives (equivalent to approx.. 140 individual substances), listed in this Annex, in cosmetic products. With this survey, the EPA wants to get an overview of:

- Which of the permitted preservatives are most frequently used in cosmetic products on the Danish market today? That is, are some preservatives used more frequently than others?
- Is there a difference in the use of preservatives for different product types?
- Are there types of cosmetic products on the market not containing preservatives?

3.2 Procedure for the survey

The survey of preservatives in cosmetic products on the Danish market was carried out by means of the following:

- Contact to the trade association SPT (the trade association for soap, perfume and chemical engineering articles)
- Contact to selected manufacturers/importers of cosmetic products on the Danish market
- Contact to selected manufacturers of preservatives and preservative systems [5] for cosmetic products on the Danish market
- Contact to selected distributors of cosmetic products
- Contact to Ecolabelling Denmark
- Search on the web for lists of ingredients of cosmetic products
- Examination of lists of ingredients of cosmetic products in shops

Some of these activities are further described below, and the results are described in Section 3.4 "Survey results".

3.2.1 Definition of types of cosmetic products

Initially in the project, a list of different types of cosmetic products was compiled. The starting point for this work is recital no. 7 of the Cosmetics Regulation (Regulation No. 1223, 2009; recital No. 7), which contains a grouping of cosmetic products. From this grouping, a list of a total of 55 different product types is compiled, presented in Appendix 5: "The number of products for each of the 55 product types." Annex 5 also states the number of products in each product type used in the survey.

[5] Preservative Systems is a system, ie. a mixture of different substances and preservatives, which together preserves the product. A preservative system may also contain substances that are not preservatives, but act like e.g. a booster for the preservatives (ie. promotes/supports the effect of the preservatives).

3.2.2 Search on the web for the lists of ingredients of cosmetic products

A general search was made on the Internet for webshops, manufacturers, etc. stating the full lists of ingredients on cosmetic products. Keywords like "list of ingredients" and "ingredients" were used in combination with various types of cosmetic products. In addition, earlier used webshops were searched, for which the project group has experienced that the full lists of ingredients are stated.

Selected lists of ingredients found via the Internet are included in the final survey, but this method was mostly used as a supplement to visits to the shops. That is, the ingredients lists found via the Internet are used primarily as supplements, so that information could be obtained on approx. 10 products of each product type.

3.2.3 Study of lists of ingredients of cosmetic products in shops

In connection with the survey, the following distributors of cosmetic products have been contacted:

- COOP
- Dansk Supermarked
- Apotekernes A.m.b.a.
- Matas

They were asked about their use of preservatives in cosmetic products (their own brands), and arrangements were made for us to be allowed to sit in one of their shops and write down lists of ingredients for a wide selection of their range (own brands as well as brands from other manufacturers) of cosmetic products.

Agreements with COOP, Dansk Supermarked, and Matas, respectively, made it possible to study lists of ingredients of cosmetic products in a Kvickly, a Bilka and a Matas shop, respectively. In addition, lists of ingredients of cosmetic products were identified in various webshops. Especially, the investigation was supplemented with products from the pharmacies, but due to lack of information on the lists of ingredients on the web, products primarily available via webshops are not included in the survey.

The aim was to find approx. 10 products from each product type, but this was not successfull in all cases. There are several reasons for this:

- For some product types, it was not possible to find 10 different products in the shops or via the Internet because the product type is not that widely distributed.
- For some product types, it soon became apparent that the use of preservatives was less common (eg. in oil based products); therefore data for 10 products were not entered in these categories.
- For product types that represented a significantly higher percentage than other product types with regard to revenue and volume, data for more than 10 products were entered. This was for hair and skin care products among others.
- After information on ingredients lists was collected, in some cases, a further division into product types was made (several product types), and therefore the survey did not include 10 products for each product type.

A total of 639 cosmetic products were selected, for which information on the contents of preservatives was recorded.

3.3 Preparation of a list of cosmetic products

In this survey, the lists of ingredients of cosmetic products were obtained as follows:

- Photographing products in shops such as Kvickly, Bilka, and Matas.
- Identifying lists of ingredients of products on the Internet - eg. in webshops and from manufacturers. Products from pharmacies have been identified like that.
- Contacting manufacturers of cosmetic products, who sent the lists of ingredients.

Of the above methods, it was the visits to the shops that gave the most information. In addition, manufacturers have provided general information about the types of preservatives they use in their cosmetic products (ie. not down to single-product level, but on a more general level).

The lists of ingredients were reviewed, and the following information for each product was noted and is therefore included in this survey:

- Product name
- Product type – according to the 55 product types listed in Section 3.2.1 "Definition of types of cosmetic products"
- Preservative with INCI-name
- Number of preservatives
- Swan labelled (yes/no)
- Products for children (yes/no)
- Rinse-off or leave-on products
- Overall grouping as used on SPT's website - is it one of the five major groups of cosmetic products: decorative cosmetics, skin care, hair care, perfumes and fragrances, and toiletries?
- Source of information - here is indicated from where the information originated (eg. the Internet or was the product seen in a particular shop)
- Date
- Price
- Manufacturer

The data entry was carried out by reading through the INCI declaration and noting the preservatives contained in the product. This approach was chosen instead of entering the entire INCI declaration, because there was no time to enter information about the preservatives for a larger number of products.

Based on this information, the results of the survey are presented, cf. Section 3.4 "Survey results".

3.4 Survey results

The survey results are divided as follows:

1. Result of contact with the industry
   1.1. Information received from manufacturers, distributors and retailers
   1.2. Information received from manufacturers of preservatives and preservative systems used in cosmetic products on the Danish market
2. Information entered from the lists of ingredients of products

3.4.1 Results of contact with the industry

3.4.1.1 Information received from manufacturers, distributors and retailers of cosmetic products

The trade association SPT was contacted to help arrange contacts with SPT members. The SPT forwarded an email from the project group calling on the 68 members within perfumes, cosmetics and personal care products to submit information about the use of preservatives in cosmetic products on the Danish market. Eight of these 68 members have supplied information to the project, ie. approx. 12 %. The market share of these eight members on the Danish market is not known. In addition, Apotekernes A.m.b.a was contacted and they created contact to their suppliers of cosmetic products to pharmacies.

Selected manufacturers of cosmetic products gave information about the distributors/ manufacturers supplying their preservatives and/or preservative systems. A selection of these distributors/manufacturers were also contacted for the purpose of asking, which preservatives and/or preservative systems they sell to manufacturers selling cosmetic products in Denmark.

Table 1 below presents the general information received from various manufacturers, distributors and retailers of cosmetic products on the Danish market regarding their use of preservatives and/or preservative systems. Each line in the table represents an example of the use of preservatives or preservative systems, ie. when three preservatives are mentioned in the same line, the company uses these three preservatives together in one or more cosmetic products. It should be noted that by this request to the manufacturers, the type of cosmetics is not always ascertained, as the manufactures speak generally about all of their cosmetic products.

The information is anonymised, deliberately not specifying company names or details of the product types. The preservatives are listed by their INCI names. Contents in percentage are indicated for each preservative (in parentheses after the name) or for the entire preservative system if indicated by the manufacturer/distributor.

Company	Preservatives / preservative system used	Typical total concentration	Comments
A	No preservatives used		Used multi-functional ingredients
B	**Phenoxyethanol, benzoic acid, dehydroacetic acid**	0.6%	The mixture can be used for Swan labelled products and is their most commonly used preservative system The company's products without preservatives are: toothpaste, nail polish remover, sun stick, and baby oil
C	**Dehydroacetic acid, benzoic acid, phenoxyethanol**, multi-functional ingredient	0.68-1.0%	The company informs that the most commonly used preservative systems are listed first The company sells products without preservatives within the following product types: hair styling foam, hair spray, eau de parfume, nail polish remover, nail polish, eye liner, lip glos, lip liner, foundation, lipstick and eye shadow
	Dehydroacetic acid, benzoic acid, polyaminopropyl biguanide, phenoxyethanol, multi-functional ingredient	0.4-1.0%	
	Diazolidinyl urea, sodium benzoate, potassium sorbate	0.1-1.0%	
	Phenoxyethanol, multi-functional ingredient	0.5-1.2%	
	Piroctone olamine	0.8-1.0%	
	Methylparaben	0.2%	
	Phenoxyethanol	0.3-0.8%	
	Methylisothiazolinone, multi-functional ingredient	0.1%	
D	**Phenoxyethanol**		The company informs that they preserve differently depending on whether it is rinse-off or leave-on products
	Sodium benzoate		
	Potassium sorbate		

Company	Preservatives / preservative system used	Typical total concentration	Comments
	Dehydroacetic acid, benzoic acid, phenoxyethanol, sodium benzoate		The company informs that the preservative they use the most is **phenoxyethanol**, that is part of the majority of their products
	Dehydroacetic acid, benzoic acid, phenoxyethanol		
	Phenoxyethanol (0.6%), potassium sorbate (0.1%), multi-functional ingredient (0.4%)		
	Phenoxyethanol (0.74%), sodium benzoate (0.25%)		
E	**Phenoxyethanol (0.98%), benzoic acid (0.06%), dehydroacetic acid (0.04%), sodium benzoate (0.004%),** multi-functional ingredient (0.07%)		This preservative system is an example of a preservative used in Swan labelled baby wipes
F	No preservative used		Uses multifunctional ingredients
G	**Imidazolidinyl urea**	0.3%	The 13 listed preservatives were all used in 2013, but many of them are on their way out. This applies to **all the parabens** and **imidazolidinyl urea**. The most important preservatives are **phenoxyethanol** and **sodium benzoate** accounting for 63% and 33%, respectively, of the company's total use of preservatives. The remaining preservatives thus only accounted for 4% of the total use in 2013. The latter six preservatives are used in special types of products
	Methylparaben	0.07-0.4%	
	Butylparaben	0.01-0.02%	
	Ethylparaben	0.03-0.2%	
	Isobutylparaben	0.005-0.008%	
	Propylparaben	0.006-0.014%	
	Phenoxyethanol	0.5-0.9%	
	Sodium benzoate	0.1-0.5%	
	Sodium dehydroacetate	0.25%	

Company	Preservatives / preservative system used	Typical total concentration	Comments
			as indicated.
	Chlorhexidine digluconate	0.04-0.2%	Cleansers
	Cetrimonium chloride	0.25-1%	Hair products
	Zinc pyrithione	1%	Dandruff shampoo
	Climbazole	0.5%	Dandruff shampoo
	Piroctone olamine	0.5-0.75%	Dandruff shampoo / special shampoo products
	Salicylic acid	0.1-0.5%	Special products
H	**Methylchloroisothiazolinone, methylisothiazolinone**		
	Sodium benzoate		
	Methylparaben		
	Propylparaben		
	Phenoxyethanol		
	Phenoxyethanol, methylparaben, ethylparaben, propylparaben		
	Phenoxyethanol, benzoic acid, dehydroacetic acid		
	Potassium sorbate		
	Phenoxyethanol, multi-functional ingredient		
	Ethylparaben		

TABLE 1
INFORMATION ON THE USE OF PRESERVATIVES FROM EIGHT DISTRIBUTORS/MANUFACTURERS OF COSMETIC PRODUCTS. THE USED PRESERVATIVES ARE HIGHLIGHTED.

3.4.2 Information received from manufacturers of preservatives

Four manufacturers of preservatives have been contacted in connection with the survey of preservatives in cosmetic products.

Of these, two manufacturers provided detailed information about the use of their preservatives, while a third has given more general information. The information is anonymised and is presented collectively in Table 2 below.

Company	Preservatives / preservative system used	Typical total concentration	Comments
1	**Sodium benzoate**	0.5-2%	The company informs that they also use multi-functional ingredients in combination with the preservatives in the preservative systems they sell.
	Phenoxyethanol	0.2-0.8%	
	Propylparaben		
	Methylparaben		
	Benzyl alcohol	0.2-0.7%	
	DMDM Hydantoin	0.3-0.6%	
	Methylchloroisothiazolinone, methylisothiazolinone		
	Phenoxyethanol, methylparaben, ethylparaben, propylparaben		
	Benzyl alcohol, multi-functional ingredient		
2	**Phenoxyethanol, benzoic acid, dehydroacetic acid**	0.5-1.0%	The company informs that this is the most commonly used mixture of preservatives. Otherwise the other specified preservatives are used alone or in combinations.
	Phenoxyethanol		
	Benzoic acid		
	Dehydroacetic acid		
	Sodium benzoate		
	Potassium sorbate		
3	**Phenoxyethanol**		The company only informs that phenoxyethanol is the most commonly used preservative.

TABLE 2
INFORMATION ON THE USE OF PRESERVATIVES FROM THREE MANUFACTURERS OF PRESERVATIVES. THE USED PRESERVATIVES ARE HIGHLIGHTED.

3.4.3 General comments from the contacted companies

In addition to information on the use of preservatives, some of the manufacturers informed that they always reduce the amount of preservatives to the exact concentration that passes a challenge test[6]. When the products are tested, they are always tested with different concentrations of preservatives.

Finally, some of the manufacturers informed that they have largely phased out the use of parabens in their products, and that this is due to the publicity of parabens in the media. In these manufacturers' opinion, this has the consequence that other preservatives must be used instead, which may have other worrying properties, such as allergenic properties. Furthermore, these other preservatives may be used in higher concentrations to be similarly effective.

Two of the preservative manufacturers informed that the various environmental labels, such as the Swan, restrict the use of more efficient and economical alternatives such as isothiazolinones, which means that many customers are limited in their choice of preserving, as many cosmetic products today are eco-labelled, and more and more cosmetic products today are Swan labelled. Often organic acids are chosen (eg. dehydroacetic acid, salicylic acid, benzoic acid, sodium benzoate, potassium sorbate), or combinations with phenoxyethanol. These preservative systems are milder, and also require optimal hygiene at the factory. The company has seen a growing number of complaints, since parabens and isothiazolinones have been replaced by milder preservative systems in cosmetic products. Milder preservation is usually more pH sensitive, and a change in pH value may mean that the preservation with organic acids, for example, loses its effect and becomes contaminated.

3.4.4 Results of study on lists of ingredients

The results presented in this section are extracted from the information on preservatives in cosmetic products that are seen in the retail sector and on the Internet. In total, data for 639 different cosmetic products were collected spread over 54 different product types presented in Section 3.2.1 "Definition of types of cosmetic products ".

As previously described, the aim was to gather information for about 10 products of each product type. However, the product types sold in large quantities in the retail sector, and thereby resulting in a large consumer exposure, have had more emphasis, as data for more products of these types have been entered. Product types which according to the survey are not sold as much in retail, or which proved not always to contain preservatives, have had less emphasis. This approach was chosen in order to better take into account the source of exposure to the preservatives. The number of products spread over the 54 product types included in this survey is shown in the table in Appendix 5.

Section 1.7 "Distribution of cosmetic products on the Danish market" indicates a percentage distribution in terms of turnover and imports (volume) of the five main groups of cosmetic products used by the SPT on their website. Import volumes are considered more important benchmarks than revenue (price), because the volumes are the most important in an exposure context.

It was fairly managed to get a similar distribution (relative to the volumes of imports) of the cosmetic products for which information has been entered in this survey, see Table 3 below. However, it is not entirely clear exactly which product types belong to which of the five main product groups (as used by the SPT). There is some uncertainty on the distribution, and of course there is a difference between comparing a percentage distribution based on turnover (DKK), import volumes (tonnes) and number of products (units).

[6] In order to establish the durability of a cosmetic product, it is necessary to carry out a challenge test, in which the preservatives are tested for antimicrobial effect.

Overall group of cosmetic products	Market in 2011 based on turnover (SPT)	Import in 2012 based on volumes (Statistics Denmark)	Number of products in this survey
Decorative cosmetics	13.5%	13%	15%
Skin care	23.5%	36%	38%
Hair case	29%	25%	23%
Perfumes and fragrances	14%	6%	9%
Toiletries	20%	20%	16%
Total	100%	100%	100%

TABLE 3
PERCENTAGE DISTRIBUTION OF THE NUMBER OF PRODUCTS INCLUDED IN THIS SURVEY COMPARED TO DISTRIBUTION PROVIDED BY THE SPT AND STATISTICS DENMARK.

The 639 products for which information has been entered cover **products from at least 116 different manufacturers/importers**. This figure represents a minimum, as names of the manufacturers/ importers in some cases were not identified (for example, where photos of the product labels are used subsequently, and the name of the manufacturer did not appear from these photos or where the name of the manufacturer did not appear from the description on the Internet). The information on preservatives collected in this project is estimated to cover a wide range of products on the market.

The entered products include both cheap products (6 DKK for a piece of hand soap) and expensive products (470 DKK for facial cream or body shampoo) and everything in between.

3.4.4.1 Identified preservatives

In the 639 cosmetic products, a total of **51 different preservatives** have been identified. This means that it is far from all of the 146 preservatives, specified in Annex V of the Cosmetics Regulation, that are used in cosmetic products on the Danish market. However, it should be noted that the method used in this survey could mean that some preservatives may have been overlooked. Table 4 below shows the preservatives identified in this survey by examining the declarations of contents in the retail sector and on the Internet. In this table, the preservatives are sorted with the most commonly used preservatives at the top. It appears that phenoxyethanol and sodium benzoate are among the most commonly used preservatives.

This survey (examination of the lists of ingredients in the retail trade and on the Internet) shows that **on average there are 2.7 preservatives in the 442 products** containing preservatives. Almost a third (31 %) of the products are free from preservatives (a total of 197 products). In the remaining 442 products, between 1 and 9 preservatives were seen, except for a single product containing 12 different preservatives. 133 of the products contain only one preservative. This survey (survey of the list of ingredients in the retail sector and on the Internet) shows that there is on average 2.7 preservatives in the 442 products containing preservatives.

The use of several different preservatives in the same product may mean that the preservatives potentiate each other in order to provide a better total preservative effect than if used alone.

When collecting information on preservatives, it was noted that eg. several shampoos from the same manufacturer could contain different preservatives, although it was the same brand of shampoo only with different flavour or function (for dry hair or curly hair).

In Table 4, the frequency of the used preservatives is indicated in percentage of all 639 products that were part of this survey, and just the 442 products in the survey containing preservatives.

By comparison of the preservatives used in Table 4 with the most commonly used preservatives from the US FDA study (referred in Section 1.8.1 "The most commonly used preservatives according to Cosmetics Europe"), it can be seen that all preservatives mentioned as the most commonly used in the FDA study are also used in Denmark. However, there are some differences in the order of the preservatives, as phenoxyethanol is the most commonly used preservative in Denmark (in this survey), followed by sodium benzoate/benzoic acid, benzyl alcohol and parabens.

Preservative	Number of the 639 products	Percentage of all selected products	Percentage of preserved products	Group number in Annex V
Phenoxyethanol	260	40.7%	58.8%	29
Sodium benzoate	142	22.2%	32.1%	1
Benzyl alcohol	108	16.9%	24.4%	34
Methylparaben	105	16.4%	23.8%	12
Potassium sorbate	69	10.8%	15.6%	4
Benzoic acid	60	9.4%	13.6%	1
Propylparaben	49	7.7%	11.1%	12
Methylisothiazolinone*	40	6.3%	9.0%	39 and 57
Dehydroacetic acid	38	5.9%	8.6%	13
Ethylparaben	38	5.9%	8.6%	12
Cetrimonium chloride	30	4.7%	6.8%	44
Methylchloroisothiazolinone	26	4.1%	5.9%	39
Butylparaben	20	3.1%	4.5%	12
Chlorphenesin	20	3.1%	4.5%	50
Sorbic acid	19	3.0%	4.3%	4
Salicylic acid	16	2.5%	3.6%	3
Isobutylparaben	15	2.3%	3.4%	12
DMDM Hydantoin	13	2.0%	2.9%	33

Preservative	Number of the 639 products	Percentage of all selected products	Percentage of preserved products	Group number in Annex V
Sodium dehydroacetate	13	2.0%	2.9%	13
Behentrimonium chloride	12	1.9%	2.7%	44
Sodium sulfite	8	1.3%	1.8%	9
Sodium salicylate	7	1.1%	1.6%	3
Quaternium-15	6	0.9%	1.4%	31
Sodium methylparaben	6	0.9%	1.4%	12
Imidazolidinyl urea	5	0.8%	1.1%	27
Sodium metabisulfite	5	0.8%	1.1%	9
Formic acid	4	0.6%	0.9%	14
Polyaminopropyl biguanide	4	0.6%	0.9%	28
2-bromo-2-nitropropane-1,3-diol	2	0.3%	0.5%	21
Benzalkonium chloride	2	0.3%	0.5%	54
Chlorhexidine	2	0.3%	0.5%	42
Diazolidinyl urea	2	0.3%	0.5%	46
Isopropylparaben	2	0.3%	0.5%	12
Sodium bisulfite	2	0.3%	0.5%	9
Sodium propylparaben	2	0.3%	0.5%	12
Triclosan	2	0.3%	0.5%	25
Chlorhexidine diacetate	1	0.2%	0.2%	42
Chlorhexidine digluconate	1	0.2%	0.2%	42
Chlorhexidine dihydrochloride	1	0.2%	0.2%	42

Preservative	Number of the 639 products	Percentage of all selected products	Percentage of preserved products	Group number in Annex V
Chloroacetamide	1	0.2%	0.2%	41
Chloroxylenol	1	0.2%	0.2%	26
Formaldehyde	1	0.2%	0.2%	5
Methyl benzoate	1	0.2%	0.2%	1a
Myrtrimonium bromide	1	0.2%	0.2%	44
Piroctone olamine	1	0.2%	0.2%	35
Potassium benzoate	1	0.2%	0.2%	1a
Propionic acid	1	0.2%	0.2%	2
Sodium hydroxy-methylglycinate	1	0.2%	0.2%	51
Sodium sorbate	1	0.2%	0.2%	4
Stearalkonium chloride	1	0.2%	0.2%	54
Steartrimonium chloride	1	0.2%	0.2%	44

* METHYLISOTHIAZOLINONE IS INDICATED IN TWO LOCATIONS IN ANNEX V (ALONE AND AS AN INGREDIENT IN A MIXTURE)

TABLE 4
PRESERVATIVES IDENTIFIED IN THIS SURVEY (RETAIL AND INTERNET).

If the information on the use of preservatives from manufacturers of cosmetic products and manufacturers of preservatives is compared with the 51 different preservatives in Table 4, it appears that *besides* the identified 51 preservatives from the survey of lists of ingredients, further two preservatives are used. However, they are only used in small amounts by one of the manufacturers of cosmetic products. The manufacturer also indicates that these two substances are used for purposes other than preservation.

- Zinc pyrithione (group number 8 in Annex V)
- Climbazole (group number 32 in Annex V)

Overall, the survey has **identified 53 preservatives**, all of which are used in cosmetic products on the Danish market. These 53 preservatives cover a total of 31 reference numbers for preservatives in Annex V of the Cosmetics Regulation.

3.4.4.2 Preservatives in rinse-off versus leave-on products

For all 639 products, it has been noted whether the product is a rinse-off or a leave-on product. In an exposure context, it is interesting to look at these two different types of cosmetic products, because the exposure to leave-on products is considered significantly larger than to rinse-off products, which are rinsed off after a short use of the product. Table 5 below shows the preservatives used frequently in rinse-off products and similarly for leave-on products.

Of the 639 products, 426 are leave-on products (67 %) and 213 are rinse-off products (33 %). It is not known whether this 2:1 distribution is due to the fact that there are generally more leave-on products on the market. 137 of the leave-on products are preservative free, and 60 of the rinse-off products are preservative free, ie. a total of 289 leave-on and 153 rinse-off products, respectively, contain preservatives.

Table 5 shows that more preservatives are used in rinse-off products (42 different preservatives) than in leave-on products (38 different preservatives). Some preservatives are used exclusively in either rinse-off products or leave-on products. Sodium salicylate is used only in rinse-off products (7 products), and polyaminopropyl biguanide is used only in leave-on products (4 products). For the remaining 17 preservatives either used only in rinse-off or leave-on products, it applies that they are only seen in one or two products.

It is not possible from the overview below to conclude that some preservatives are only used in one of the two categories of products - on the contrary, it seems that the vast majority of preservatives is used in both rinse-off and leave-on products.

Rinse-off products (213 in total, 153 containing preservative)		**Leave-on products (426 in total, 289 containing preservative)**	
Preservative	**Number of products of 153**	**Preservative**	**Number of products of 289**
Sodium benzoate	75 (49%)	Phenoxyethanol	186 (64%)
Phenoxyethanol	74 (48%)	Methylparaben	75 (26%)
Benzyl alcohol	37 (24%)	Benzyl alcohol	71 (25%)
Benzoic acid	30 (20%)	Sodium benzoate	67 (23%)
Methylparaben	30 (20%)	Potassium sorbate	46 (16%)
Methylisothiazolinone	29 (19%)	Propylparaben	37 (13%)
Methylchloroisothiazolinone	23 (15%)	Benzoic acid	30 (10%)
Potassium sorbate	23 (15%)	Ethylparaben	30 (10%)
Dehydroacetic acid	16 (10%)	Dehydroacetic acid	22 (8%)
Cetrimonium chloride	14 (9%)	Chlorphenesin	19 (7%)

Rinse-off products (213 in total, 153 containing preservative)		Leave-on products (426 in total, 289 containing preservative)	
Preservative	**Number of products of 153**	**Preservative**	**Number of products of 289**
Propylparaben	12 (8%)	Butylparaben	17 (6%)
Behentrimonium chloride	9 (6%)	Cetrimonium chloride	16 (6%)
DMDM Hydantoin	8 (5%)	Sorbic acid	15 (5%)
Ethylparaben	8 (5%)	Isobutylparaben	12 (4%)
Salicylic acid	8 (5%)	Sodium dehydroacetate	12 (4%)
Sodium salicylate	7 (5%)	Methylisothiazolinone	11 (4%)
Sodium sulfite	7 (5%)	Salicylic acid	8 (3%)
Sodium methylparaben	5 (3%)	DMDM Hydantoin	5 (2%)
Sorbic acid	4 (3%)	**Polyaminopropyl biguanide**	4 (1.4%)
Butylparaben	3 (2%)	Behentrimonium chloride	3 (1,0%)
Imidazolidinyl urea	3 (2%)	Formic acid	3 (1.0%)
Isobutylparaben	3 (2%)	Methylchloroisothiazolinone	3 (1.0%)
Quaternium-15	3 (2%)	Quaternium-15	3 (1.0%)
Sodium metabisulfite	3 (2%)	Imidazolidinyl urea	2 (0.7%)
2-bromo-2-nitropropane-1,3-diol	2 (1.3%)	**Isopropylparaben**	2 (0.7%)
Benzalkonium chloride	2 (1.3%)	Sodium metabisulfite	2 (0.7%)
Chlorhexidine	2 (1.3%)	**Triclosan**	2 (0.7%)
Chlorhexidine diacetate	1 (0.7%)	**Chloroacetamide**	1 (0.3%)
Chlorhexidine digluconate	1 (0.7%)	**Chloroxylenol**	1 (0.3%)
Chlorhexidine dihydrochloride	1 (0.7%)	Diazolidinyl urea	1 (0.3%)
Chlorphenesin	1 (0.7%)	**Formaldehyde**	1 (0.3%)

Rinse-off products (213 in total, 153 containing preservative)		Leave-on products (426 in total, 289 containing preservative)	
Preservative	**Number of products of 153**	**Preservative**	**Number of products of 289**
Diazolidinyl urea	1 (0.7%)	**Potassium benzoate**	1 (0.3%)
Formic acid	1 (0.7%)	Sodium bisulfite	1 (0.3%)
Methyl benzoate	1 (0.7%)	Sodium methylparaben	1 (0.3%)
Piroctone olamine	1 (0.7%)	Sodium propylparaben	1 (0.3%)
Propionic acid	1 (0.7%)	Sodium sulfite	1 (0.3%)
Sodium bisulfite	1 (0.7%)		
Sodium dehydroacetate	1 (0.7%)		
Sodium hydroxymethylglycinate	1 (0.7%)		
Sodium propylparaben	1 (0.7%)		
Sodium sorbate	1 (0.7%)		
Steartrimonium chloride	1 (0.7%)		
In total 42 different preservatives		**In total 38 different preservatives**	

TABLE 5
PRESERVATIVES USED IN RINSE-OFF AND LEAVE-ON PRODUCTS, RESPECTIVELY. PRESERVATIVES ONLY SEEN IN EITHER RINSE-OFF OR LEAVE-ON PRODUCTS ARE HIGHLIGHTED IN THE RELEVANT COLUMNS.

3.4.4.3 Preservatives in the five main SPT-groups

Appendix 6 lists the preservatives seen in the 639 products when they are divided into the five main groups used by the SPT: decorative cosmetics, skin care, hair care, perfumes and fragrances, and toiletries. This appendix shows that the use of preservatives is special in the group of perfumes and fragrances, where 50 % of the products do not contain preservatives, and 31 % of the products contain benzyl alcohol, which also has perfuming properties. Furthermore, it appears that more preservatives are used in the hair care and skin care groups compared to the other three groups of cosmetic products. The main features of the comparison of the use of preservatives in the five main SPT groups are given in Table 6 below.

SPT group	Overall picture of the use of preservatives
Decorative cosmetics	• Used in a total of 20 different preservatives • 35% of the products are not preserved • The three most commonly used preservatives are *: – phenoxyethanol (67%)

SPT group	Overall picture of the use of preservatives
	– methylparaben (35%) – propylparaben (24%)
Skin care	• Used in a total of 34 different preservatives • 24% of the products are not preserved • The three most commonly used preservatives are *: – phenoxyethanol (71%) – sodium benzoate (32%) – methylparaben (27%)
Hair care	• Used in a total of 33 different preservatives • 32% of the products are not preserved • The three most commonly used preservatives are *: – phenoxyethanol (57%) – benzyl alcohol (40%) – sodium benzoate (37%)
Perfumes and fragrancies	• Used in a total of 15 different preservatives • Many products (50%) are not preserved • The three most commonly used preservatives are *: – benzyl alcohol (62%) – is also a fragrance chemical – phenoxyethanol (28%) – benzoic acid (14%)
Toiletries	• Used in a total of 20 different preservatives • 31% of the products are not preserved • The three most commonly used preservatives are *: – sodium benzoate (63%) – phenoxyethanol (35%) – benzoic acid (26%)

* THE MOST COMMONLY USED PRESERVATIVES ARE ALL EXPRESSED IN PERCENTAGE OF THE PRODUCTS CONTAINING PRESERVATIVES, IE. PRESERVATIVE FREE PRODUCTS DO NOT COUNT.

TABLE 6
THE OVERALL PICTURE OF THE USE OF PRESERVATIVES IN THE FIVE SPT GROUPS OF COSMETIC PRODUCTS.

Generally, the following conclusions can be mentioned when comparing the incidence of preservatives in the five main groups presented in Appendix 6:

- Phenoxyethanol is the most commonly used preservative in decorative cosmetics, hair care and skin care products, and is used as the second most commonly used preservative in toiletries. Phenoxyethanol is also the most commonly used preservative in perfumes and fragrances, apart from the fact that approx. 80 % of the products in this group are either not preserved or contain the fragrance chemical benzyl alcohol. Phenoxyethanol is used in 16 % of the cases alone and in 84 % of the cases together with one or more other preservatives – most commonly together with one, two or three other preservatives, but in a few products up to 8 other preservatives. These other preservatives are typically sodium benzoate, benzoic acid and/or dehydroacetic acid, but may also be others, for instance parabens.
- Sodium benzoate is often used as a preservative in skin care products, hair care products, and toiletries, but hardly ever in decorative cosmetics and perfumes and fragrances.
- Parabens (as a group) seem to be used much more frequently in decorative cosmetics, skin care and hair care products than in toiletries and perfumes and fragrances.

3.4.4.4 Preservatives in products for children

Of the 639 products included in this survey, 36 products corresponding to 6 % are marketed directly for children or babies. Of these 36 products, 11 were without preservatives, and in the remaining 25 products, 10 different preservatives were identified. For products for children, it also applies that approx. one third of the products are not preserved. These products are baby oils, toothpaste, sun lotions, suncreen spray, shampoos and lip balms. The preservatives are indicated in Table 7 below. The table indicates the percentage of the products for children containing the various preservatives. The sum here is more than 100 %, because there is more than one preservative per product. In the products for children, an average of 2.7 preservatives per product is used, which is the same number as the average number of preservatives used in the 442 products containing preservatives in this survey (cf. Section 3.4.4.1 "Identified preservatives ").

It appears from Table 7 that primarily five preservatives are used in products for children, and these are typically used in the following combinations:

- Sodium benzoate (alone)
- Phenoxyethanol/benzoic acid/dehydroacetic acid
- Phenoxyethanol/potassium sorbate
- Sodium benzoate/phenoxyethanol
- Phenoxyethanol/sodium benzoate/benzoic acid/dehydroacetic acid

Preservative	Number of 36 products	Percentage of products marketed for children/ babies	Percentage of preserved products for children/ babies
Phenoxyethanol	15	42%	60%
Sodium benzoate	15	42%	60%
Benzoic acid	9	25%	36%
Dehydroacetic acid	8	22%	32%
Potassium sorbate	4	11%	16%
Methylparaben	2	6%	8%
Benzyl alcohol	1	3%	4%
Ethylparaben	1	3%	4%
Methylisothiazolinone	1	3%	4%
Sorbic acid	1	3%	4%

TABLE 7
PRESERVATIVES IN PRODUCTS FOR CHILDREN.

Compared with the previous survey of cosmetic products for children in 2006, see Appendix 3: "Previous studies of cosmetic products", the use of parabens has dropped significantly. In the previous study, five out of the six most commonly used preservatives were parabens, while parabens in products for children have not been equally seen in this survey (where only three of the 25 products for children containing preservatives contain parabens and these were, as shown in Table

7 above, the permitted methylparaben and ethylparaben). Like this project, the previous 2006 survey studied various types of cosmetic products, but 208 different products for children were studied then, whereas this survey has only studied a total of 36 products for children.

3.4.4.5 Preservatives in Swan labelled products

Of the 639 products included in this survey, 88 products corresponding to 14 % are Swan labelled products. The percentage of Swan labelled cosmetic products on the Danish market is not known, but it is assumed that the percentage of the market is fairly representative, as the products included in this survey were selected by volume as they are presented in shops.

Of these 88 products, 23 products are preservative free, corresponding to approx. a quarter (26 %), whereas approx. a third of all the 639 examined products are not preserved. It is not known why Swan labelled products appear to be preserved more often than the average for this survey. The reason why Swan labelled products appear to be preserved more often than the average for this study is not known precisely, but it may be related to Swan labelled products being product types, which often require preservation. In the 65 Swan labelled products containing preservatives, 8 different preservatives have been identified. The preservatives are indicated in Table 8 below. The table indicates the percentage of the Swan labelled products containing the various preservatives. The sum is more than 100%, because there is more than one preservative per product. In the Swan labelled products an average of 2.6 preservatives per product is used, which is slightly less than the average number of preservatives in all tested products in this survey.

It appears from Table 8 that primarily five preservatives are used in the Swan labelled products, and these are the same preservatives used in products for children. In Swan labelled products, preservatives are typically used in the following combinations:

- Phenoxyethanol (alone)
- Sodium benzoate (alone)
- Phenoxyethanol/benzoic acid/dehydroacetic acid
- Phenoxyethanol/potassium sorbate
- Sodium benzoate/phenoxyethanol
- Phenoxyethanol/sodium benzoate/benzoic acid/dehydroacetic acid

Preservative	Number of 88 products	Percentage of 88 products	Percentage of 65 products
Phenoxyethanol	48	55%	74%
Sodium benzoate	36	41%	55%
Benzoic acid	22	25%	34%
Dehydroacetic acid	20	23%	31%
Potassium sorbate	15	17%	23%
Sorbic acid	3	3%	5%
Sodium dehydroacetate	1	1%	2%
Sodium sulfite	1	1%	2%

TABLE 8
PRESERVATIVES IN SWAN LABELLED PRODUCTS.

According to Ecolabelling Denmark, no specific preservatives are allowed to use in Swan labelled cosmetic products. Ecolabelling Denmark informed that it is often the demand to bioaccumulation and content of sensitising substances, the preservatives are unable to meet. See Section 2.2 "Swan labelling of cosmetic products." This survey shows that few preservatives are actually used in the Swan labelled products, and they are typically the same five preservatives either alone or in combination.

3.4.4.6 Rarely used preservatives

Table 9 indicates the preservatives that are only seen in 1 or 2 products of the 639 studied products. In the right column, the product type, in which the preservatives are seen, is marked in order to examine whether these preservatives are used in specific kinds of cosmetic products. It appears that the vast majority of these preservatives are present in common cosmetic products such as soaps, hair dyes, shampoos, deodorants, hair styling products, etc. Overall, it can be concluded that these more rare preservatives are not used very often, but when used, they are commonly occurring in cosmetic products such as soaps, shampoos, etc. However, with the following exceptions:

- Some of the chlorhexidine-based preservatives appear to be used in hair dyes or in different types of disinfectant products, such as mouth rinse.
- Formaldehyde is used exclusively in nail care products and other nail products. In these products formaldehyde is hardly used as a preservative, but rather as a reinforcing agent as formaldehyde can polymerise keratin in nails (Nørgaard Andersen et al, 2008).

Preservative	Number of products of 639	Seen in the product type
2-bromo-2-nitropropane-1,3-diol	2	Liquid hand soap
Benzalkonium chloride	2	Liquid hand soap, facial products for blemished skin
Chlorhexidine	2	Hair dyes, hair bleaching products
Diazolidinyl urea	2	Facial masks, hair styling products – wax/gel/paste
Isopropylparaben	2	Lip balms /lip gloss
Sodium bisulfite	2	Deodorants, depilatories
Sodium propylparaben	2	Toothpaste, eye pencils
Triclosan	2	Deodorants, after shave products
Chlorhexidine diacetate	1	Mouth rinse liquid
Chlorhexidine digluconate	1	Hair dyes
Chlorhexidine dihydrochloride	1	Make-up remover and cleansers
Chloroacetamide	1	Hair styling products – wax/gel/paste

Preservative	Number of products of 639	Seen in the product type
Chloroxylenol	1	Foundation, BB cream, concealer
Formaldehyde	1	Nail care products or other nail products
Methyl benzoate	1	Solid hand soap
Piroctone olamine	1	Hair shampoo
Potassium benzoate	1	Cleaning wipes
Propionic acid	1	Facial products for blemished skin
Sodium hydroxymethylglycinate	1	Facial soap
Sodium sorbate	1	Body scrub
Steartrimonium chloride	1	Hair dyes

TABLE 9
RARELY USED PRESERVATIVES.

3.4.4.7 Product types without preservatives

This survey shows that some types of cosmetic products typically do not contain preservatives, or that within the product type there is an excess of the studied products that do not contain preservatives. To all the below mentioned product types it applies that 50 % or more of the products in the product type do not contain preservatives. However, it should be noted that for some of the product types, the number of selected products in the survey is low and does not necessarily give a representative picture of the market.

- Nail polish (10 of 10 products)
- Oral products (not including mouth wash) (2 of 2 products)
- Body oils/massage oils (9 of 10 products)
- Hair styling products – hair spray (18 of 23 products)
- Bath oils (3 of 4 products)
- Nail polish remover (5 of 7 products)
- Hair bleaching products (2 of 3 products)
- Solid hand soap (6 of 9 products)
- Lip balms/lip gloss (11 of 18 products)
- Shaving products men/women (7 of 11 products)
- Toothpaste (7 of 12 products)
- Deodorants (20 of 35 products)
- Lipstick/lip liner (6 of 11 products)
- Perfumes/eau de toilette (7 of 13 products)
- Skin tonic (8 of 16 products)

Common for some of these product types is the fact that they are either oil-based (contain no water), solids (contain no water), or products with a higher alcohol content. The conclusion is that a part of the cosmetic products not containing water or containing alcohol does not contain preservatives. However, there are still products on the market of this type that do contain preservatives.

It should be noted that the use of preservatives is complex and will depend on the actual formulation (composition) of each product. Many preservatives are, for example, only able to function in a particular type of formulation. As an example, organic acids will not be able to perform their preservative properties in an alkaline formulation. Therefore, the use of a specific preservative for a product/product type depends on how the product is formulated (composed), but also on many other factors such as use, packaging, water/oil content, etc. (Varvaresou et al., 2009).

3.4.4.8 Product types with "different" uses of preservatives

The 55 different product types are reviewed to assess whether there are product types in which phenoxyethanol is not the most commonly used preservative, and where it is not one of the product types, which in most cases will be without preservatives, ie. does not contain water or is based on alcohol.

The only product types standing out are the following:

- Facial masks, where the use of methylparaben and propylparaben is as widespread as the use of phenoxyethanol.
- Body shampoo, liquid hand soap, mouth rinse and toothpaste, where sodium benzoate is the most commonly used preservative - this is consistent with the general picture of toiletries where sodium benzoate is the most commonly used preservative (see Section 3.4.4.3 Preservatives in the five main SPT-groups).
- Hair conditioner, where the mixture of methylisothiazolinone and methylchloroiso-thiazolinone is just as used as phenoxyethanol.
- Hair dyes, where sodium sulfite is used almost as often as phenoxyethanol. Six of the 8 products where sodium sulfite is seen used are hair dyes.
- Hair shampoo, where sodium benzoate is used just as often as phenoxyethanol.
- Hair styling products – foam/mousse, where cetrimonium chloride is used just as often as phenoxyethanol.
- Eye liners where methylparaben is the most commonly used preservative.

3.5 Conclusions from the survey

The overall conclusions from the survey are as follows:

- A total of 53 preservatives used in cosmetic products on the Danish market have been identified. These 53 preservatives cover a total of 31 of the 58 reference numbers for preservatives in Annex V of the Cosmetics regulation.
- 31 % of the 639 surveyed products were preservative free.
- Manufacturers of cosmetics products mention that some of the identified preservatives are not used for their preserving properties, but primarily because of other functions (these preservatives are multi-functional ingredients).
- Manufacturers of cosmetics products mention that there has been a change in the use of preservatives - the use of parabens is decreasing, which is confirmed when looking at children's products.
- Phenoxyethanol is generally the most commonly used preservative - either alone or in combination with other preservatives. Compared with previous survey studies, this has not changed significantly. Phenoxyethanol was (along with parabens) the most commonly used preservative in virtually all of the previous studies.

- The use of preservatives in rinse-off products compared to leave-on products is virtually the same.
- Typically, a much smaller range of preservatives is used in products for children and Swan labelled products. This is due to the fact that not all preservatives can meet the requirements for Swan labelled products about bioaccumulation and sensitisation. Here, these five preservatives are primarily used in various combinations:
  - Phenoxyethanol
  - Sodium benzoate
  - Benzoic acid
  - Dehydroacetic acid
  - Potassium sorbate
- Most cosmetic products that do not contain water or are based on alcohol are not preserved. However, such products containing preservatives still exist on the market.
- Several different kinds of preservatives are used in hair care and skin care products compared to the other three groups of cosmetic products, ie. perfumes and fragrances, decorative cosmetics and toiletries (33 and 35 different preservatives compared to 15, 20 and 21 different preservatives).
- Parabens (as a group) seem to be used much more frequently in decorative cosmetics, skin care and hair care products than in toiletries and perfumes and fragrances.
- Comparison with previous survey studies of cosmetic products shows that the use of parabens is decreasing, which is also confirmed by the manufacturers who supplied information for this survey. In a previous study of cosmetic products for children, parabens were the most commonly used preservatives, whereas this survey shows that parabens are very rarely used in products for children. It should be emphasised that this study only showed parabens used in 3 of the 36 products for children, and these were either methylparaben or ethylparaben. This means that all the studied products meet the interim Danish Statutory order prohibiting the use of certain parabens in cosmetic products for children below the age of 3.

4. Survey of the use as a biocidal active substance

Preservatives may be subject to two legislations, depending on whether they are used in a cosmetic product or in a biocidal product. It is therefore of interest to compare the list of approved biocidal active substances with the substances in Annex V of the Cosmetics Regulation, and thereby determine whether there are substances no longer allowed to be used as biocidal active ingredients, but allowed in cosmetics - ie. included in Annex V.

Protection against unintended microbial growth (preservation) is comprised by the biocides legislation, which does not, however, apply to cosmetic products. Therefore, it is possible that the approx. 140 preservatives (58 reference numbers in Annex V of the Cosmetics Regulation) can also be used as biocidal active substances. When used in biocidal products, the substances are subject to the rules of EC Regulation 1451/2007 and the new EU Biocides Regulation (528/2012).

In connection with the preparation of the Biocides Directive, a list was introduced – a socalled gross list of existing biocidal active substances in the EU. This list is shown in Annex I to Commission Regulation (EC) No 1451/2007. As a supplement to Annex I, a list of biocidal active substances was prepared, which is to be reassessed as part of the EU's 10-year work program for the study of active substances in biocidal products. Each substance will be assessed in relation to application in a number of listed product types. The list is shown in Annex II to Commission Regulation (EC) No 1451/2007.

Biocidal active substances will for the assessed combinations of biocidal active substances/product types either be included in the list of approved biocidal active substances (Annex I, IA of the Biocidal Products Directive) or placed on a list of substances not allowed to use for such purposes. The EU list of prohibited biocidal active substances *"Existing active substances for which a decision of non-inclusion into Annex I or Ia of Directive 98/8/EC has been adopted"* thus includes substances not permitted for use as active substances in biocidal products. For some active substances, the decision that they are not permitted for use is limited to certain product types.

Until the EU has assessed all biocidal active substances, some biocidal products will not be subject to EU approval requirements. It depends on whether the active substance in the biocidal product has been approved, rejected or is under assessment. During the transition period, some biocidal products continue to be covered by the Danish approval rules.

Biocidal products are classified according to the Biocides Directive in 22 different product types (PT; see also Appendix 7 for an explanation of the individual PTs), including preservatives, disinfectants and preservatives (eg. wood preservatives and slimicides), pest control (eg. rodenticides, insecticides) and antifouling agents (antifouling). Biocidal product types relevant to this project are:

- PT 6: Preservatives for products during storage
- PT 7: Film preservatives
- PT 8: Wood preservatives
- PT 9: Fibre, leather, rubber and polymerised materials preservatives
- PT 11: Preservatives for liquid-cooling and processing systems
- PT 13: Working or cutting fluid preservatives

- PT 22: Embalming and taxidermist fluids

These above biocidal product types may contain active substances that can also be used as preservatives in cosmetic products.

Preservatives may be comprised by two legislations, depending on whether they are used in a cosmetic product or in a biocidal product. It is therefore of interest to compare the lists of approved biocidal active substances with the substances in the Cosmetics Regulation's Annex V to determine whether there are substances that may no longer be used as biocidal active substances, but are allowed in cosmetics – ie. included in Annex V.

All 144 preservatives in Annex V of the Cosmetics Regulation are displayed in the socalled gross list of existing biocidal active substances in the EU (December 2013). The list is shown in Annex I to Commission Regulation (EC) No 1451/2007. A total of 64 of the 144 substances (44 %) were not found on the gross list of all previously approved biocidal active substances (see Annex I), which means that these substances have not been assessed in relation to the biocidal legislation, and hence there is no data to retrieve here. Of these 64 substances, 11 were found in cosmetic products on the Danish market (see Appendix I, the column "In Annex I").

Furthermore, the Annex V preservatives (those allowed in cosmetics) have been looked up in Annex I[7] (Annex I, IA to the Biocides Directive) and the statutory order 528/2012 (the Biocidal Products Regulation), which is the list of approved biocidal active substances. This list is yet very short (only 58 approved biocidal active substances in total, 27 wood preservatives PT8, 1 slimicide PT12, 12 rodenticides PT14, 15 insecticides PT18, and 3 repellents PT19; entries made in December 2013). None of the 144 preservatives permitted in cosmetics are found on this list, which means that none of the preservatives permitted in cosmetics are currently approved as biocidal active substances according to the Biocides Directive, but slightly more than half of them are either under review, and thus will be approved at a later date, or is being phased out (see Table 10).

The substances have also been looked up in the *non-inclusion*[8] list of phased out biocidal active substances (Table 10). Here it appears that many of the substances originally included in Annex I (the gross list - Annex I to Commission Regulation (EC) No 1451/2007) have now been phased out in single or multiple biocidal product types over the past years. Several of them are, however, still in the review program[9] (Annex II of Commission Regulation (EC) No 1451/2007) for one or more biocidal product types (Table 10).

Preservative	CAS no.	In Annex I*	Phased out** "–" INDICATES THAT THE SUBSTANCE IS NOT INDICATED ON THE LIST	Re-assessment***
Behentrimonium chloride	17301-53-0	No	-	No
Benzalkonium chloride	8001-54-5	Yes	-	No
Benzoic acid	65-85-0	Yes	Commission Decision 2008/809/EC phased out 25/10/2009 PT1, PT2, PT6 Commission Decision 2010/72/EU phased out	PT3, PT4

[7] http://echa.europa.eu/web/guest/information-on-chemicals/biocidal-active-substances
[8] http://ec.europa.eu/environment/108biocides/pdf/list_dates_product_2.pdf
[9] http://ec.europa.eu/environment/chemicals/biocides/pdf/list_participants_applicants_subs.pdf

Preservative	CAS no.	In Annex I*	Phased out** "–" INDICATES THAT THE SUBSTANCE IS NOT INDICATED ON THE LIST	Re-assessment***
			09/02/2011 PT11 Commission Decision 2010/675/EU phased out 01/11/2011 PT20	
Benzyl alcohol	100-51-6	Yes	-	No
2-bromo-2-nitropropane-1,3-diol	52-51-7	Yes	Commission Decision 2008/809/EC phased out 25/10/2009 PT1, PT3, PT4, PT13 Commission Decision 2010/72/EU phased out 09/02/2011 PT7, PT10	PT2, PT6, PT9, PT11, PT12, PT22
Butylparaben	94-26-8	Yes	-	No
Cetrimonium chloride	112-02-7	Yes	-	No
Chlorhexidine	55-56-1	No	-	No
Chlorhexidine diacetate	56-95-1	Yes	-	No
Chlorhexidine digluconate	18472-51-0	Yes	Commission Decision 2011/391/EU phased out 01/07/2012 PT3, PT6, PT13 Commission Decision 2010/72/EU phased out 09/02/2011 PT7, PT9, PT10, PT11	No
Chlorhexidine dihydrochloride	3697-42-5	Yes	-	No
Chlorphenesin	104-29-0	Yes	-	No
Chloroacetamide	79-07-2	Yes	Commission Decision 2011/391/EU phased out 01/07/2012 PT3, PT6, PT13 Commission Decision 2010/72/EU phased out 09/02/2011 PT7, PT9, PT10, PT11	No
Chloroxylenol	1321-23-9	Nej	-	No
Dehydroacetic acid	520-45-6	Yes	-	No
Diazolidinyl urea	78491-02-8	Yes	Commission Decision 2008/809/EC, phased out 25/10/2009 PT6, PT7	No
DMDM Hydantoin	6440-58-0	Yes	Commission Decision 2010/72/EU phased out 09/02/2011 PT11, PT12 Commission Decision 2008/809/EC phased	PT6, PT13

Preservative	CAS no.	In Annex I*	Phased out** "–" INDICATES THAT THE SUBSTANCE IS NOT INDICATED ON THE LIST	Re-assessment***
			out 25/10/2009 PT2	
Ethylparaben	120-47-8	Yes	-	No
Formaldehyde	50-00-0	Yes	Commission Decision 2011/391/EU phased out 01/07/2012 PT1, PT5, PT9, PT23 Commission Decision 2010/675/EU phased out 01/11/2011 PT4, PT6 Commission Decision 2008/681/EC phased out 21/08/2009 PT11, PT12, PT13 Commission Regulation (EC) 1849/2006 phased out 03/01/2008 PT18, PT21	PT2, PT3, PT22
Formic acid	64-18-6	Yes	Commission Decision 2007/565/EC phased out 22/08/2008 PT18 Commission Decision 2008/809/EC phased out 25/10/2009 PT1, PT13 Commission Regulation (EC) 1048/2005 phased out 01/09/2006 PT8 Commission Decision 2010/72/EU phased out 09/02/2011 PT9	PT2, PT3, PT4, PT5, PT6, PT11, PT12
Imidazolidinyl urea	39236-46-9	Yes	-	No
Isobutylparaben	4247-02-3	Yes	-	No
Isopropylparaben	4191-73-5	No	-	No
Methylchloroisothiazolinone	26172-55-4	Yes	-	PT6, PY11, PT12, PT13
Methylisothiazolinone****	2682-20-4	Yes	Commission Decision 2010/72/EU phased out 09/02/2011 PT7, PT9, PT10, PT22 Commission Decision 2008/809/EC phased out 25/10/2009 PT2, PT4	PT6
Methyl benzoate	93-58-3	No	-	No
Methylparaben	99-76-3	Yes	-	No
Myrtrimonium bromide		No	-	No
Quaternium-15	4080-31-3	Yes	Commission Decision 2010/72/EU phased out	PT6, PT12, PT13

Preservative	CAS no.	In Annex I*	Phased out** "–" INDICATES THAT THE SUBSTANCE IS NOT INDICATED ON THE LIST	Re-assessment***
			09/02/2011 PT9 (applies to both CAS no.)	
Phenoxyethanol	122-99-6	Yes	Commission Decision 2010/72/EU phased out 09/02/2011 PT7, PT10, PT11	PT1, PT2, PT4, PT6, PT13
Piroctone olamine	68890-66-4	Yes	-	No
Polyaminopropyl biguanide	28757-47-3	No	-	No
Potassium benzoate	582-25-2	No	-	No
Potassium sorbate	24634-61-5	Yes	Commission Decision 2008/809/EC phased out 25/10/2009 PT1, PT2, PT3, PT4, PT5 Commission Decision 2010/72/EU phased out 09/02/2011 PT7, PT9, PT10	PT6, PT8
Propionic acid	79-09-4	Yes	-	No
Propylparaben	94-13-3	Yes	-	No
Salicylic acid	69-72-7	Yes	Udfases 01/02/2014, no descision reference PT1	PT2, PT3, PT4
Sodium benzoate	532-32-1	Yes	Commission Decision 2008/809/EC phased out 25/10/2009 PT1, PT2, PT6 Commission Decision 2010/675/EU phased out 01/11/2011 PT11, PT20	No
Sodium bisulfite	7631-90-5	Yes	Commission Decision 2008/809/EC phased out 25/10/2009 PT1, PT2, PT4, PT5, PT6, PT13 Commission Decision 2010/72/EU phased out 09/02/2011 PT9, PT11, PT12, PT20, PT22 Commission Regulation (EC) 1849/2006 phased out 03/01/2008 PT21	No
Sodium dehydroacetate	4418-26-2	Yes	-	No
Sodium hydroxymethylglycinate	70161-44-3	Yes	Commission Decision 2010/72/EU phased out 09/02/2011 PT7	PT6
Sodium metabisulfite	7681-57-4	Yes	Commission Decision 2008/809/EC phased out 25/10/2009 PT1, PT2, PT4, PT5, PT6,	No

Preservative	CAS no.	In Annex I*	Phased out** "–" INDICATES THAT THE SUBSTANCE IS NOT INDICATED ON THE LIST	Re-assessment***
			PT13 Commission Decision 2010/72/EU phased out 09/02/2011 PT9, PT11, PT12, PT20, PT22 Commission Regulation (EC) 1849/2006 phased out 03/01/2008 PT21	
Sodium methylparaben	5026-62-0	Yes	-	No
Sodium propylparaben	35285-69-9	Yes	-	No
Sodium salicylate	54-21-7	Yes	-	No
Sodium sorbate	7757-81-5	No	-	No
Sodium sulfite	7757-83-7	Yes	Commission Decision 2008/809/EC phased out 25/10/2009 PT1, PT2, PT4, PT5, PT6, PT13 Commission Decision 2010/72/EU phased out 09/02/2011 PT9, PT11, PT12, PT20, PT22 Commission Regulation (EC) 1849/2006 phased out 03/01/2008 PT21	No
Sorbic acid	110-44-1	Yes	Commission Decision 2008/809/EC phased out 25/10/2009 PT1, PT2, PT3, PT4, PT5 Commission Decision 2010/72/EU phased out 09/02/2011 PT7, PT9, PT10 Commission Decision 2008/681/EC phased out 21/08/2009 PT8	PT6
Stearalkonium chloride	8001-54-3	No	-	No
Steartrimonium chloride	112-03-8	No	-	No
Triclosan	3380-34-5	Yes	Commission Decision 2010/675/EU phased out 01/11/2011 PT3	PT1, PT2, Pt7, Pt9

* ANNEX I TO COMMISSION REGULATION (EC) NO. 1451/2007

** THE EU LIST OF PROHIBITED BIOCIDAL ACTIVE SUBSTANCES "EXISTING ACTIVE SUBSTANCES FOR WHICH A DECISION OF NON-INCLUSION INTO ANNEX I OR IA OF DIRECTIVE 98/8/EC HAS BEEN ADOPTED". "–" INDICATES THAT THE SUBSTANCE IS NOT INDICATED ON THE LIST

*** ANNEX II TO COMMISSION REGULATION (EC) NO. 1451/2007

**** METHYLISOTHIAZOLINONE IS INDICATED TWICE IN ANNEX V (ALONE AND AS A COMPONENT IN THE MIXTURE WITH METHYLCHLOROISOTHIAZOLINONE)

TABLE 10
IDENTIFIED PRESERVATIVES IN PRODUCTS ON THE DANISH MARKET SURVEYED IN THIS PROJECT AND THEIR USE AS BIOCIDAL ACTIVE SUBSTANCES (ENTRIES IN VARIOUS LISTS WERE MADE DECEMBER 2013).

As no biocidal active substances have yet been approved for use in biocidal product types relevant to this project, it is not possible to find published data indicating the reason why some substances have been phased out as biocidal active substances. The project's authors assess that this is because the manufacturers in many cases no longer want to use the particular substance as a biocidal active substance in the particular product type, and therefore have not submitted a dossier to get the substance reassessed. To include a biocidal active substance from the old gross list (Annex I to Commission Regulation (EC) No 1451/2007) in the reassessment program, a manufacturer or a group of manufacturers must submit a dossier on the substance for the specific product types, for which they want approval. Last date to sign up a biocidal active substance for reassessment was 28 March 2002. Substances for which this has not been done will be automatically phased out. Phasing out needs not result from specific adverse health or environmental effects. Annex 1 shows that for most of the substances, various product types are still included in the reassessment program.

The reassessment program is underway, and as can be seen from the list of approved biocidal active substances (Annex I, IA of the Biocides Directive) and the statutory order 528/2012 (Biocides Regulation), there are not yet any permitted active substances in the product types of interest to this project, with the exception of IPBC (PT 6) which has been listed in the beginning of 2014. The assessment of biocidal active substances has long been delayed. Therefore, the EU extended the deadline for the work to and including 2024. To achieve the goal of completing assessments in 2024, the Member States have agreed in the future to finalise approx. 50 active substances per year. The product types relevant for this project are planned to be completed between 2020 and 2023. A reassessment report (CAR: Competent Authority Report) will be available once the reassessment of each active substance has been completed. The public version of the reassessment report will be available on CIRCABC's website[10] when it is ready.

Entries in the biocidal lists indicate that the majority of the most commonly used preservatives in cosmetic products on the Danish market is no longer used as biocidal active substances or only in a limited number of the total of 22 different biocidal product types. None of the most commonly used preservatives have been approved yet as biocidal active substances under the Biocides regulation (52872012) (entries made in December 2013). Some of the preservatives have never been used or allowed as biocidal active substances, but this applies mainly to preservatives which are only found in a few Danish cosmetic products.

Eventually, data can be generated for approval of a substance as a biocidal active substance, which can also be interesting in connection with the use of the substances in cosmetic products. At present it is too early for this project to use data from the biocidal assessments because the European authorities have only just started the reassessment program.

[10] https://circabc.europa.eu/faces/jsp/extension/wai/navigation/container.jsp

5. Prioritising the preservatives

As previously mentioned, 144 individual substances and a total of 58 reference numbers for preservatives are allowed to use as preservatives in cosmetic products (Appendix I: Annex V to the Cosmetics Regulation). The following describes the criteria used to prioritise which preservatives to further examine in terms of their environmental and health properties. The prioritising is based on the following information, and is indicated below in Table 11:

- Focus has been on the preservatives seen used in products on the Danish market, including their use as biocidal active substances. However, it was taken into account that some preservatives may be interesting to prioritise, even though this survey did not find any in products on the Danish market.
- The classification of the preservatives in ECHA's Classification & Labelling Inventory database[11].
- SCCS's opinion of preservatives individually or of groups of preservatives.
- Assessment in relation to their impact on the environment

The classifications of all 144 substances have been found in ECHA's Classification & Labelling Inventory database (C&L Inventory database). For substances without harmonised classifications, Appendix 1 shows the reported classification, notified by most companies (ie. notification to ECHA as self-classification of the substance). The classifications of the 144 substances are in Appendix 1 listed in two columns, while Table 11 only indicates the harmonised classification:

1. Harmonised classification – the harmonised classification specified here if any; if not, "no" is indicated.
2. Notified classification – the registrant's classification is indicated here. The classification notified by most companies has been indicated.

It is also indicated for all 144 substances whether the SCCS has made an opinion of the substances and their use in cosmetic products. An opinion by the SCCS for the substance or the substance group is indicated by a "yes" in the column "SCCP opinion" and an indication of publishing year. If the opinion by the SCCS specifies a MoS value (Margin of Safety), this value is indicated in the column "Human tox MoS."

Finally, it has been examined for the use of prioritising, whether an opinion has been made for the preservatives in relation to the final PBT criteria, and thus their impact on the environment.

Based on the above information, 25 preservatives have been selected in agreement with the Environmental Protection Agency, which are considered to be the most relevant to proceed with in this project with regard to their use and potential health and environmental properties. Subsequently, a detailed screening of the environmental and health properties of these substances was carried out (see Chapters 5.1 and 5.2). See Table 11 below.

[11] http://echa.europa.eu/web/guest/information-on-chemicals/cl-inventory-database

Refe-rence no. in Annex V	Preservative	CAS no.	SCCP opinion	Human tox MoS (mg/kg/d)	Harmonised classification	Seen in no. of products in this survey *	Reason for prioritising
1	Sodium benzoate	532-32-1	SCCP/0891/2005	206	No	142	One of the most commonly used preservatives in products on the Danish market, according to this survey and the general the picture of use of preservatives in the EU (Steinberg, 2010)
3	Salicylic acid	69-72-7	SCCNFP/0522/2001	133	No	16	Older SCCP, MoS around 100
4	Sorbic acid	110-44-1	-	-	No	19	One of the most commonly used preservatives in cosmetic products in the EU (Steinberg, 2010)
5	Formaldehyde	50-00-0	SCCNFP/587/2002	Not calculated	Acute Tox. 3 * H301 Acute Tox. 3 * H311 Skin Corr. 1B H314 Skin Sens. 1 H317 Acute Tox. 3 * H331 Carc. 2 [12]H351	1	No MoS calculation; health (allergies/cancer) considerations. Draft for biocidal CA reports available
8	Zinc pyrithione	13463-41-7	SCCNFP/0671/2003 + SCCS/1512/2013	Not calculated in 2003, but in 2013 applied for permission to use a concentration of 2% - here MoS was 76	No	0	Not seen in any of the products mentioned in this project, but is used in dandruff shampoos; dangerous for the environment; considered safe by the SCCS, but earlier assessment that has been repeated in 2013, when the applicant applied for an increase in the permitted concentration from 1.0% to 2.0% in rinse-off hair care products for dandruff. The MoS calculation showed, however,

[12] An assessment as Carc 1 is suggested in the EU

							that this cannot be permitted.
9	Sodium Sulfite	7757-83-7	SCCNFP/0648/2003	Not calculated	No	8	Interesting to clarify both environment and health
	Sodium Betabisulfite	7681-57-4	SCCNFP/0648/2003	Not calculated	Acute Tox. 4 * H302 Eye Dam. 1 H318	5	
12	Methylparaben	99-76-3	SCCS/1348/2010	Not calculated	No	105	One of the most commonly used preservatives in cosmetic products in the EU (Steinberg, 2010) Interesting to clarify environmental impact
12	Propylparaben	94-13-3	SCCS/1348/2010 SCCS/1446/2011	46.6	No	49	One of the most commonly used preservatives in cosmetic products in the EU (Steinberg, 2010) Interesting to clarify environmental impact
13	Dehydroacetic acid	520-45-6	-	-	No	38	Lack of data
16	Thimerosal	54-64-8	-	-	No	0	Not seen in any of the products included in this survey; lack of data. Focus on mercury consumption
17	Phenyl mercuric acetate	62-38-4	-	-	Acute Tox. 3 * H301 Skin Corr. 1B H314 STOT RE 1 H372 ** Aquatic Acute 1 H400 Aquatic Chronic 1 H410	0	Not seen in any of the products included in this survey; lack of data. Focus on mercury consumption
21	2-Bromo-2-nitropropane-1,3-diol	52-51-7	0125/1999	Not calculated	Acute Tox. 4 * H302 Acute Tox. 4 * H312 Skin Irrit. 2 H315 Eye Dam. 1 H318 STOT SE 3 H335	2	Lack of data; dangerous for the environment One of the most commonly used preservatives in cosmetic products in the EU (Steinberg, 2010)

					Aquatic Acute 1 H400		
27	Imidazolidinyl urea	39236-46-9	SCCNFP/586/2002	Not calculated	No	5	No MoS calculation; allergy considerations. One of the most commonly used preservatives in cosmetic products in the EU (Steinberg, 2010)
29	Phenoxyethanol	122-99-6	Data has been summoned for an assessment of the substance (http://ec.europa.eu/consumers/sectors/cosmetics/files/pdf/cfd_phenoxy_en.pdf)	-	Acute Tox. 4 H302 Eye Irrit. 2 H319	260	One of the most commonly used preservatives in cosmetic products in the EU (Steinberg, 2010) No SCCP opinion; but a new opinion is being prepared by the EU
32	Climbazole	38083-17-9	SCCS/1506/2013 SCCS/1500/2013	Values between 13 and 701 SCCS assesses that Climbazole is safe when using 2 or fewer products containing the substance. When using multiple products, the substance is assessed not to be safe.	No	0	Not seen in any of the products included in this project survey; MoS under 100 in some cases; dangerous for the environment
33	DMDM Hydantoin	6440-58-0	-	-	No	13	Lack of data; allergy considerations. Draft for biocidal CA reports may be available. One of the most commonly used preservatives in cosmetic products in the EU (Steinberg, 2010)
34	Benzyl alcohol	100-51-6	Opinion on the safety of benzyl alcohol in parenteral medicinal products, adopted on 10	Not calculated	Acute Tox. 4 * H302 Acute Tox. 4 * H332	108	One of the most commonly used preservatives in cosmetic products in the EU (Steinberg, 2010) No MoS calculation in old opinion

			February 1999				
35	1-Hydroxy-4-methyl-6-(2,4,4-trimethylpentyl)-2 pyridon, piroctone olamine	68890-66-4	SCCNPF/0525/2001	Not calculated	No	0	Dangerous for the environment
39	Mixture of 5-Chloro-2-methyl-isothiazol-3(2H)-one and 2-Methylisothiazol-3(2H)-one with magnesium chloride and magnesium nitrate	55965-84-9 26172-55-4 2682-20-4	SCCS/1238/2009	7368	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	26	Allergy considerations
42	Chlorhexidine	55-56-1	-	-	No	2	Lack of data; dangerous for the environment
44	Cetrimonium chloride	112-02-7	SCCS/1246/2009	192	No	30	Dangerous for the environment; frequent use in hair care products
46	Diazolidinyl urea	78491-02-8	SCCNFP/586/2002	Not calculated	No	2	No MoS calculation; allergy considerations One of the most commonly used preservatives in cosmetic products in the EU (Steinberg, 2010)
50	Chlorophenesin	104-29-0	-	-	No	20	Lack of data One of the most commonly used preservatives in cosmetic products in the EU (Steinberg, 2010)
57	Methylisothiazolinone	2682-20-4	SCCNFP/0805/2004	633	No	40	Allergy considerations One of the most commonly used preservatives in cosmetic products in the EU (Steinberg, 2010)

* A total of 639 products were surveyed

TABLE 11

PRESERVATIVES SELECTED FOR HEALTH AND ENVIRONMENTAL SCREENING WITH STATEMENT OF REASONS FOR THEIR PRIORITIES.

5.1 Screening – environmental impacts

The environmental impacts of the substances have been screened against the PBT criteria (Persistent/Bioaccumulative/Toxic). Data particularly from REACH registrations are used in the assessment of the substances. In cases where these data were not available or insufficient, the Aquire database and the EU database ESIS were used supplemented with Episuite calculations for a QSAR evaluation of the substances' possible impact on the environment. The results of the screening are summarised in the summary table below (Table 12) and lists the toxicity to aquatic organisms, persistence in the environment and potential for bioaccumulation of the substances. If the assessment of the individual substance gives rise to classification either as persistent (P), bioaccumulative (B) or toxic (T), it is highlighted in the table.

The criteria for environmental impacts are the following:

- The substances are considered to be toxic and meet the criteria for toxicity (T), if EC50 <0.01 mg/L and/or NOEC <0.01 mg/L, and if
- the substance is classified as CMR (Carcinogenic, Mutagenic, Reprotoxic). The substances are assessed to be persistent (P) if they do not meet the requirements for ready biodegradability, see OECD guideline No. 301, and
- potentially degradable, see OECD guideline No. 302. The substances are assessed to be bioaccumulative (B) if BCF> 2000 L/kg or Log Pow ≥ 4.5.

Reference no. in Annex V	Preservative	Biodegradability	Bioaccumulative	Toxicity	Overall assessment
1	Sodium benzoate	The substance is readily biodegradable according to OECD Guideline No. 301. (REACH registration data)	The substance has a Log P_{ow} = -2.27. (REACH registration data)	LC50 (96h) fish: 484 mg/l; NOEC (144h) fish = 10 mg/l; EC50 (96t) Crustaceans > 100 mg/l; EC50 (72h) Algae > 30,5 mg/L, NOEC (72h) Algae = 0.09 mg/l. $PNEC_{ferskvand}$ = 0.13 mg/l $PNEC_{saltvand}$ = 0.013 mg/l (AF = 50/500 fresh/marine) (REACH registration data).	Sodium benzoate has low to moderate toxicity to aquatic organisms, is readily biodegradable and is not expected to bioaccumulate in aquatic organisms.
3	Salicylic acid	The substance is readily biodegradable according to OECD Guideline No. 301. (REACH registration data) Not expected to be hydrolysed (QSAR) (REACH registration data)	The substance has a Log P_{ow} = 2.25 at 25 °C. (REACH registration data)	LC50 (96h) fish: 1370 mg/l; EC50 (48h) Crustaceans = 870 mg/l; NOEC (21d) Crustaceans =10 mg/l; EC50 (72h) Algae > 10 mg/l; $PNEC_{ferskvand}$ = 0.2 mg/l, $PNEC_{saltvand}$= 0.02 mg/l, (AF = 50/500 fresh/marine) (REACH registration data)	Salicylic acid has low to moderate toxicity to aquatic organisms, is readily biodegradable and is not expected to bioaccumulate in aquatic organisms.
4	Sorbic acid	The substance is readily biodegradable according to OECD Guideline No. 301. (REACH registration data) The estimated half-life in air is approx. 0.637 days (QSAR) (REACH registration data)	The substance has a Log P_{ow} = 1.32 which is below the limit value for bioaccumulation of 4.5 (REACH registration data)	LC50 (96h) = 75 mg/l; EC50 (48h) Crustaceans =70 mg/l; NOEC (21d) Crustaceans = 50 mg/l; NOEC (72t) Algae = 6,47 mg/l; $PNEC_{ferskvand}$ = 0.129 mg/l, $PNEC_{saltvand}$ = 0.0129 mg/L (AF = 50/500 fresh/marine) (REACH registration data)	Sorbic acid has moderate toxicity to aquatic organisms, is readily biodegradable and is not expected to bioaccumulate in aquatic organisms.
5	Formaldehyde	The substance is readily biodegradable according to OECD Guideline No. 301. (REACH registration data); Degradation air: DT50 = 1.7 d; The substance cannot hydrolyse as there are no hydrolysable groups (REACH registration	The substance has a Log P_{ow} = 0.35 (25 °C) which is below the limit value for bioaccumulation of 4.5 (REACH registration data)	LC50 (96t) fish = 6.7 mg/l; NOEC (28d) fish > 48 mg/l; EC50 (48h) Crustaceans = 5.8 mg/l, EC50 (72h) Algae = 4.89 mg/l; $PNEC_{ferskvand}$ = 0.47 mg/l, $PNEC_{saltvand}$ = 0.47 mg/l (AF = 10/10 fresh/marine) (REACH registration data) (EC50 (48h) *Daphnia pulex* = 5.8 mg/l, PNECaqua of 5.8 µg/l (OECD SIDS, 2002))	Formaldehyde has moderate toxicity to aquatic organisms, is readily biodegradable and is not expected to bioaccumulate in aquatic organisms. Formaldehyd is classified as carcinogenic and meets the criteria for **toxicity (T)** in the PBT criterium.

		data)		(RIVM Report (2002) Negligible Concentration (NC) = 0.0018 mg/l uses an uncertainty factor of 100 (NC = HC5 /100)) Harmonised classification: Carc. 2 (H351) **(T)**	
8	Zinc pyrithione	The degradation of zinc pyrithione in the environment is very complex and a number of decomposition products are formed. The aerobic degradation of zinc pyrithione causes formation of omadine disulfide, which is further degraded to several heterocyclic compounds that can be characterised as persistent (Madsen et al, 2000). However, these heterocyclic compounds are known to have low toxicity and low potential for bioaccumulation (Rasmussen, 2007).	The substance has a Log P_{ow} = 0.9 (25 °C, pH =7) BCF =11 (fish) (REACH registration data)	(Fish (28d) NOEC = 1.22 µg/l; Invertebrate (28d) NOEC = 2.28 µg/l; Algae (120h) NOEC = 0.46 µg/l (REACH registration data) **(T)**	Zinc pyrithione is not readily biodegradable **(P)**, has hiigh toxicity to aquatic organisms **(T)** and is not expected to bioaccumulate in aquatic organisms.
9	Sodium sulfite	Not readily biodegradable (Epi-Suite) **(expected P)**	The substance has a Log P_{ow} = -7.78 (Episuite: inorganic compound (Outside Estimation Domain) BCF 3162 (regression method)	LC50 (96h) Fish = 316 mg/l; NOEC (34d) > 316 mg/l; NOEC (21d) Crustaceans > 10 mg/l; EC50 (96h) Algae = 63 mg/l; NOEC (96h) Algae = 37.8 mg/l; $PNEC_{ferskvand}$ = 1.33 mg/l; $PNEC_{saltvand}$ = 0.133 mg/l (AF 10/100 fresh/marine) (REACH registration data)	Sodium sulfite and Sodium beta bisulfite are not expected to be readily biodegradable (**expected P**). The substances are also expected not to bioaccumulate in aquatic organisms and have low to medium toxicity in the aquatic environment.
9	Sodium Betabisulfite	Not readily biodegradable (Epi-Suite) **(expected P)**	The substance has a Log P_{ow}= -3.7 (25 °C) IUCLID	LC50 (96t) Fish = 147 mg/l; EC50 (48h) Crustaceans = 89 mg/l; NOEDC (21d) Crustaceans > 10 mg/l; EC50 (72h) Algae = 43.8 mg/l; EC10 (72h) Algae =33.3 mg/l $PNEC_{ferskvand}$ = 1 mg/l; $PNEC_{saltvand}$= 0.11 mg/l	

				(AF 10/100 fresh/marine) (REACH registration data)	
12	Methylparaben	The substance is readily biodegradable according to OECD Guideline No. 301. (REACH registration data); Hydrolysis: Methylparaben does not hydrolyse in cold and hot water.	The substance has a Log P_{ow}= 1.98 (REACH Registrerings data)	LC50 (96h) = 59.5 mg/l; EC50 (48t) Crustaceans = 11.2 mg/l; NOEC (21d) Crustaceans = 0,2 mg/l; EC50 (72h) = 91 mg/l; EC10 (72t) = 31 mg/L; $PNEC_{ferskvand}$ =0.004 mg/l; $PNEC_{saltvand}$ =0.0004 mg/l (AF 50/500 fresh/marine) (REACH registration data)	Methylparaben has low to medium toxicity to aquatic organisms, is readily biodegradable and is not expected to bioaccumulate in aquatic organisms.
12	Propylparaben	The substance is readily biodegradable according to OECD Guideline No. 301. (REACH registration data)	The substance has a Log P_{ow}= 2.34 (REACH registration data)	LC50 (96h) Fish = 6.4 mg/l; EC50 (48h) Crustaceans = 15.4 mg/l; EC50 (72h) = 16 mg/l; NOEC (72h) = 2.1 mg/l; $PNEC_{ferskvand}$ = 0.0064 mg/l; $PNEC_{saltvand}$ = 0.00064 mg/l (AF 1000/10000 fresh/marine) (REACH registration data)	Propylparaben has low to medium toxicity to aquatic organisms, is readily biodegradable and is not expected to bioaccumulate in aquatic organisms.
13	Dehydroacetic acid	The substance is readily biodegradable (Epi-suite)	BCF = 92-182 (Fish, Aquire Database)	E(L)C50 > 100 mg/l (short term exposure) Epi-suite	Dehydroacetic acid has low to medium toxicity to aquatic organisms, is readily biodegradable and is not expected to bioaccumulate in aquatic organisms.
16	Thimerosal	The substance is readily biodegradable (Epi-suite)	The substance has a Log P_{ow} = -1.88 (Epi-suite)	H400, H410 (notifiedc lassification) = R50/53 (EC50 < 1 mg/l) (LC50 fish (48h) = 1.1 mg/l, Aquire database)	Thimerosal has high toxicity to aquatic organisms, is readily biodegradable and is not expected to bioaccumulate in aquatic organisms.
17	Phenyl mercuric acetate	Not readily biodegradable (Epi-suite) **(expected P)**	BCF fish = 80-100 (4d) Aquire Database Log Pow = 0.71 (Epi-suite)	H400, H410 (harmonised classification) = R50/53 (EC50 < 1 mg/l) EC50 (24t) Algae = 6 µg/l; EC50 (96h) Crustaceans = 500 µg/L; LC50 (96h) Fish = 8.6 µg/l (Aquire database) **(T)**	Phenyl mercuric acetate has high toxicity to aquatic organisms **(T)**. Phenyl mercuric acetate is not expected to be readily biodegradable **(expected P)**, but does not bioaccumulate in aquatic organisms.
21	2-Bromo-2-nitropropane-	The substance is readily	The substance has a Log P_{ow}=	LC50 (96h) Fish = 35.7 mg/l; NOEC (49d) =	2-Bromo-2-nitropropane-

	1,3-diol	biodegradable according to OECD Guideline No. 301. Air DT50=12.1d; Hydrolysis: DT50= 2.4h (REACH registration data)	0.24 (24 °C, pH =7) (REACH registration data)	21.5 mg/l; EC50 (48h) Crustaceans = 1.4 mg/l; NOEC (1d) Crustaceans = 0.27 mg/l; EC50 (72h) Algae = 0.25 NOEC (72h) Algae = 0.08 mg/l; $PNEC_{ferskvand}$ = 0,01 mg/l, $PNEC_{saltvand}$= 0.0008 mg/l (REACH registration data)	1,3-diol has medium to high toxicity to aquatic organisms, is readily biodegradable and is not expected to bioaccumulate in aquatic organisms.
27	Imidazolidinyl urea	The substance is readily biodegradable according to OECD Guideline No. 301. Hydrolysis: (read across) DT50 = 12h (REACH registration data)	The substance has a Log P_{ow}= -8.28; BCF = 3.162 (Epi-suite)	LC50 (24h) Fish > 1000 mg/l; (read across with analogous substances for impact on crustaceans and algae) $PNEC_{ferskvand}$ = 5.78 ug/l; $PNEC_{saltvand}$ = 0.58 ug/l (REACH registration data)	Imidazolidinyl urea is expected to have low toxicity to aquatic organisms, is readily biodegradable and is not expected to bioaccumulate in aquatic organisms.
29	Phenoxyethanol	The substance is readily biodegradable according to OECD Guideline No. 301. (REACH registration data) Half-life in air: DT50 =11.8h; Hydrolysis: DT50 > 1year. (REACH registration data)	The substance has a Log P_{ow} = 1.2 (23 °C, pH = 7); BCF (calculated) = 0.3493 (REACH registration data)	LC50 (96h) Fish = 344 mg/l; NOEC (34d) = 23 mg/l; EC50 (48h) Crustaceans > 500 mg/l; NOEC (21d) Crustaceans = 9.43 mg/l; EC50 (72t) Algae = 625 mg/l; NOEC (72h) Algae = 70 mg/l; $PNEC_{ferskvand}$ = 0.943 mg/l; $PNEC_{saltvand}$ = 0.0943 mg/l (REACH registration data)	Phenoxyethanol has low toxicity to aquatic organisms, is readily biodegradable and is not expected to bioaccumulate in aquatic organisms.
32	Climbazole	The substance is not readily biodegradable according to OECD Guideline No. 301. (REACH registration data). Hydrolysis: stable (REACH registration data) **(P)**	The substance has a Log P_{ow} = 3.83 (REACH registration data)	NOEC (21d) Crustaceans = 0.1 mg/l; EC10 (72h) Algae = 26 ug/l; $PNEC_{ferskvand}$ = 0.52 mg/l; $PNEC_{saltvand}$ =0.0552 mg/l (AF 50/500 fresh/marine) (REACH registration data)	Climbazole has high toxicity to aquatic organisms (does not, however, meet the requirement of T (log Pow > 4.5), cf. PBT criteria), is not readily biodegradable **(P)** and may potentially bioaccumulate in aquatic organisms.
33	DMDM Hydantoin	The substance is readily biodegradable according to OECD Guideline No. 301. (REACH registration data) Hydrolysis: DT50: pH4 > 1 year, pH 7 < 1 d, pH 9 < 1 d; Half-life in air (read across) (t1/2): 878 d	The substance has a Log P_{ow} = -2.9; BCF (calculated) = 0.08 (REACH registration data)	LC50 (96h) Fish > 82,3 mg/l; EC50 (48h) Crustaceans = 29.1 mg/l; EC50 (72h) Algae = 11 mg/l; EC10 (72h) Algae = 5.1 mg/l; $PNEC_{ferskvand}$ = 0.51 mg/l; $PNEC_{saltvand}$ = 0.051 mg/l (AF = 10/100 fresh/marine) (REACH registration data)	DMDM Hydantoin has medium toxicity to aquatic organisms, is readily biodegradable and is not expected to bioaccumulate in aquatic organisms.

		(REACH registration data)			
34	Benzyl alcohol	The substance is readily biodegradable according to OECD Guideline No. 301. (REACH registration data)	The substance has a Log P_{ow} = 1.1 (20°C and 25 °C) (REACH registration data)	LC50 (96h) Fish = 460 mg/l; EC50 (48h) Crustaceans = 230 mg/l; NOEC (21d) Crustaceans = 51 mg/l; EC50 (72h) Algae = 770 mg/l; NOEC (72h) Algae = 310 mg/l $PNEC_{ferskvand}$ = 1 mg/l; $PNEC_{saltvand}$ =0.1 mg/l (AF =50/500 fresh/marine) (REACH registration data)	Benzyl alcohol has low toxicity to aquatic organisms, is readily biodegradable and is not expected to bioaccumulate in aquatic organisms.
35	1-Hydroxy-4-methyl-6-(2,4,4-trimethylpentyl)-2 pyridon, piroctone olamine	The substance is readily biodegradable according to OECD Guideline No. 301. (REACH registration data)	The substance has a Log P_{ow}= 3.86 (20.5 °C , pH =4) (REACH registration data)	LC50 (96h) Fish = 1.89 mg/l; EC50 (48h) Crustaceans = 1.8 mg/l; NOEC (21d) Crustaceans = 128 µg/l; EC50 (72h) Algae = 10.8 mg/l; EC10 (72h) Algae = 6.3 mg/l; $PNEC_{ferskvand}$= 2.6 µg/l, $PNEC_{saltvand}$ = 0.26 µg/l (AF = 50/500 fresh/marine) (REACH registration data)	1-Hydroxy-4-methyl-6-(2,4,4-trimethylpentyl)-2 pyridon, piroctone olamine has medium to high toxicity to aquatic organisms, is readily biodegradable and may potentially bioaccumulate in aquatic organisms (does not, however, meet the requirement of T (log Pow > 4.5)), cf. PBT criteria
39	Mixture of 5-Chloro-2-methyl-isothiazol-3(2H)-one and 2-Methylisothiazol-3(2H)-one with magnesium chloride and magnesium nitrate	Not readily biodegradable (Epi-Suite) (confirmed by H410) **(expected to fulfil P)**	The substance has a Log P_{ow} = -0.83 (Epi-Suite)	H400, 410 (Harmonised classification) = R50/53 (EC50 < 1 mg/l) (ESIS)	Mixture of 5-Chloro-2-methyl-isothiazol-3(2H)-one og 2-Methylisothiazol-3(2H)-one with magnesium chloride and magnesium nitrate, Methylchloroisothiazolinone Methylchloroisothiazo linone and methylisothiazolinone have high toxicity to aquatic organisms and are not expected to be readily biodegradable **(expected P)**, and are also not expected to bioaccumulated in aquatic organisms.
39	Methylchloroisothiazolinone	Photodegradation: (T1/2= 6.3-18.2d) 90% after 60.3d; Hydrolysis: T1/2, pH =9; 13d (25 °C) (IUCLID) Not readily biodegradable (Epi-Suite) **(expected P)**	The substance has a Log P_{ow} = -0.75 (20 °C) (IUCLID)	EC50 (96h) Fish = 1.6 mg/l; EC50 (48h) Crustaceans = 4.71 mg/l; NOEC (21d) Crustaceans = 0.172 mg/l; EC50 (120h) Algae = 0.31 mg/l; NOEC (120h) Algae =0.25 mg/l (IUCLID) LC50 (96h) Fish = 180 µg/L; NOEC (36d) Fish = 20 µg/l; EC50 (48h) Crustaceans = 120 µg/l; NOEC (21d) Crustaceans = 100 µg/l; EC50	

				Algae (72h) = 10 µg/l (AQUIRE)	
39	Methylchloroisothiazolinone and methylisothiazolinone	Not readily biodegradable (Epi-Suite) **(expected P)**	The substance has a Log P_{ow} = -0.83 (Epi-Suite)	EC50 (48h) Crustaceans = 140 µg/l; LC50 (96h) Fish = 240 µg/l (AQUIRE)	
42	Chlorhexidine	The substance is not readily biodegradable according to OECD Guideline No. 301. (REACH registration data) photodegr. (read across) <1.3h (REACH registration data) **(P)**	The substance has a Log P_{ow} > 4.5 (QSAR) exp =0.08; BCF(calculated) = 3 (REACH registration data)	REACH registration data: LC50 (96h) Fish = 1.4 mg/l; $PNEC_{ferskvand}$ = 0.0012 mg/l $PNEC_{saltvand}$ = 0.00012 mg/l (AF = 10/100 fresh/marine) Read across, NOEC, invertebr. = 11.6 µg/l)(REACH registration data)	Chlorhexidine has medium to high toxicity to aquatic organisms. Chlorhexidine is not readily biodegradable **(P)**. The substance is potentially biodegradable, but experimental data did not confirm this.
44	Cetrimonium chloride	The substance is readily biodegradable according to OECD Guideline No. 301. (REACH registration data) photodegr. DT50 = 0.32 d (calculated); Hydrolysis: stable; (REACH registration data)	The substance has a Log P_{ow} = 3.08; BCF (calculated) = 70.8 (REACH registration data)	LC50 (96h) Fish = 0.19 mg/l; $PNEC_{ferskvand}$ = 0.00068 mg/l; $PNEC_{saltvand}$ = 0.000068 mg/l (AF =10/100 fresh/marine) (read across *daphnia magna* (21d) NOEC value = 0.0068 mg a.s./l.) (REACH registration data) EC50 (48h) Crustaceans = 7 µg/l; LC50 (96h) Fish = 60 µg/l (AQUIRE)	Cetrimonium chloride has high toxicity to aquatic organisms. Cetrimonium chloride is readily biodegradable and is not expected to bioaccumulate in aquatic organisms.
46	Diazolidinyl urea	(Potentially biodegr.) Hydrolysis: pH 7 DT50 < 1h. (REACH registration data)	The substance has a Log P_{ow} < 0.9 (REACH registration data)	LC50 (96h) Fish > 67 mg/l; EC50 (48h) Crustaceans = 58 mg/l; EC50 (72h) Algae = 5.78 mg/l, NOEC (72h) Algae = 1.6 mg/l $PNEC_{ferskvand}$ = 5.78 µg/l; $PNEC_{saltvand}$ = 0.58 µg/l (AF = 1000/10000 fresh/marine) (REACH registration data)	Diazolidinyl urea has medium toxicity to aquatic organisms. Diazolidinyl urea is potentially biodegradable and is not expected to bioaccumulate in aquatic organisms.
50	Chlorphenesin	Readily biodegradable (Epi-Suite)	The substance has a Log P_{ow} = 1.5 (Epi-suite)	Acute toxicity > 100 mg/l (Epi-suite)	Chlorphenesin has low toxicity to aquatic organisms. Chlorphenesin is expected to be readily biodegradable and is not expected to bioaccumulate in aquatic organisms.
57	Methylisothiazolinone	Not readily biodegradable (Epi-Suite) **(expected P)**	The substance has a Log P_{ow} = -0.83 (Epi-Suite)	EC50 (48h) Crustaceans = 140 µg/l; EC50 (96h) Fish = 60 µg/l (AQUIRE)	Methylisothiazolinone has high toxicity to aquatic organisms. Methylisothiazolinone is not expected to be readily biodegradable

					(expected P) and is not expected to bioaccumulate in aquatic organisms.

TABLE 12
SCREENING OF IMPACTS ON THE ENVIRONMENT OF SELECTED PRESERVATIVES.

Six of the substances (groups) meet the criteria to be either persistent (P) or toxic (T) to aquatic organisms. These substances are:

- Formaldehyde (T)
- The sulphites (reference no. 9 in Annex V) (expected P)
- Climbazole (P)
- Mixture of 5-Chloro-2-methylisothiazol-3(2H)-one and 2-Methylisothiazol-3(2H)-one with magnesium chloride and magnesium nitrate (expected P)
- Chlorhexidine (P)
- Methylisothiazolinone (expected P)
- Zinc pyrithione (T)

Only one substance meets the criteria to be both persistent and toxic. This substance is:

- Phenyl mercuric acetate (P, T)

The screening for environmental impacts shows that none of the selected substances/substance groups meet the criteria for being PBT substances (where all three criteria must be met). None of the substances meet the criteria to be bioaccumulative (B). One substance, however, is both persistent and have toxic impacts on aquatic organisms. This substance has not been seen in the 639 cosmetic products on the Danish market, surveyed in this project, but has been used in mascaras and cleansing products for eye makeup[13].

5.2 Screening – health impacts

A screening of health impacts and an assessment of the data available on the substances have been made for the selected preservatives. Table 13 shows the screening. The following impacts were searched for:

- Allergenic properties of the substances
- Other impacts, including impacts by repeated exposure and possible mutagenic/carcinogenic/reprotoxic properties of the substances (in the table such an impact is only given if it has been found for the substance)
- NOAEL value (No observed adverse effect level) for use in risk assessment
- Assessment of whether new data are available (less than 5-10 years old)

Data are mainly identified in available SCCP opinions (stated in Table 13 with date of publishing) or other data available on the Internet, such as REACH dossier, CIR reports (Cosmetic Ingredient Reports), JECFA reports (Joint FAO/WHO Expert Committee on Food Additives) or in a few cases, where documents are available in connection with the application of the substance as a biocide.

A data search has been made for the substances, in which the following sources have been examined for relevant literature:

- Cosing (http://ec.europa.eu/consumers/cosmetics/cosing/)
- Toxnet (http://toxnet.nlm.nih.gov/)
- JECFA (http://apps.who.int/ipsc/database/evaluations/search.aspx)
- Inchem (http://www.inchem.org/)
- Cosmetic Ingredient Review (CIR) Compendium 2010 eller CIR website (http://www.cir-safety.org/)
- ECHA database, kun for REACH registrerede stoffer (http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances)
- Pubmed (http://www.ncbi.nlm.nih.gov/pubmed)

For hits on Toxnet (Toxline) and PubMed, titles have been skimmed for relevance

[13] WHO, 2011. http://www.who.int/ipcs/assessment/public_health/mercury_flyer.pdf

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Refe-rence no. in Annex V	Preservative	SCCS opinion and MoS	Sensibilisation	Other impacts	NOAEL (mg/kg bw/day)	Assessment of available data	Overall assessment
1	Sodium benzoate	SCCP/0891/2005 MoS: 206	No sensitisation based on data in animals. No immunological contact urticaria in humans (SCCS opinion, 2005)	Skin absorption set to 100% due to lack of data (SCCS opinion, 2005)	500 (from a 4-generation reprotoxic study) (SCCS opinion, 2005)	SCCP opinion from 2005 stating MoS calculation of 206 mg/kg bw/day. There is a REACH dossier on the substance, but this does not use more recent data to illustrate the health impacts of the substance.	Approved for use in food. A safety margin of 206 has been calculated for the substance. The substance benzoic acid has been assessed and approved as an active substance in product types 3 and 4 (EU Commission, 2013), and a public report is available. Additional data for the substance are not expected to be available in the open literature. On this background, the substance was not selected for further analysis.
3	Salicylic acid	SCCNFP/0522/2001 MoS: 133	Not sensitising (SCCNFP, 2001)	Skin absorption set to 20% (SCCNFP, 2001)	75 (from an oral teratogenicity study in rats)(SCCNFP, 2001)	SCCP opinion from 2001 stating MoS calculation of 133. No recent data to illustrate the health impacts of the substance have been found.	A safety margin of 133 has been calculatedfor the substance, safe. Additional data for the substance are not expected to be available in the open literature. On this background, the substance was not selected for further analysis.
4	Sorbic acid	No SCCS opinion	Not sensitising (Anonymous, 1988)		2500 (rat oral) (JECFA)	There is no SCCP opinion on this substance. There is a REACH dossier on the substance, but many impacts have been assessed using read across. More recent	Sorbic acid is also approved for use in foods. Additional data for the substance are not expected to be available in the open literature. On this background, the substance was not selected for further analysis.

						data have not been found for the substance.	
5	Formaldehyde	SCCNFP/587/2002 MoS: Not calculated	Skin sensitiser. At the Center for allergy the substance is seen to cause allergy in 1.2% of the cases[14] – a number that has been decreasing over the last 10 years (probably due to decreasing consumption of the substance).	Suspected of causing cancer. Prohibited in aerosol products.	15 (rat oral)	There is a 12 years old SCCP opinion from 2002, where MoS is not calculated. There are volumes of data on formaldehyde, which have been collected in a LOUS (list of undesirable substances) project in 2014.	Formaldehyde has been classified as Muta2 and Carc1B (in force 1.4.14) (ECHA, 2014), which means that the substance after this date is no longer allowed to be used in cosmetic products - unless it meets the requirements of Article 15, paragraph 2. As formaldehyde in the future may be removed from cosmetic products, it was not selected for further analysis.
8	Zinc pyrithione	SCCNFP/0671/2003 MoS: Not calculated SCCS/1513/2013 Mos calculated for a higher concentration than the allowed.	Not sensitising in most studies (SCCNFP, 2003)	Dermal absorption varies from 0.03 to 3.4% (SCCNFP, 2003)	0,5 (oral rat from to-year study due to neurotoxicity) (SCCNFP, 2003)	There is an 11 years old SCCP opinion from 2003, where MoS is not calculated, but it concludes that zinc pyrithione has moderate acute and sub-chronic toxicity. There is a REACH dossier on the substance. There is also a NOAEL of 0.5 mg/kg bw/day in a study from 2004. A new opinion from 2013 has just been published - here it is concluded that the new evaluation confirms the previous opinion	Zinc pyrithione should be studied further, as the substance has harmful impacts on the environment and has a relatively low NOAEL.

[14] http://www.videncenterforallergi.dk/allergi-blandt-eksempatienter-konserveringsmidler.html

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						(SCCNFP/0671/03) on the safe use of zinc pyrithione for preservative purposes in cosmetic rinse-off hair care products at a maximum concentration of 1.0 %. However, zinc pyrithione, when used in a concentration up to 2.0% as anti-dandruff agent in rinse-off hair care products, is not safe for the consumer.	
9	Sodium sulfite Sodium Beta-bisulfite	SCCNFP/0648/2003 SCCNFP/0648/2003 MoS: Not calculated	Not sensitising (SCCNFP, 2003)	Dermal absorption <10% (SCCNFP, 2003). IARC assesses that there is no evidence of carc in animal studies (IARC, 1992).	72 (oral rat 3-generation reprotoxic study) (expressed as sulfur dioxide) (SCCNFP, 2003)	There is an 11 years old SCCP opinion from 2003.	SCCNFP assessed in 2003 that inorganic sulfites and bisulfites are safe to use in cosmetic products within the allowed concentrations. Further data for the substances are not expected to be available in open literature. Therefore, the substance group was not selected for further analysis.
12	Methylparaben	SCCS/1348/2010 MoS: Not calculated	Not sensitising (SCCS, 2010)		1000 (oral rat) (SCCS, 2010)	The substance is well documented both in the publicly available literature and in an SCCP opinion.	The substance is assessed to be well-studied in cosmetic products, and has been assessed in the EU. Therefore, the substance was not selected for further analysis.
12	Propylparaben	SCCS/1348/2010 SCCS/1446/2011 MoS: 46,6	Not sensitising	Dermal absorption 3.7% Found to be endocrine disruptive in animal studies (SCCS, 2011)	2 (rat subcutane 17 days study with butylparaben) (SCCS, 2011)	The substance is well documented both in the publicly available literature and in several SCCP opinions.	Found to be mildly endocrine disruptive in animal studies, but is assessed by SCCS to be safe for use in adults. In Denmark there has since 2011 been a national ban on the use of

							the substance in cosmetic products for children under 3 years of age. As the substance is well-studied and regulated in the EU, it wasnot selected for further analysis.
13	Dehydroacetic acid	No SCCP opinion	Not sensitising (Anonymous, 1985)	Max conc. 0.6% acid and not allowed in aerosols	100 (oral rat 2-year study) (Anonymous, 1985)	There is no SCCP opinion for this substance. There is a CIR report from 1985 (Anonymous, 1985) Further data for the substance have not been available in open literature.	Irritating effect, but is assessed to be safe at conc <0.6%. Additional data for the substance are not expected to be available in open literature and therefore the substance was not selected for further analysis.
16	Thimerosal	No SCCP opinion	Sensitising (EMEA, 1997)	Found to be foetotoxic, teratogenic and reprotoxic (EMEA, 1997)	No data for determining NOAEL The provisional tolerable weekly intake of mercury is 0.3 mg per person (60 kg), which can/should also be used for this preservative (EMEA, 1997)	There is no SCCP opinion for the substance. When searching PubMed, there are some more recent data (> year 2000) on thimerosal based on the use in vaccines.	Contains mercury, which is in focus in the Danish Environmental Protection Agency. There are some more recent data on the substance, however, related to a different use than in cosmetics. Because of the mercury content, the substance is selected for further analysis.
17	Phenyl mercuric acetate	No SCCP opinion	Sensitising (Norwegian Climate and Pollution Agency, 2010)	Target organ was found to be the kidney in a repeated dose study (Norwegian Climate and Pollution Agency, 2010)	0.0084 (2-years oral study in rats – impacts on the kidneys) (Norwegian Climate and Pollution Agency, 2010)	There is no SCCP opinion for the substance. A comprehensive report has been published in connection with Annex XVII restriction (Norwegian Climate and Pollution Agency, 2010). Further data for the substance have not	Contains mercury, which is in focus in the Danish Environmental Protection Agency. Limited by Annex XVII of the REACH regulation. Must not be manufactured, marketed or used as substances or in mixtures after October 10, 2017, if the concentration of mercury in the mixtures is equal to or more than 0.01% by weight

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						been available in open literature.	(Norwegian Climate and Pollution Agency, 2010). Since the substance thus becomes restricted in the near future, it makes no sense to select it for further analysis in this project.
21	2-Bromo-2-nitropropane-1,3-diol	0125/1999 MoS: Not calculated	Not sensitising in animal studies, A few cases of sensitisation in humans (SCCS, 1999)	Liberates formaldehyde. When degraded in water, small amounts of formaldehyde are generated. Dermal absorption 40% rat (SCCS, 1999)	20 (subchronic oral study in rats) (SCCS, 1999)	There is an old SCCP opinion from 1999. There are some data on formaldehyde releasers and sensitisation, eg. de Groot et al, 2010 and Latorre et al, 2011. There is a REACH dossier for the substance. Further data for the substance have not been available in open literature.	Releases formaldehyde, which has been classified as mutagenic (Muta2) and carcinogenic (Carc 1B) (valid from 1.4.14) (ECHA; 2014). In the REACH dossier on the substance, it is assessed to constitute a low risk to the general public by dermal exposure. Not many new data on the substance, but data on formaldehyde releasers could generally be interesting to investigate further. It is therefore assessed that this will bring news for the formaldehyde-releasing substances.
27	Imidazolidinyl urea	SCCNFP/586/2002 MoS: Not calculated	Mild sensitisation in guinea pig and in a higher concentration (2%) in humans (SCCNFP, 2002) At the Center for allergy the substance is seen to cause allergy	Liberates formaldehyde	28 (oral rat) (CIR, 1980)	There is a 12 years old SCCP opinion from 2002. There are some data on formaldehyde releasers and sensitisation, eg. de Groot et al, 2010 and Latorre et al, 2011.	Releases formaldehyde, which has been classified as mutagenic (Muta2) and carcinogenic (Carc 1B) (valid from 1.4.14) (ECHA; 2014). Not many new data on the substance, but data on formaldehyde releasers could generally be interesting to investigate further. It is therefore assessed that

			in 0.5% of the cases[15] – a number that has been decreasing over the last 10 years (probably due to the decreasing consumption of the substance)				this will bring news for the formaldehyde-releasing substances.
29	Phenoxyethanol	Data have been summoned for an opinion of the substance (http://ec.europa.eu/consumers/sectors/cosmetics/files/pdf/cfd_phenoxy_en.pdf)	Not sensitising (Anonymous, 1990)		80 (oral rat from a 90 days study); The French authorities have in their assessment used a NOAEL of 164 mg/kg bw/day based on a study from 1996, as the study in which a NOAEL of 80 mg/kg bw/day was observed is not publicly available (ANMS, 2012). In the ECHA database of registered substances, other higher NOAEL values are reported for phenoxyethanol, which are newer than the one used from	There is no SCCP opinion for the substance, but an initiative to make one has been initiated.There is a CIR report from 1990 (Anonymous, 1990)	MoS is significantly lower than 100 in use for children, according to a French assessment from 2012 (ANSM, 2012) based on a study from 1996. This substance is therefore suitable for further evaluation, especially because of the frequent use and as phenoxyethanol in many cases will probably replace the parabens. The substance is selected for further analysis.

[15] http://www.videncenterforallergi.dk/allergi-blandt-eksempatienter-konserveringsmidler.html

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					1996.		
32	Climbazole	SCCS/1506/2013 SCCS/1500/2013 MoS: Values between 13-701	Not sensitising (SCCS, 2013)	Dermal absorption rinse-off product from *in vitro* human skin 0.15%. In vivo pigs skin 2-3.5% from leave-on product (SCCS, 2013)	5 (oral rat) (SCCS, 2013)	New SCCP opinion from 2013 with calculation of MoS.	MoS is low and indicates a risk if several products with climbazole are used daily. The conclusions are given in a new SCCP opinion and it is not expected that further review of the substance will provide any news, and therefore the substance was not selected for further analysis.
33	DMDM Hydantoin	No SCCP opinion	Not sensitising in working solution	Formaldehyde releaser	220 (oral rat from a 90 days study)	There is no SCCP opinion for the substance. There are data in connection with the use as a biocidal active substance. There is also a CIR report from 1988 (Anonymous, 1988) and a REACH dossier. Furthermore, there are some data on formaldehyde releasers and sensitisation, eg. de Groot et al, 2010 and Latorre et al, 2011	Releases formaldehyde, which has been classified as mutagenic (Muta2) and carcinogenic (Carc 1B) (valid from 1.4.14) (ECHA; 2014). The substance is being reassessed in biocidal context (CA biocide report) as a biocide product type 6 and 13, and a CA draft report may be available. As there is no SCCP opinion of the substance, it could be interesting to study the substance in connection with the use in cosmetic products, for which data from biocidal use - if they can be obtained.
34	Benzyl alcohol	Opinion on the safety of benzyl alcohol in parenteral medicinal products, adopted on 10 February 1999 No SCCP opinion	Both positive and negative results in sensitisation studies in animals are seen . A maximum incidence of sensitisation of 1% in patch test studies in		400 (oral rat from a 90 days study) (SIDS, 2001)	There is a CIR report from 2001 (Anonymous, 2001) and a SIDS (Screening Information Data Set) report from 2001 (SIDS, 2001)	Benzyl alcohol is one of the 26 fragrances that are mandatory to declare on the label. Based on data from the 2001 benzyl alcohol is assessed by the CIR Expert Group as being safe for use in cosmetic products in concentrations up il 5%.

			humans has been reported. For several decades sensitisation has not been observed in workers (SIDS, 2001)				The available data waere insufficient to support the safety of the substance in cosmetic products, where the primary route of exposure is inhalation. They also concluded that benzyl alcohol is safe for use in hair dyes in concentrations up to 10%. Data indicate no problems when used in cosmetic products, and therefore the substances was not selected for further analysis.
35	1-Hydroxy-4-methyl-6-(2,4,4-trimethylpentyl) -2 pyridon,	SCCNPF/0525/2001 MoS: Not calculated	Not sensitising in a Guinea pig maximisation test (GPMT) (SCCNPF, 2001)		100 (oral rat 90 days study) (SCCNPF, 2001)	There is a 13 years old SCCP opinion from 2001, in which MoS is not calculated. It is concluded in the opinion that MoS cannot be calculated due to insufficient data. The data search did not show any new data since the publication of the SCCP opinion.	The data search showed no new data for the substance even though the opinion from 2001 concluded that there were insufficient data to make a risk assessment. No new data for the substance were found by data search, although in the opinion from 2001, it was concluded that there was insufficient data to perform a risk assessment. Further analysis is not expected to provide any new information on the substance.
39	Mixture of 5-Chloro-2-methyl-isothiazol-3(2H)-one and 2-Methylisothiazol -3(2H)-one with	SCCS/1238/2009 MoS: 7368	Strongly sensitising in animals DCMI 1.7 µg a.i./cm², CMI/MI (14.05% a.i) human sensitising EC3 30 ppm (0,75 µg a.i./cm²). The frequency of	Dermal absorption is set to 100% due to problems with measuments both in in vitro og in vivo studies (SCCS, 2009).	2.8 mg a.i./kg bw/day Kathon™ 886 (from a reprotoxic study (P1 gen) used for MoS calculation (Rohm and Haas, 1998)	A more recent SCCP opinion with a high MoS calculation of systemic effects. Some literature on the sensitising effects.	Despite a low concentration in cosmetic products, there are general problems of sensitisation. The use in rinse-off products is safe in terms of systemic effects. The substance is already under review in the EU, and is expected to be prohibited in leave-on products.

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	magnesium chloride and magnesium nitrate		contact allergy to MCI/MI is still high in European patients with eczemas by recommended use (SCCS, 2009).				Therefore, no further analysis of the substance will be made in this project.
42	Chlorhexidine	No SCCP opinion	Sensitising, chlorhexidine is a hapten (Anonymous, 1993) Chlorhexidine is used for disinfection of the skin and mucous membranes in medicine and dentistry. Long-term exposure may cause contact sensitisation and allergic contact eczema (Liippo et al, 2011)	Low oral and dermal absorption (Anonymous, 1993). May contain the carcinogenic contamination p-chloroaniline (Anonymous, 1993).	25 (rat oral from a 2-year study (Anonymous, 1993)	There is no SCCP opinion for the substance, but a CIR report from 1993. There are some more recent data on the substance, but mainly for other uset han in cosmetic products. There are also some American reports on the substance based on it use as a disinfectant (Anonymous, 1993)	Chlorhexidine may cause sensitisation. Based on data from 1993, chlorhexidine is assessed by the CIR Expert Group to be safe for use in cosmetic products in a concentration <0.14%. It is assessed that further analysis of the substance in this project will not add further knowledge about the substance, and therefore this substance is not evaluated further in this project.
44	Cetrimonium chloride	SCCS/1246/2009 MoS: 192	Not sensitising (SCCS, 2009)	Dermal absorption rat 3.15% (SCCS, 2009)	10 (oral rat from a 1-year study) (SCCS, 2009)	More recent SCCP opinion with a calculated MoS of 192	SCCS in 2009 concluded that the substance does not give cause for concern to health in specific concentrations, and therefore this substance is not evaluated further in this project.
46	Diazolidinyl urea	SCCNFP/586/2002 MoS: Not calculated	Sensitising (Anonymous, 1990) At the Center for allergy, the substance is seen to cause allergy	Releases formaldehyde (SCCNFP, 2002)	200 (oral rat from a 90 days study) (Anonymous, 1990)	There is a 12 years old SCCP opinion from 2002, where MoS is not calculated. Furthermore, only old toxicological data of the	Releases formaldehyde, which has been classified as mutagenic (Muta2) and carcinogenic (Carc 1B) (valid from 1.4.14) (ECHA; 2014).

			in 0.8% of the cases[16] – a number that has been decreasing over the last 10 years (probably due to decreasing consumption of the substance)			substance have been found (< 1990). Derudover er der kun fundet gamle toksikologiske data på stoffet (< 1990). However, there are some data on formaldehyde releasers and sensitisation, eg. de Groot et al, 2010 and Latorre et al, 2011	Based on data from 1990 and earlier, Diazolidinyl Urea has been assessed by the CIR Expert Group to be safe for use in cosmetic products in a concentration < 0.5%. Additional data specific for the substance are not expected to be available in the open literature, and therefore this substance is not evaluated further in this project.
50	Chlorphenesin	No SCCP opinion	Not sensitising (CIR, 2012)	Dermal absorption 60% (CIR 2012)	10 (oral rat from a 28-days study) (CIR 2012)	There is no SCCP opinion for the substance, but a CIR report from 2012.	Based on a more recent CIR report, chlorphenesin has been assessed to be safe to use in cosmetic products in concentrations of 0.32% in rinse-off products and 0.3% in leave-on products. Therefore, it is assessed that further analysis of the substance in this project will not add further knowledge about the substance, and therefore this substance is not evaluated further in this project.
57	Methylisothiazolinone	SCCNFP/0805/2004 MoS: 633	Sensitising, but not approved for working concentration (SCCNFP, 2004)	Dermal absorption in vitro rat skin 80% (SCCNFP, 2004)	19 (oral rat 90 days study)(SCCNFP, 2004)	There is a 10 years old SCCP opinion from 2004 for the substance	A high MoS has been found for the substance in terms of systemic effects, which means that the substance is safe in terms of systemic effects. Methylisothiazolinone is sensitising andis, acc. Allergy Research Centre on cosmetics ingredient that often cause allergies. Methylisothiazolinone is

[16] http://www.videncenterforallergi.dk/allergi-blandt-eksempatienter-konserveringsmidler.html

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							sensitizing and according to the Allergy Research Centre, it is the cosmetic ingredient that causes allergy most often. The substance has been reassessed in the EU, and the substance is expected to be regulated in the near future. Therefore, the substance was not selected for further analysis.

TABLE 13
SCREENING OF HEALTH IMPACTS OF SELECTED PRESERVATIVES.

Based on the above screening of the selected preservatives, it is assessed that for formaldehyde releasing substances it would be advantageous to make extended hazard identifications based on their allergenic effects. In addition, the substances release formaldehyde, which has been classified as mutagenic (Muta2) and carcinogenic (Carc 1B) (ECHA, 2014). This classification of formaldehyde means that formaldehyde after 26 September 2015 must no longer be used in cosmetic products unless it meets the requirements of Art. 15 paragraph. 2. As there are just older SCCP-opinions on the substances, it is interesting to further investigate them. It might be 1-2 of the substances:

- Diazolidinyl urea
- DMDM Hydantoin
- Imidazolidinyl urea
- 2-bromo-2-nitropropane-1,3-diol

The screening shows that mainly for DMDM Hydantoin, data are available from its use as a biocidal active substance, which can be used in a hazard assessment, but these data could not be obtained for this project, but Imidazolidinyl urea may be selected as well. The classification of formaldehyde means that after 26 September 2015, Formaldehyde can no longer be used in cosmetic products unless it meets the requirements of Art. 15 paragraph 2. As formaldehyde has been classified, formaldehyde releasing substances are likely to be re-evaluated by the SCCS in the near future.

For phenoxyethanol the Margin of Safety (MoS) is significantly lower than 100 by use for children according to the latest assessment of the substance by France (ANSM, 2012), and this substance is therefore suitable for further evaluation, in particular because of the frequent use and considering the fact that phenoxyethanol is likely to replace the parabens in many cases.

Zinc pyrithione should be investigated further as the substance may have harmful impacts on the environment and a relatively low NOAEL for health impacts. Apparently, the substance is rarely used as a preservative.

The last substance group considered to be of interest for further assessment in this project is the two preservatives containing mercury. However, the two substances were not found in cosmetic products on the Danish market in connection with the survey of 639 products in this project. Generally, the use of mercury is required to be limited. The substances are:

- Thimerosal
- Phenyl mercuric acetate

Thimerosal has been and still is to a lesser extent used as adjuvant in vaccines, and therefore some more recent literature describing the impacts on health is available. Therefore this substance was selected instead of phenyl mercuric acetate, which will be limited in the near future, as it is listed in Annex XVII of the EU chemicals legislation REACH, which is a list of substances that may present a risk to health and environment. When a substance is included in this list, it means that it is either prohibited to produce, market or use the substance, or that the substance is subject to other restrictions as described in Annex XVII.

Therefore, it is suggested to prepare hazard identifications for the following 4 substances:

- DMDM Hydantoin
- Imidazolidinyl urea
- Zinc pyrithione
- Thimerosal

This project will not make a hazard identification of phenoxyethanol, but will use a NOAEL value from the French study (ANSM, 2012) as the basis for the safety assessment of phenoxyethanol made

below in Chapter 9. In addition, a newer NOAEL value from a REACH dossier is used. According to information from SPT there are also newer studies that may be relevant.

Data in the hazard assessment are presented following the template in the existing SCCS Notes of Guidance, and carried out so that it follows the template for hazard assessment of cosmetic ingredients according to SCCS guidelines (SCCS, 2012). Similarly, the exposure assessments are performed in accordance with the rules specified in these guidelines for applied dose, frequency, and surface area, etc.

6. Analyses

On the basis of the preservatives prioritised for hazard and risk assessments, it was determined in cooperation with the EPA to select 30 cosmetic products for analyses of contents of phenoxyethanol. The purpose was to gain a greater knowledge of the content of phenoxyethanol in different types of cosmetic products. These measured concentrations of phenoxyethanol have subsequently been used directly in a risk assessment of the use of phenoxyethanol in various cosmetic products.

The 30 cosmetic products were selected among the 639 products, for which the lists of ingredients were studied in the preliminary survey in the project. In these 639 products, phenoxyethanol appeared from the lists of ingredients in 197 cases. 30 of these 197 cosmetic products were selected and subsequently bought for chemical analyses of contents of phenoxyethanol. The selection criteria were the following:

- Cosmetic products from several manufacturers were selected
- Several products types were selected
- Primarily leave-on products were selected, as these products have the highest exposure, but 5 rinse-off products were selected as well
- Half of the leave-on products were selected as full body products (ie. bodylotion and sunscreen), as these products have the highest exposure
- Minimum 5 sunscreens were selected
- Minimum 5 products specifically aimed at children were selected
- Minimum 5 Swan labelled products were selected
- Products containing a different number of preservatives were selected, ie. probably with different preservative systems as well

6.1 Analytical method – quantitative analysis of phenoxyethanol

Phenoxyethanol was analysed quantitatively by true duplicate determination using internal Eurofins methods. True duplicate determination means that two identical samples are taken from the same product, and are then treated as two individual samples throughout the analysis. The test material was extracted with solvent, and the content in the solvent was determined by the method given in Table 14 below. Applied solvent and detection limit and analytical uncertainty are stated in Table 14 as well.

Solvent	Principle	Analytical parameter	Detection limit	Analytical uncertainty (U_m)
Water or dichlormethan Partitioned with methanol:water Approx. 1 g test for 33 ml water	HPLC-DAD	Phenoxyethanol	33 mg/kg (0.0033%)	20%

U_m (%) = the expanded measurement uncertainty = 2 x RSD%. See also www.eurofins.dk. Keyword: measurement uncertainty.

TABLE 14
APPLIED ANALYSIS METHOD.

6.2 Analytical results – quantitative analysis of phenoxyethanol

The analytical results of the 30 analysed products are indicated in Table 15 below. The products are listed so that products of the same product type are placed one after another in the table. In addition to the analytical results of phenoxyethanol, product type, category (ie. whether the product is Swan labelled, for example, use for children or leave-on/rinse-off), price per liter, and the preservatives listed in the list of ingredients are indicated.

For each product, two values are listed for the analytical result - the two values measured by true duplicate determination.

It can be seen from the analytical results that all products comply with the permitted amount of phenoxyethanol of max. 1 % (w/w). The identified concentrations of phenoxyethanol are between 0.10 % and 0.89 %. One product contains <0.0033 % phenoxyethanol, ie. below the detection limit of 33 ppm), and probably does not contain phenoxyethanol, despite the fact that it is indicated on the ingredients list.

There is no pattern in the amount of phenoxyethanol and the number of preservatives. Products with only one preservative (phenoxyethanol) have a content concentration of 0.23 % - 0.70 %, whereas a content concentration of phenoxyethanol of between 0.10 % and 0.80 % was measured for products with more preservatives (4 and 5 different preservatives). Different products containing the same preservative system do not seem to contain the same amount of phenoxyethanol, which not surprisingly shows that different manufacturers vary in the amount of different preservative systems to optimise the amount for their specific products.

Lab-no.	Product type	Category	Price per litre	Preservatives according to the ingredients list	Analytical result content of phenoxyethanol	
					% (w/w)	% (w/w)
1-AC	Facial creams (day and night)	Swan labelled, leave-on	DKK 780	Phenoxyethanol Sodium benzoate	0.83%	0.84%
2-BL	Bodylotion/creams	Leave-on	DKK 1475	Phenoxyethanol	0.23%	0.23%
3-BL	Bodylotion/creams	Leave-on	DKK 738	Phenoxyethanol Ethylparaben Methylparaben Potassium sorbate	0.10%	0.10%
4-BL	Bodylotion/creams	Swan labelled, leave-on	DKK 220	Phenoxyethanol Sodium benzoate	0.48%	0.47%
5-BL	Bodylotion/creams	Swan labelled, leave-on	DKK 92	Phenoxyethanol Sodium benzoate	0.47%	0.47%
6-BL	Bodylotion/creams	Leave-on	DKK 300	Phenoxyethanol Sodium benzoate	0.84%	0.85%

Lab-no.	Product type	Category	Price per litre	Preservatives according to the ingredients list	Analytical result content of phenoxyethanol	
					% (w/w)	% (w/w)
7-BLE	Bodylotion/creams for "eczema skin"	Leave-on	DKK 948	Benzoic acid Chlorphenesin Phenoxyethanol	0.35%	0.35%
8-BLE	Bodylotion/ creams for "eczema skin"	Leave-on	DKK 798	Benzoic acid Chlorphenesin Phenoxyethanol	0.50%	0.50%
9-BS	Bodyscrub	Rinse-off	DKK 775	Sodium salicylate Phenoxyethanol Sodium benzoate	0.87%	0.87%
10-DEO	Deodorants	Leave-on	DKK 639	Phenoxyethanol Potassium sorbate Sorbic acid	0.50%	0.51%
11-DEO	Deodorants	Swan labelled, leave-on	DKK 379	Phenoxyethanol Benzoic acid Dehydroacetic acid	0.47%	0.47%

Lab-no.	Product type	Category	Price per litre	Preservatives according to the ingredients list	Analytical result content of phenoxyethanol	
					% (w/w)	% (w/w)
12-FC	Various foot products	Leave-on	DKK 913	Phenoxyethanol Chlorphenesin Methylparaben Ethylparaben Butylparaben Propylparaben Potassium sorbate	0.56%	0.56%
13-BBC	Foundation, BB cream, concealer	Leave-on	DKK 6,500	Phenoxyethanol	0.69%	0.69%
14-HC	Hand cream	Leave-on	DKK 153	Methylparaben Phenoxyethanol Potassium sorbate Propylparaben Benzyl alcohol	0.39%	0.40%
15-HF	Depilatories	Rinse-off	DKK 400	Phenoxyethanol Potassium sorbate	< 0.0033%	< 0.0033%
16-IS	Intimate care products	Rinse-off	DKK 260	Sodium benzoate Phenoxyethanol	0.61%	0.61%

Lab-no.	Product type	Category	Price per litre	Preservatives according to the ingredients list	Analytical result content of phenoxyethanol	
					% (w/w)	% (w/w)
17-RM	Make-up remover and cleansers	Rinse-off	DKK 925	Phenoxyethanol Ethylparaben Methylparaben Benzyl alcohol Methylisothiazolinone	0.78%	0.80%
18-RM	Make-up remover and cleansers	Rinse-off	DKK 700	Sodium benzoate Phenoxyethanol	0.49%	0.50%
19-MS	Mouth rinse liquid	Rinse-off	DKK 78	Benzyl alcohol Phenoxyethanol	0.30%	0.30%
20-RS	Cleaning wipes	Leave-on	DKK 2.00*	Phenoxyethanol Methylparaben Methylisothiazolinone Benzyl alcohol	0.24%	0.24%
21-RC	Anti wrinkle creams and serum	Leave-on	DKK 2,792	Phenoxyethanol Methylparaben Benzyl alcohol	0.62%	0.62%
22-RC	Anti wrinkle creams and serum	Leave-on	DKK 5,832	Phenoxyethanol	0.49%	0.49%

Lab-no.	Product type	Category	Price per litre	Preservatives according to the ingredients list	Analytical result content of phenoxyethanol	
					% (w/w)	% (w/w)
23-SOL	Sunscreen/sun oil	Swan labelled, for children, leave-on	DKK 281	Phenoxyethanol Benzoic acid Dehydroacetic acid	0.49%	0.49%
24-SOL	Sunscreen/sun oil	For children, leave-on	DKK 610	Phenoxyethanol	0.70%	0.69%
25-SOL	Sunscreen/sun oil	For children, leave-on	DKK 490	Phenoxyethanol Methylparaben Ethylparaben Benzyl alcohol	0.49%	0.50%
26-SOL	Sunscreen/sun oil	Swan labelled, for children, leave-on	DKK 350	Phenoxyethanol Benzoic acid Dehydroacetic acid	0.50%	0.50%
27-SOL	Sunscreen/sun oil	Swan labelled, for children, leave-on	DKK 466	Phenoxyethanol Benzoic acid Dehydroacetic acid	0.50%	0.49%

Lab-no.	Product type	Category	Price per litre	Preservatives according to the ingredients list	Analytical result content of phenoxyethanol	
					% (w/w)	% (w/w)
28-VS	Wipes	For children, leave-on	DKK 0.61*	Phenoxyethanol Sodium benzoate	0.51%	0.51%
29-VS	Wipes	Swan labelled, leave-on	DKK 0.90*	Phenoxyethanol Sodium benzoate Potassium sorbate Benzoic acid	0.86%	0.86%
30-ØC	Eye creams	Leave-on	DKK 7,933	Phenoxyethanol Benzoic acid Dehydroacetic acid	0.87%	0.89%

* THE PRICE IS INDICATED PER WIPE IN THE PACKAGE

TABLE 15

ANALYTICAL RESULTS OF THE 30 COSMETIC PRODUCTS SELECTED FOR ANALYSES FOR CONTENT OF PHENOXYETHANOL .

7. Hazard identification

The hazard identifications of the selected substances have been made to follow the template for hazard identification of cosmetic ingredients under SCCS Guidelines (SCCS, 2012). All toxicological endpoints are included, and significant hazards identified are briefly summarised, and if possible a NOAEL for the risk assessment has been identified. If more recent data are not identified, data from the last SCCP opinion on the substance are given in the assessment.
Data for the selected substances have been widely searched in accessible databases on the Internet, similar to the searches made in connection with the screenings (Chapter 5).

7.1 DMDM Hydantoin

Dimethylol dimethyl hydantoin (DMDM Hydantoin) is a preservative that functions by releasing formaldehyde, which is classified for its mutagenic (Mut2) and carcinogenic (Carc 1B) properties. It is used in the cosmetics industry and is found in products such as shampoos, hair conditioners, hair gels and skin care products.
DMDM Hydantoin is also used as a biocidal active substance, and a draft assessment of the substance as a biocidal active substance should be available. However, it has not been possible for the project group to gain access to this report, and therefore these data are not included in the hazard identification.

7.1.1 Chemical identity

$C_7H_{12}N_2O_4$

7.1.1.1 Primany name/INCI name

DMDM Hydantoin

7.1.1.2 CAS no.

6440-58-0

7.1.2 Acute toxicity

7.1.2.1 Acute oral toxicity

According to REACH registration (ECHA, 2014a), an LD50 in rats of 1572 mg/kg extrapolated from Glycoserve II was observed in a study from 1991 (product containing DMDM Hydantoin).

7.1.2.2 Acute dermal toxicity

According to REACH registration (ECHA, 2014a), an LD50 in New Zealand White rabbits of 1052 mg/kg extrapolated from Glycoserve II was observed in a study from 1998 (product containing DMDM Hydantoin).

7.1.2.3 Acute inhalation toxicity

No new studies have been identified since CIR's review (1988):
Four groups of 10 Sprague-Dawley rats were exposed to a 55% DMDM Hydantoin solution in drop form for 4 hours. Each of the 4 groups, respectively, was exposed to concentrations of 0.0, 13.7, 126.8 or 377.8 mg/L in an inhalation chamber. The animals were observed for signs of toxicity during the exposure period, and for two weeks thereafter. All animals survived. Dry pigmented material was noticed around the snouts of 3 animals in the mid dose group (126.8 mg/L) and 5

animals in the high dose group (377.8 mg/L) on the second day of exposure; no nasal discharge was visible on day 3. No significant dose-related effects could be observed by microscopic examination of tissues from the trachea, bronchi, lungs, liver and kidneys (CIR, 1988).
Ten adult male Sprague-Dawley rats were exposed to 55% DMDM Hydantoin for one hour (204 mg/L). During the exposure period, signs of discomfort were observed in the animals in the form of gasping for breath and closed eyes. The animals were sacrificed two weeks after exposure, and no remarkable pathological tissue changes were found in either the control or the experimental groups (CIR, 1988).

7.1.3 Irritation

7.1.3.1 Skin irritation

According to REACH registration (ECHA, 2014a), mild irritation, which was fully reversible within 72 hours, was observed in a study of New Zealand White rabbits from 1998.

7.1.3.2 Mucosal irritation/eye irritation

According to REACH registration (ECHA, 2014a), mild irritation at a dose of 52.6 mg/kg, which was fully reversible in less than 4 days, was observed in a study of New Zealand White rabbits from 1998.

7.1.4 Skin sensitisation

According to REACH registration (ECHA, 2014a), no skin sensitisation was observed in guinea pigs in two studies from 1998 and 2001, respectively.
A recent review explained that there is a correlation between formaldehyde allergy and patch test reactions to DMDM Hydantoin (de Groot et al, 2010).

7.1.5 Dermal absorption

No new studies since CIR's review (1988). A study was reported in Sprague-Dawley rats which were applied radioactive DMDM Hydantoin dorsally (on their backs). After 72 hours, more than 90% of the applied dose was recovered. More than 98% of the recovered DMDM Hydantoin was limited to the application site, which indicates that the dermal absorption in rats does not exceed 2%; however, with the uncertainty that only 90% of the applied substance was recovered in the study. The highest counts of radioactivity outside the site of application were found in the gastrointestinal tract, liver and bone marrow. For most tissue samples, there was no evidence of accumulation of DMDM Hydantoin or its metabolites. DMDM Hydantoin and its metabolites are excreted primarily in the urine. The amount of radioactivity in the urine decreased approx. 6 times over a 72-hour period. The radioactivity in faeces remained fairly constant and significantly lower than in the urine.

7.1.6 Repeated toxicity

7.1.6.1 Repeated (28 days) oral / dermal / inhalation toxicity

No available data.

7.1.6.2 Sub-chronic (90 days) oral / dermal / inhalation toxicity

Dermal:
Thirty-two New Zealand White rabbits were divided into two groups of 8 males and 8 females. 55% DMDM Hydantoin (0.0012 g/kg) was applied on the shaved backs of the experimental group once a day and 5 days/week for 28-91 days. Six animals from each group were sacrificed after 28 days of treatment. The remaining 10 rabbits in each group were sacrificed after 91 days. No pharmacological or toxicological signs were observed during the treatment period. Macroscopic skin changes could be seen post mortem. Skin changes included erythema, desquamation, and crusting, swollen and rough surfaces. Furthermore, acute epidermal necrosis and acanthosis were observed. The pathological changes were assessed to be related to DMDM Hydantoin (CIR, 1988).

According to REACH registration (ECHA, 2014a), NOAELs of 440 mg/kg and 4.4 mg/kg for systemic and local doses, respectively, of DMDM Hydantoin were calculated in a study in New Zealand White rabbits.
In another study in New Zealand White rabbits from 1983, macroscopic skin changes on the application site were observed. A NOAEL of 540 mg/kg was calculated (ECHA, 2014a).
A read across study (DM hydantoin) from 1994 showed a NOEL of 390 mg/kg in rats. No adverse effects were seen from the registration other than one death, which was not considered dose-related (ECHA, 2014a).

Oral:
In an oral 90-days study with Glydant® from the REACH dossier, a NOEL for DMDM Hydantoin of 220 mg/kg bw was calculated (the study was conducted on a product, and therefore the dose levels shall be converted to active substance) (ECHA, 2014a).

7.1.6.3 Chronic (> 12 months) toxicity
No new studies since CIR's review (1988).

7.1.7 Reproduction toxicity
7.1.7.1 Two-generation reproduction toxicity
In a read across study from 1994 (with DM hydantoin, the data of which may be used to say something about DMDM), it was concluded that DM hydantoin is not a reproductive toxin, but there might be an effect on lactation (ECHA, 2014a).

7.1.7.2 Teratogenicity
A read across study (DM hydantoin) from 1988 calculated a NO(A)EL of 1000 mg/kg in New Zealand White rabbits (ECHA, 2014a).
A read across study (DM hydantoin) from 1992 in New Zealand White rabbits calculated a NOAEL of 375 mg/kg for maternal toxicity and 1000 mg/kg for embryo toxicity (ECHA, 2014a).
Another read across study from 1992 calculated a NO(A)EL of 1000 mg/kg in rats for DM hydantoin (ECHA, 2014a).

7.1.8 Mutagenicity / genotoxicity
7.1.8.1 Mutagenicity / genotoxicity *in vitro*
Positive Ames test in Salmonella *typhimurium* (ECHA, 2014a).
Positive in mouse lymphoma L5178Y cells (ECHA, 2014a)
Positive in chromosomal aberration test (hamster ovary) (ECHA, 2014a).
Positive in "DNA damage and repair assay" in rat-hepatocytes (ECHA, 2014a).

7.1.8.2 Mutagenicity / genotoxicity *in vivo*
According to REACH registration (ECHA, 2014a), no genotoxic effect was found in a micronucleus assay in mice.

7.1.9 Carcinogenicity
According to REACH registration (ECHA, 2014a), no carcinogenicity was found in 2 read across studies from 1994 (DM hydantoin) in mice and rats, respectively.

7.1.10 Toxicokinetics
According to REACH registration (ECHA, 2014a), no bioaccumulation was observed in a read across study (DM hydantoin) in rats from 1991.

7.1.11 Photo-induced toxicity
7.1.11.1 Phototoxicity/photoirritation and photosensitisation
No available data.

7.1.11.2 Phototoxicity/photomutagenicity/photoclastogenicity

No available data.

7.1.12 Human data

2453 patients, of whom 13.9% had a history of atopic dermatitis (AD) underwent a patch test (Shaughnessy et al, 2014). The result of the patch test showed that patients with AD were statistically more likely to respond positively than patients without AD. AD was associated with contact hypersensitivity particularly to the substances DMDM Hydantoin and imidazolidinyl. The authors concluded from their study that patients with AD should avoid the use of skin care products preserved with formaldehyde releasers.
Shaughnessy et al (2014) also found that four of the five formaldehyde releasers (Quaternium-15, imidazolidinyl urea, DMDM Hydantoin and 2-bromo-2-nitropropane-1,3-diol) showed significantly higher allergic reactions in patients with AD than in patients without AD; something they did not find for formaldehyde. The allergenic potency of the majority of the known formaldehyde releasers, but not of formaldehyde alone, suggests that it is the structure of the formaldehyde releaser that causes an allergic reaction, more than the low release of formaldehyde. This was also studied by Kireche M et al (2010), who also found indications to the fact that the formaldehyde releaser in itself can cause allergies, which has nothing to do with the release of formaldehyde.

Between January 2000 and December 2010, Travassos et al (2011) collected information on the specific cosmetic products causing allergic contact eczema and the individual sensitising ingredient therein. In 621 cases of 959 volunteers, the sensitising reaction was due to other than fragrances. In 58% of the cases, preservatives were responsible. Of the 130 reactions to formaldehyde releasers, 40 concerned 2-bromo-2-nitropropane-1,3-diol, 37 concerned DMDM Hydantoin, 29 concerned diazolidinyl urea, 22 concerned imidazolidinyl urea and 2 concerned quaternium-15.

7.1.13 Special studies

No available data.

7.1.14 Conclusion

DMDM Hydantoin has low acute toxicity both by oral and dermal exposure. The substance is a slightly skin and eye irritant. The substance is seen to have a slightly allergenic potential in laboratory animals, but human data show that DMDM Hydantoin may cause allergies in humans. Data from DM hydantoin cannot be considered relevant for read across to DMDM Hydantoin in relation to allergy, as DM hydantoin does not release formaldehyde. The substance is genotoxic in a number of *in vitro* studies, but there is also a negative *in vivo* micronucleus study, and since the substance has not been found to be carcinogenic, it is assessed to be non-mutagenic.
It is concluded that there is a lack of data for several endpoints. The critical effect is considered to be the allergenic potential of the substance, as it has shown an allergenic effect in humans. Disregarding allergy, a 90-day study can be used for a MoS calculation giving a NOEL of 220 mg/kg bw. The dermal absorption is set as a worst case to 10 % based on the uncertainty inherent in the available data from a rat study, but is probably lower for humans.

7.2 Imidazolidinyl urea

According to literature, imidazolidinyl urea is a commonly used preservative world-wide (especially in combination with parabens). The substance may release formaldehyde, which is classified for its mutagenic (Muta2) and carcinogenic (Carc 1B) properties.

As described in the screening of the substance, there is a 12 year old SCCP opinion from 2002 of the substance (SCCNFP, 2002). This opinion, however, deals more with the opportunity for analytical methods of the substance than assessment of its potentially harmful effects. To find a description of the harmful effects, we must go back to 1980, where a Cosmetic Ingredient Review (CIR) was made on the substance. As more recent data could not be found, the old data from 1980 are presented here. In the CIR from 1980, the substance is assessed to be safe to use in concentrations up to 5 % in cosmetic products; however, the conclusion suggests that there are no data on kinetics, long-term studies, studies of mutagenic effect as well as human studies of phototoxicity and photosensitivity for the substance.
Due to the release of formaldehyde, which must not exceed 0.2 % in cosmetic products, imidazolidinyl urea in the opinion of 2002 is considered to be safe in a concentration of 0.6% in cosmetic products (SCCNFP; 2002).

7.2.1 Chemical identity

N,N'-Methylenebis[N'-[3-(hydroxymethyl)-2,5-dioxoimidazolidin-4-yl]urea]

Imidazolidinyl urea is soluble only in polar solvents. In aqueous solution it decomposes and may thereby release formaldehyde. Formaldehyde release from imidazolidinyl urea in an aqueous solution increases with increasing pH and temperature of the solution as well as with increasing storage period. One molecule of imidazolidinyl urea can release 4 molecules of formaldehyde under strict conditions. The total content of free formaldehyde in a product containing 0.6% imidazolidinyl urea would correspond to a release of 0.186 % formaldehyde (SCCNFP, 2002).

7.2.1.1 Primary name/INCI name

Imidazolidinyl urea

7.2.1.2 CAS no.

39236-46-9

7.2.2 Acute toxicity

7.2.2.1 Acute oral toxicity

In rats and mice, respectively, LD50 values were seen from 7.2-11.3 g/kg bw by oral exposure (CIR, 1980).

7.2.2.2 Acure dermal toxicity

In rats, an LD50 value of > 8 g/kg bw was found by dermal exposure of rabbits (CIR, 1980).

7.2.2.3 Acute inhalation toxicity

Based on inhalation studies in rats, it is concluded that LC50 is > 5 mg/l when imidazolidinyl urea is administered to rats continuously for one hour (CIR, 1980).

7.2.3 Irritation

7.2.3.1 Skin irritation

Older studies in rats and rabbits show no or just mild skin irritation (CIR, 1980).

7.2.3.2 Mucosal irritation/eye irritation

Imidazolidinyl urea is not an eye irritant based on studies in rats and rabbits (CIR, 1980).

7.2.4 Skin sensitisation

Formaldehyde releasers, such as imidazolidinyl urea, are the common cause of allergic contact eczema (Lundov et al, 2010; Latorre et al, 2011).
Imidazolidinyl urea sensitised 60-70 % of the tested Dunkin Hartley female guinea pigs in a dose-dependent way. The animals were patch tested with 1, 5, and 10% imidazolidinyl urea in petrolatum. The animals were assessed after 48 hours (Andersen et al, 1984).
Similarly, imidazolidinyl urea was found to be a sensitiser after dermal application of 25 µl of a 10, 25 or 50 % solution of CBA/Ca-mouse daily for three days. The exposure induced significant radioactive thymidine incorporation in local lymph nodes four days after the last treatment with imidazolidinyl urea (Basketter & Scholes, 1992).

7.2.5 Dermal absorption

No available data.

7.2.6 Repeated toxicity

7.2.6.1 Repeated (28 days) oral/dermal/inhalation toxicity

Five male and female albino rabbits were exposed to doses of imidazolidinyl urea in powder form at their shaved backs for 6 hours/day, 5 days/week for three weeks. Used concentrations were 20, 45, 90 and 200 mg/kg bw/day. The only treatment-related effects reported were slight to mild inflammatory and focal ulcerative effect (CIR, 1980).

7.2.6.2 Sub-chronic (90 days) oral/dermal/inhalation toxicity

In a 90 days study in rats orally exposed to imidazolidinyl urea in doses of 0, 6, 28, 130 and 600 mg/kg bw, reduced growth in male rats exposed to doses of 130 and 600 mg/kg bw was found. Hematolytical, biochemical or pathological changes in these animals were not observed. As a worst case, a NOEL of 28 mg/kg bw/day can be set from this study based on reduced growth in animals that were exposed to higher concentrations (CIR, 1980).

A 90-day toxicity study in rats exposed orally to 1,300 mg of imidazolidinyl urea/kg bw/day, no apparent toxic effects were observed. The experimental details are not available (Clariant, 2002).

7.2.6.3 Chronic (> 12 months) toxicity

No available data.

7.2.7 Reproduction toxicity

7.2.7.1 Two-generation reproduction toxicity

Imidazolidinyl urea induced a slight increase in the number of resorptions and/or foetal deaths in the uterus on day 17 in albino mice orally intubated with 30, 95, and 300 mg/kg bw/day from day 6 to day 15 of gestation. However, different abnormalities were not found in soft tissue or bone tissue compared to the control group. It was concluded that imidazolidinyl urea is slightly foetotoxic, but not teratogenic in mice (Sutton Laboratories, 1973b).

7.2.7.2 Teratogenicity

No available data.

7.2.8 Mutagenicity / genotoxicity

7.2.8.1 Mutagenicity / genotoxicity *in vitro*

Imidazolidinyl urea was mutagenic in Salmonella typhimurium TA98 and TA100 in concentrations up to 1,500 mg/plate (Seifried, 2003).

7.2.8.2 Mutagenicity / genotoxicity *in vivo*

No available data.

7.2.9 Carcinogenicity
No available data.

7.2.10 Toxicokinetics
No available data.

7.2.11 Photo-induced toxicity
7.2.11.1 Phototoxicity/photoirritation and photosensibilisation
No available data.

7.2.11.2 Phototoxicity / photomutagenicity / photoclastogenicity
Imidazolidinyl urea was described as not phototoxic in Hartley female guinea pigs after intradermal injections of doses of 1-5 % on their shaved backs and subsequent radiation with FL20E and FL20BLB light for 30 minutes. This treatment was repeated 24 and 48 hours after the first injection, but no reaction was observed (CIR, 1980).

7.2.12 Human data
In a 5-year retrospective study (Latorre et al, 2011) conducted in six Spanish hospitals on patients with positive patch test reactions to formaldehyde or any of the seven formaldehyde releasers, it was found that the most common allergens were formaldehyde (1.72 %), imidazolidinyl urea (1.05 %), quaternium-15 (0.88 %) and diazolidinyl urea (0.79 %). Patients with hypersensitivity only to formaldehyde had a higher frequency of dermatitis related to work (25%) than patients with hypersensitivity only to formaldehyde releasers (9.5 %).

As described in the hazard identification of DMDM Hydantoin, 2453 patients, of whom 13.9% had a history of atopic dermatitis (AD), underwent a patch test (Shaughnessy et al, 2014). The results of the patch tests showed that patients with AD were statistically more likely to respond positively than patients without AD. AD was associated with contact hypersensitivity to the substances imidazolidinyl urea and DMDM Hydantoin in particular. The authors concluded from their study that patients with AD should avoid the use of skin care products preserved with formaldehyde releasers.
Shaughnessy et al (2014) also found that four of the five formaldehyde releasers (Quaternium-15, imidazolidinyl urea, DMDM Hydantoin and 2-bromo-2-nitropropane-1,3-diol) showed significantly higher allergic reactions in patients with AD than in patients without AD; something they did not find for formaldehyde. This allergenic potency of the majority of the known formaldehyde releasers, but not formaldehyde alone, suggests that it is the structure of the formaldehyde releaser that causes an allergic reaction, more than the low release of formaldehyde..

Between January 2000 and December 2010, Travassos et al (2011) collected information on the specific cosmetic products causing allergic contact dermatitis, and the sensitising cosmetic ingredients in these products. In 621 cases out of 959 affected, the allergenic ingredient was other than fragrances. In 58 % of the cases, preservatives were responsible. Of the 130 reactions to formaldehyde releasers, 40 concerned 2-bromo-2-nitropropane-1 ,3-diol, 37 concerned DMDM Hydantoin, 29 concerned diazolidinyl urea, 22 concerned imidazolidinyl urea, and 2 concerned quaternium-15.

At the Center for Allergy (2014), the substance is shown to cause allergy in 0.5 % of the incoming cases of patients with known cases of allergy - a figure that has been decreasing over the last 10 years, probably due to falling consumption.

7.2.13 Special studies
No available data.

7.2.14 Conclusion

Imidazolidinyl urea has low acute toxicity both at oral and dermal exposure. The substance causes no or only slight skin and eye irritation at single exposure. The limited data do not suggest a toxicological effect of repeated exposure. In one 90 days study, decreased growth was found and based on this, a NOEL of 28 mg/kg bw/day was established.
The critical effect is considered to be the allergenic potential of the substance, but it has not been possible from the available studies to set a NOAEL for this effect. Human data from patch tests show that imidazolidinyl urea, like other formaldehyde releasers, may cause contact allergy.
The data search shows that the toxicological effects are not well-examined, since there are no available data on the mutagenic and carcinogenic potential beyond a single *in vitro* study showing a positive mutagenic effect. In addition, the kinetics, including dermal absorption, is poorly or not at all described. As a basis for the MoS calculation (effects beside allergy), a NOEL of 28 mg/kg bw/day and a dermal absorption of 100 % are used.

7.3 Thimerosal

Thimerosal is an abbreviation of the chemical name of the substance sodium ethyl mercurithiosalicylate. It is an organic mercury compound, which has been used as a preservative in various pharmaceutical products, including vaccines, immune globulin preparations and anti-toxins, as well as in cosmetic products.
Thimerosal consists in weight of 50 % mercury, which is metabolised to thiosalicylate and ethyl mercury.
For cosmetic products in the EU and the US, thimerosal is only allowed to use in eye products such as eyeliners and mascara. In the USA, such products may contain 0.0065 % mercury and only if it is considered that there are no are safer alternatives (FDA, 2000), while the limit in the EU is 0.007 % (EC, 2009).

7.3.1 Chemical identity

$C_9H_9HgNaO_2S$

7.3.1.1 Primary name/INCI name

Sodium ethyl mercurithiosalicylate / Thimerosal

7.3.1.2 CAS no.

54-64-8

7.3.2 Acute toxicity

In 1931, Powell & Jamieson found that the maximum non-lethal doses of thimerosal were at 20 mg/kg in rabbits and 45 mg/kg in rats (Powell & Jamieson, 1931).

7.3.2.1 Acute oral toxicity

Magos et al (1985) compared the toxicity of ethyl mercury (mercury derivative of thimerosal) and methyl mercury (the mercury compound on which the guidelines for the use of thimerosal are based) in adult male and female rats receiving 5 daily doses equimolar concentrations of ethyl or methyl mercury by gavage. Magos concluded that ethyl mercury is less neurotoxic than methylmercury.

7.3.2.2 Acute dermal toxicity

No available data.

7.3.2.3 Acute inhalation toxicity

Blair et al (1975) observed no histopathological changes in brain or kidney of squirrel monkeys dosed with 418 µg or 2280 µg thimerosal intranasally for 190 days.

7.3.3 Irritation

7.3.3.1 Skin irritation

No available data.

7.3.3.2 Mucosal irritation/eye irritation

It has been shown that thimerosal containing eye drops may cause allergic conjunctivitis in patients (Tosti & Tosti, 1988).

7.3.4 Skin sensitisation

Hypersensitivity to thimerosal is relatively common and can be determined by patch testing, but is rarely clinically relevant (Admani & Jacob, 2014). As thimerosal is found in certain ophthalmic solutions (e.g. contact lens cleaners) as well as in some types of eye make-up, there may be a clinical relevance for patients with dermatitis around the eyes (Admani & Jacob, 2014).
In a Norwegian study, 1,236 adults were patch tested with 24 allergens, including thimerosal. The test showed that 1.9 % of the tested persons was allergic to thimerosal (Videncenter for Allergi, 2014).
In a German study conducted in 1997/98, 1141 subjects aged 25-74 years were tested. Here it was found that 4.7 % of the tested subjects were allergic to thimerosal (Videncenter for Allergi, 2014).

7.3.5 Dermal absorption

No available data.

7.3.6 Repeated toxicity

7.3.6.1 Repeated (28 days) oral / dermal / inhalation toxicity

No available data.

7.3.6.2 Sub-chronic (90 days) oral / dermal / inhalation toxicity

No available data.

7.3.6.3 Chronic (> 12 months) toxicity

No available guideline-studies of chronic toxicity of more than 12 months duration.

7.3.7 Reproduction toxicity

No studies available of thimerosal's effect on reproduction, but according to EMEA, a study showed that methyl mercury affects spermatogenesis in mice at 1 mg Hg/kg body weight (EMEA, 1996). Furthermore, a treatment study for 3 months with daily oral doses of methyl mercury hydroxide (0.05 to 0.09 mg/kg body weight) resulted in an increased frequency of reproductive failure (non-conception, abortion) in non-human primates (EMEA, 1996).

7.3.7.1 Two-generation reproduction toxicity

No available data.

7.3.7.2 Teratogenicity

An increased number of dead and aborted foetuses (rats and rabbits) and an increased number of absorptions (rats) were reported for animals treated with daily intraperitoneal injections of thimerosal in doses of 7 or 70 mg/kg on days 6-18 of gestation (EMEA , 1996).
It was also shown that methyl mercury is foetotoxic in mice (2.5-7.5 mg / kg) and teratogenic in rats and may cause behavioural changes in monkeys exposed to 0.05-0.07 mg/kg per day during gestation (EMEA, 1996).

7.3.8 Mutagenicity / genotoxicity

7.3.8.1 Mutagenicity / genotoxicity *in vitro*

Negative Ames test (*Salmonella typhimurium*) (Zeiger et al, 1987).

Positive *in vitro* micronucleus test in hamster V79 cells (Seelbach et al, 1993).
Induction of micronucleus in human lymphocyte assay thimerosal concentrations between 0.05 and 0.5 µg/mL (Westphal et al, 2003).
According to HSDB (2009), Leopardi and employees observed in a micronucleus test, cytotoxicity in male mice (C57B1 nexC3H/Cne) injected with 20 mg/kg thimerosal.
In vitro studies have shown that 0.03 mM thimerosal enhances the "tubulin assembly" in pig's brains (HSDB, 2009).
Gene mutations, numerical chromosomal aberrations and spindle effects were studied in human lymphocyte cultures exposed to thimerosal. Hyperdiploidy might be caused by thimerosal without direct dose relationship, and spindle functions were also affected. Tetraploid and/or endoreduplication of cells could be induced by thimerosal without dose relationship (HSDB, 2009).
It can be concluded that thimerosal is genotoxic in some *in vitro* studies and cytotoxic at high concentrations.

7.3.8.2 Mutagenicity / genotoxicity *in vivo*
No available data.

7.3.9 Carcinogenicity
According to the EMEA one study attempted to evaluate the carcinogenicity of thimerosal, but due to lack of protocols, no conclusion could be reached (EMEA, 1996).

7.3.10 Toxicokinetics
A study measured the total mercury content in blood, urine and stool samples from a total of 61 infants 3-28 days after vaccination with either thimerosal-containing or thimerosal-free vaccines (Pichichero, 2002). The content of mercury in the blood did not exceed the safety concentration of 29 nmol/L in any of the infants. The half-life of ethyl mercury was estimated to be 7 days (95 % CI 4-10 days).

7.3.11 Photo-induced toxicity
7.3.11.1 Phototoxicity/photoirritation and photosensitisation
No available data.

7.3.11.2 Phototoxicity / photomutagenicity / photoclastogenicity
No available data.

7.3.12 Human data
There are several examples of acute mercury poisoning from thimerosal-containing products in the medical literature with thimerosal doses from about 3 mg/kg to several hundred mg/kg. These reports include gammaglobulin and hepatitis B immunoglobulin with thimerosal as a preservative, chloramphenicol containing 1000 times the correct dose of thimerosal, ear lavage with thimerosal of a child with drainage, treatment of omphalocele in infants with thimerosal, and a suicide attempt with thimerosal. The reported injuries include local necrosis, acute hemolysis, disseminated intravascular coagulation, acute tubular necrosis, and damage to the central nervous system including drowsiness, coma and death (HSDB, 2009; FDA, 2014).
In a study in infants routinely vaccinated with thimerosal-containing vaccines, Pichichero et al (2002) found that the content of mercury in the blood did not exceed the safety values specified in the guidelines for methyl mercury. Furthermore, mercury disappeared from the blood of infants exposed to thimerosal faster than would be expected for methyl mercury and the excreted significant amounts of mercury in the faeces. The results suggest that there are differences in the way that thimerosal and methyl mercury are distributed, metabolised and excreted (Pichichero et al, 2002).

7.3.13 Special studies
No available data.

7.3.14 Conclusion
Thimerosal is acute toxic and toxic after repeated dosing. Especially foetuses and newborn children are expected to be the most sensitive. It can be concluded that the documentation is insufficient and that it is not possible to obtain a NOAEL from animal studies to be used for MoS calculation. It can also be concluded that the proportion of persons who test positive for allergy to thimerosal is between 1.9 and 4.7 %. It has not been possible to find a threshold value for sensitisation for this substance.
For the calculation of MoS for the substance, the provisional tolerable weekly intake of mercury of 0.3 mg/kg bw/week could be used, established by the EMEA (1997), equivalent to 0.04 mg/kg bw/day, and set a dermal absorption to 100 %, as there are no data for dermal absorption of the substance.

7.4 Zinc pyrithione
Zinc pyrithione (ZPT) is a zinc complex with fungi and bacteriostatic properties, which is also used in the treatment of seborrheic dermatitis besides as a preservative in cosmetic products. ZPT is also used as a biocide in antifouling paints for ships and boats.

7.4.1 Chemical identity
$C_{10}H_8N_2O_2S_2Zn$

7.4.1.1 Primary name/INCI name
Zinc pyrithione

7.4.1.2 CAS no.
13463-41-7

7.4.2 Acute toxicity
Intraperitoneal injection of ZPT resulted in LD50 values of 36 mg/kg for rats and 500 mg/kg for mice (SCCS, 2013).
Intravenous injection of 25 mg/kg ZPT was lethal in both dogs and monkeys within 24 hours. Doses of 15 and 20 mg/kg produced a slight cholinergic effect in dogs, but did not result in deaths. One of two Yorkshire pigs died by injection with 20 mg/kg, and 10 mg/kg was found to be a lethal dose in rabbits (SCCS, 2013).

7.4.2.1 Acute oral toxicity
According to the most recent opinion from the SCCS (2013), LD50 values have been estimated in several studies in different species. In rats and mice, respectively, from 92-266 mg/kg and 160-1000 mg/kg have been observed, and in dogs an LD50 of 600 mg/kg has been observed.
For specific ZPT-containing products, an LD50 of 2.5 g/kg for a 'cream shampoo' has been observed in rats and of 3.0 ml/kg for a 'lotion shampoo' (SCCS, 2013).
In dogs, an ED50 (emetic dose = vomiting dose) has been established of approx. 0.05 g/kg which gives an ED50 to LD50 ratio of 1:125 and 1:42, respectively, for 'cream shampoo' and 'lotion shampoo' (SCCS, 2013).

7.4.2.2 Acute dermal toxicity
In albino rabbits, LD50 values have been observed ranging from <2.000 mg/kg to 10,000 mg/kg (SCCS, 2013).
According to REACH registration of ZPT, an LD50 of 2.000 mg/kg has been observed in New Zealand White rabbits (ECHA, 2014).

A shampoo containing 2 % ZPT was tested in rabbits in doses of 2.5; 5.0; 10.0 or 20.0 g/kg. No clinical signs were observed except in 2 of the 4 animals that were tested at the highest dose. In these two animals a slight and transient depression was observed (SCCS, 2013).

7.4.2.3 Acute inhalation toxicity

In a study in 5 male and 5 female rats, an LC50 value of 5.08 mg/l could be calculated. According to REACH registration, in three studies in rats were derived LC50 values of > 1.03 mg/l, > 0.6 mg/l and 0.14 mg/l, respectively (ECHA, 2014).

7.4.3 Irritation

7.4.3.1 Skin irritation

In MAK (2012), 3 skin irritation studies are described:
6 New Zealand White male rabbits were exposed to 0.5 g of ZPT for 4 hours. Skin reactions were assessed at 0.5, 1, 24, 48 and 72 hours. After 0.5-1 hours, a slight erythema was observed in three animals and edemas in two animals. After 24 hours there was no redness and edemas were reduced. After 48 hours, also edemas disappeared.
The dermal irritation of a 20 % suspension of ZPT with 5 daily applications was examined in three animal models (rabbits, guinea pigs and mice). This induced slight irritation as well as a marginal epidermal hyperplasia and increased hair growth.
In a Buehler test in 10 male guinea pigs, 6 hours of treatment with 0.4 ml of a 48 % dispersion did not cause skin irritation.

7.4.3.2 Mucosal irritation/eye irritation

SCCS (2013) concluded on the basis of a number of studies that the irritation potential of shampoo in the eyes of rabbits was not increased by adding ZPT.
MAK (2012) refers to two studies in New Zealand White rabbits, which concluded that ZPT is a severe eye irritant.

7.4.4 Skin sensibilisation

Several studies in guinea pig have concluded that ZPT did not cause skin sensitisation (SCCS, 2013).

According to REACH registration, 2 of 20 guinea pigs were sensitised and it was concluded that ZPT may cause sensitisation by skin contact (ECHA, 2014).

ZPT alone or as part of a cosmetic product showed a low potential for skin sensitisation in a number of skin tests on humans. However, a conclusion of the studies in some of the cases is not possible because of skin irritation in the form of erythema (SCCS 2013).

7.4.5 Dermal absorption

In SCCNFP (2003) it was concluded that based on animal studies, the dermal absorption of ZPT ranges from 0.03-3.4 %. Human clinical studies with a shampoo containing 2 % ZPT (either in combination with a leave-on product containing 0.1 and 0.25 % ZPT or just with a leave-on product containing 0.25% zinc pyrithione) have shown an excretion of up to 0.22 % ZPT with the urine. Taking into account that additional ZPT could have been separated at a later date as well as possible excretion with faeces and possible detention in tissues, SCCS reaches the conclusion that most likely dermal absorption is not above 1 % (SCCS, 2014).

7.4.6 Repeated toxicity

7.4.6.1 Repeated (28 days) oral / dermal / inhalation toxicity

In a 28 days study of dermal neurotoxicity in rats, the lowest no effect dose was 25 mg/kg/day (SCCS, 2013).

7.4.6.2 Sub-chronic (90 days) oral / dermal / inhalation toxicity

Based on observations of muscle atrophy in the hind limbs of rats in a 90-day oral study, a NOEL of 0.5 mg/kg/day was determined (SCCS, 2013).

7.4.6.3 Chronic (> 12 months) toxicity

In a 2-year feeding study of Wistar rats, a NOEL of 0.5 mg/kg/day was determined based on observations of hind limb paralysis (SCCS, 2013). As there were other effects that the study did not account for, this NOAEL value has in the recent opinion of the substance been assessed to be a LOAEL (lowest-observed-adverse-effect level) (SCCS, 2014).

7.4.7 Reproduction toxicity

7.4.7.1 Two-generation reproduction toxicity

From a read-across from sodium pyrithione in rats, a NOAEL of 1.5 mg/kg/day was established for parental toxicity in the form of weakening of hind legs, and atrophy of skeletal muscles. Two 2-generation studies in rats showed a NOAEL of 3.5 mg/kg/day (as the highest dose of 4.5 mg/kg/day was reduced to 3.5 mg/kg/day after the first week of lactation) for effects on fertility (litter size and survival, etc.), and NOAELs of 1.5 and 0.5 mg/kg bw/day for male and female rats, respectively (SCCS, 2013).

7.4.7.2 Teratogenicity

Studies in rats and rabbits showed that 2.5 mg/kg/d were the highest concentration given orally with no effect (SCCS, 2013).

No teratogenicity observed in rats treated with ZPT concentrations up to 100 mg/kg/day (SCCS, 2013).

A number of tests have been carried out where shampoo containing ZPT was applied topically to rabbits and pigs. Concentrations up to 400 mg/g/day were used, but no teratogenicity was observed (SCCS, 2013).

7.4.8 Mutagenicity / genotoxicity

7.4.8.1 Mutagenicity / genotoxicity *in vitro*

SCCS (2013) refers to 2 Ames test studies where no mutagenicity was observed.

In a Comet Assay, damage to DNA strands was observed by treatment with 100-500 nM zinc pyrithione (SCCS, 2013).

The REACH registration refers to a number of *in vitro* studies with negative results. One study showed chromosomal aberrations (ECHA, 2014).

7.4.8.2 Mutagenicity / genotoxicity *in vivo*

The REACH registration refers to 3 studies, none of which found mutagenicity or genotoxicity (ECHA, 2014).

7.4.9 Carcinogenicity

No carcinogenicity was observed in mice and rats by lifelong dermal exposure to 100 mg/kg bw/day or oral exposure of 2.5 mg/kg/day ZPT (SCCS, 2014).

7.4.10 Toxicokinetics

The distribution of radioactivity in tissues after oral administration of labelled ZPT showed that radioactivity was rapidly cleared from the blood, and that it was primarily excreted in the urine. The remaining radioactivity was low (4.5 % of dose). ZPT was distributed in the whole body, and was not concentrated in any particular tissue.
All tested animal species (rat, rabbit, dog and monkey) biotransform ZPT in qualitatively the same way indicating that it is metabolised similarly in humans (SCCS, 2013).

7.4.11 Photo-induced toxicity

7.4.11.1 Phototoxicity/photoirritation / photosensitisation

No available data.

7.4.11.2 Phototoxicity / photomutagenicity / photoclastogenicity

No available data.

7.4.12 Human data

The effect of ZPT in shampoo on human skin was evaluated at concentrations of 0.2, 0.4 or 2.0 % for 64 consecutive days. There was no observed skin irritation or changes in skin pigmentation (SCCS, 2013).
A case is described in which a patient responded to a shampoo containing 2 % ZPT. The patient had 7 years earlier had a similar reaction after using a hair cream with a lower level of ZPT. Another report described a case of eczema of the scalp and face after using a shampoo containing 2 % ZPT (SCCS, 2013).
A number of studies have studied the skin sensitisation potential of ZPT. SCCS concluded in 2013 on this basis that ZPT at worst is a very weak allergen (SCCS, 2013).

7.4.13 Special studies

SCCS (2013) refers to a number of special studies and concludes that reversible hind limb paralysis is the most prominent effect in rats after repeated oral administration of ZPT, and that this is likely due to an effect of pyrithione on the Ca2+ channels. However, from these studies, no conclusions in relation to human impact can be made.

7.4.14 Conclusion

ZPT is acute toxic after oral dosing and by inhalation. It may cause severe eye damage. ZPT has been shown to be neurotoxic, and studies show that there is a threshold. It is the pyrithione part of the molecule that via an increased influx of Ca2+ into the cells activates this non-selective cation, which depolarises the nerve cells and provides the neurotoxic effects as seen in the form of hind legs paralysis in rats. The relevance to humans cannot be determined from these studies.

Several studies with repeated dosing have been made with ZPT. From these studies, it is possible to set a NOAEL of 0.5 kg/kg bw/day. From a chronic study, 0.5 mg/kg body weight/day has been concluded as a viable oral NOAEL covering the neurotoxic effects of pyrithiones, but as there are other effects that have not been accounted for in the study, this value is consideres a LOAEL value (SCCS, 2014).

Although there are signs that sensitisation is possible, human studies have not confirmed that ZPT is other than a possible weak sensitiser. For the MoS calculation, a LOAEL of 0.5 mg/kg bw/day is used, which converted with a factor 3 gives a NOAEL of 0.167 mg/kg body weight/day at 100 % bioavailability.

8. Exposure assessment

Realistic worst case exposure scenarios are established for the selected preservatives for the relevant use situations. The selected preservatives are:

- DMDM Hydantoin
- Imidazolidinyl urea
- Zinc pyrithione
- Thimerosal
- Phenoxyethanol

The following information from the survey is relevant to the five selected preservatives:

- DMDM Hydantoin was most commonly observed to be used with 2 -11 other preservatives in the tested products. Only in one product DMDM Hydantoin was used as the only preservative.
- Imidazolidinyl urea was most commonly observed to be used with 2-3 other preservatives in the tested products. Only in one product, Imidazolydinyl urea was used as the only preservative.
- According to information from the manufacturers, Zinc pyrithone is used for dandruff shampoo. Zinc pyrithone has not been observed to be used in the tested products, but only 3 dandruff shampoos are included in the survey.
- Thimerosal has not been observed in the tested products nor has it been indicated by the manufacturers. According to Cosing, Thimerosal is used in eye products[17] and according to WHO, it is used worldwide in creams and soaps for bleaching of the skin and in eye makeup cleansing products and mascaras[18]. According to EU Regulation on cosmetic products (EU Regulation 1223, 2009) Thimerosal can only be used in eye products in the EU.
- Phenoxyethanol is the most commonly used preservative according to the survey, and is used alone or with other preservatives. Phenoxyethanol has been identified in a large number (43) of the 55 product types.

Table 16 provides an overview of the types of products in which the selected preservatives are observed according to the survey. It appears that phenoxyethanol is used in virtually all types of cosmetic products. In this project, it has therefore been possible to perform exposure calculations with the measured values in excess of the maximum permitted concentration for the product types where the content of phenoxyethanol was analysed (see Chapter 6 "Analyses").

[17] According to Cosing, used in eye products (http://ec.europa.eu/consumers/cosmetics/cosing/index.cfm?fuseaction=search.details_v2&id=28141)
[18] http://www.who.int/ipcs/assessment/public_health/mercury_flyer.pdf?ua=1

Preservative	Product types observed in the survey	Information from manufacturers	Product types for which exposure calculations are performed
DMDM Hydantoin	Hair conditioner (2) Hair care products (2) Hair shampoo (4) Hair styling products - foam/mousse (1) Hair styling products - aqueous hairspray (1) Hair styling products - wax/gel/paste (2) Makeup remover and cleansers (1)	Not stated to be used by the 8 manufacturers of cosmetic products who provided information to this projekt. Sold by 1 og the 3 manufacturers of preservatives who provided information to this project. The product types in which it is used are not stated.	Hair conditioner Hair repair Hair shampoo Hair styling products Hairspray Cleansers (face)
Imidazolidinyl urea	Facial masks (2) Hair conditioner (1) Mascara (1) Powder/blush (1)	Stated to be used by 1 of the 8 manufacturers of cosmetic products. It is also stated that the use of this preservative is on the way out. Not stated to be sold by the 3 manufacturers of preservatives.	Facial masks Hair conditioner Mascara Powder/blush
Zinc pyrithione	Not observed in any products (but only 3 dandruff shampoos are included in this survey)	Stated to be used by 1 of the 8 manufacturers of cosmetic products in dandruff shampoo. Not stated to be sold by the 3 manufacturers of preservatives.	Dandruff shampoo
Thimerosal	Not observed in any products	Not stated either by manufacturers of cosmetic products or preservatives	Eye products

Preservative	Product types observed in the survey	Information from manufacturers	Product types for which exposure calculations are performed
Phenoxy-ethanol	Observed in 43 of the 55 product types in the survey. Most commonly (percentage) observed in: Mascara (13/87%) Hand cream (10/83%) Foundation, BB cream (14/82%) Wet wipes (9/75%) Hair styling – aqueous hairspray (3/75%) Bodylotion (14/70%)	Stated to be used by 6 of the 8 manufacturers of cosmetic products using preservatives. Used for a variety of products. Stated to be sold by 3 of 3 manufacturers of preservatives.	Aftersun lotion/spray Facial creams Bodylotion Bodylotion/creams for ”eczema skin” Bodyscrub Deodorants (roll-on) Liquid hand soap Foot cream Foundation, BB cream Hand cream Hair conditioner Hair shampoo Intimate soap Mouthwash Cleanser (face) Cleansing wipes Anti-wrinkle creams Foambath/bath gel Sunscreen/sun oils Wet wipes Eye creams

TABLE 16
OVERVIEW OF PRODUCT TYPES IN WHICH THE SELECTED PRESERVATIVES APPEAR. NUMBER OF PRODUCTS PER PRODUCT TYPE IS STATED IN BRACKETS.

8.1 Method for assessment of exposure calculation

The exposure assessment for preservatives in cosmetic products is based on the maximum permitted concentration of preservatives in cosmetic products (according to EU Regulation 1223, 2009), and for phenoxyethanol also on the specific content concentrations measured by quantitative analysis (see Chapter 6 "Analyses"). Generation of exposure scenarios for the selected preservatives is described below and follows SCCS Notes of Guidance, version 8 (SCCS, 2012).

The systemic exposure dosage (Systemic Exposure Dosage, SED) is set in a worst-case scenario for a model person (adult of 60 kg or baby of 5.3 kg depending on product type) using the default parameters specified by the SCCS (2012). Where there is a standard parameter in SCCS, the default

values are used for body area from the REACH Guidance Documents from ECHA (ECHA R.15, 2012).

The daily exposure is calculated using the formula below, where SED – the daily exposure dosage – is calculated as the product of the daily applied amount (AA), the concentration of the substance in the product (C), the absorption through the skin expressed in percentage (dermal absorption, DA_p), and a retention factor (R_f) that takes into account rinse-off products, divided by the body weight (BW)[19].

$$SED\ (mg/kg\ bw/day) = \frac{AA\ (mg/day) \times Rf\ \times C\ (\%)/100\ \times\ DAp\ (\%)/100}{BW\ (kg)}$$

8.1.1 Method for calculation of total exposure

The total exposure when using several product types containing the same preservative can be calculated by adding the estimated systemic exposure dosage for each product type. The total systemic exposure dosage (SED_{total}) is calculated using the following formula:

$$SED_{total} = SED_{produkttype\ 1} + SED_{produkttype\ 2} + \ldots + SED_{produkttype\ n}$$

If the same preservative is used in the different product types, the exposure to preservatives is calculated from a worst-case scenario, where the total exposure to a realistic number of daily used cosmetic products is set to 17.4 g/day, or 269 mg/kg BW/day, and based on this calculate safety margin (MoS) (SCCS, 2012).

In this project, the exposure is also calculated case-by-case for all the product types described in the survey. This calculation shows that the daily exposure also comes close to the 17.4 g/day, see section 8.4 below.

8.2 Exposure scenarios

The following exposure scenarios are calculated in this project:

- Calculation is made on the product types in which the selected preservatives are used (indicated in Table 16) for a standard person of 60 kg (female).
- The maximum permitted concentrations for the preservatives are used - but where measurements have been made of the concentration (here phenoxyethanol), both the maximum permitted concentration and the highest measured concentration are used in the analysis.
- Calculation is made on scenarios with and without sunscreen (corresponding to a winter and a summer scenario) for the preservatives used in sunscreens according to the survey, ie. exclusively phenoxyethanol.
- Calculaton is also made on scenarios using wet wipes on a baby's diaper area, as this area may be especially sensitive and have a higher absorption. This is assessed to be relevant only for phenoxyethanol.

8.3 Data used in the exposure calculations

This section contains an overview of the data used in the exposure calculations:

The general anatomical data used for exposure calculations are indicated in Table 17.

[19] Formlen er en kombination af formlen angivet side 69 i SCCS (2012) og beregningerne foretaget i Tabel 3 side 71. Bl.a. svarer AA som angivet i denne rapport til A/BW i SCCS (2012).

Parameter	Value used	Comments	Reference
Body weight adults (BW)	60 kg	SCCS states that the standard value for adults is 60 kg.	SCCS, 2012
Body weight baby (BW)	5.3 kg	A 3-month old baby's weight of 5.3 kg is used. The value is referred in SCCS opinion.	SCCS/1446/11
Body area adults	17 500 cm^2	Body area for adult women.	SCCS, 2012
Body area baby (3 months)	310 cm^2	Body area for a 3-month old baby.	SCCS/1446/11

TABLE 17
ANATOMICAL DATA USED IN THE EXPOSURE CALCULATIONS.

Data concerning the daily amount used and the retention factor are indicated for the different product types in Table 18. The amounts are stated per kg body weight (bw), ie. 60 kg, see Table 17. These two values (amount/kg bw and retention factor) are multiplied to the value indicated in the column "calculated daily exposure in mg/kg bw/day". Some of the products are used frequently, and studies have shown that the frequency of use may affect the amount used of the product per time. Thus, a reduction of the used amount of the most commonly used products is seen. It is indicated if the values are from SCCS Notes of Guidance 8th rev.Table 3 (SCCS, 2012).

Product type	Relatively daily used amount (mg/kg bw/day)	R_f (no unit)	Calculated daily exposure in mg/kg bw/day	Comments
Aftersun lotion/ spray	11.54	1	11.54	Here it is assumed that adults use 0.5 mg/cm^2 once per day, ie half the amount of sunscreen applied per day (18 g/day). This product is used in the periods during where sunscreen may also be used, i.e. in 4 out of 52 weeks
Facial masks	24.14	0.1	2.41	Here it is assumed that the same amount is used as for facial creams. Some products are staying on for a while and then rinsed off, whereas others need to stay on overnight. A retention factor R_f = 0.1 is used assuming that very few facial masks stay on the skin overnight.
Facial creams	24.14	1	24.14	The exposure appears from SCCS (2012), Table 3.
Bodylotion	123.20	1	123.20	The exposure appears from SCCS (2012), Table 3.

Product type	Relatively daily used amount (mg/kg bw/day)	R_f (no unit)	Calculated daily exposure in mg/kg bw/day	Comments
Bodylotion/ creams for "eczema skin"	123.20	1	123.20	Here it is assumed that the same amount is used as for normal bodylotion. The exposure appears from SCCS (2012), Table 3.
Bodyscrub	130.33	0.01	1.30	Here it is assumed that the same amount is used as for estimated daily use of bodylotion/creams, but as it is quickly removed, a retention factor of 0.01 is used.
Deodorants (roll-on)	22.08	1	22.08	The exposure appears from SCCS (2012), Table 3.
Liquid hand soap	333	0.01	3.33	The exposure appears from SCCS (2012), Table 3.
Foot cream	24.14	1	24.14	Here, a proportional value based on feet's area is used. The area of women's feet (1001 cm^2) is almost identical to the face area (1028 cm^2) (ECHA R.15, 2012). Application of foot cream twice daily is recommended, which is also is assumed for facial creams. Therefore, the value for facial cream is used here.
Foundation/ BB cream	7.90	1	7.90	For foundation/BB cream, the value indicated for liquid foundation is used. The exposure appears from SCCS (2012), Table 3.
Hand cream	32.70	1	32.70	The exposure appears from SCCS (2012), Table 3.
Hair conditioner	60.33	0.01	0.60	The exposure of 0.60 appears from SCCS (2012), Table 3.
Hair repair	60.33	0.1	6.03	It is assumed that the used amount is identical to that of hair conditioner. However, some hair repairs are stay-on products, and therefore an R_f value corresponding to hair styling products of 0.1 is chosen.
Hair shampoo	150.49	0.01	1.51	The exposure appear from SCCS (2012), Table 3.
Hair styling products	57.40	0.1	5.74	The exposure appear from SCCS (2012), Table 3.
Hairspray	57.40	0.1	5.74	It is not specified, whether hair spray is covered by hair styling products in SCCS (2012), Table 3. However, this is assumed to be the case. That is,

Product type	Relatively daily used amount (mg/kg bw/day)	R_f (no unit)	Calculated daily exposure in mg/kg bw/day	Comments
				the same values are used for hairspray and other hair styling products.
Intimate soap	77.79	0.01	0.78	It is assumed that the consumption of intimate soap is a quarter of the consumption of body shampoo/shower gel (18 670 mg).
Mascara	0.42	1	0.42	The exposure appear from SCCS (2012), Table 3.
Mouthwash	325.40	0.1	32.54	The exposure appear from SCCS (2012), Table 3.
Powder/blush	1.67	1	1.67	There are no indicated amounts specifically for powder. It is assumed that the amount used is 5 times the value used for eye shadow (0.33 mg/kg).
Clenser (face)	83.33	0,1	8.33	The amount indicated for makeup remover is used. The exposure appear from SCCS (2012), Table 3.
Cleansing wipes	66.67	1	66.67	A weighing of a wipe has shown that it only weighs about 6 g (5.64 g). After evaporation (drying) of the liquid in cleansing wipe, the wipe is weighed to 1.83 g. That is, the fluid on the wipe is measured to 3.81 g. 4 g is therefore used in the calculations.
Anti-wrinkle creams	24.14	1	24.14	The amount indicated for facial creams is used. The exposure appear from SCCS (2012), Table 3.
Foambath/bath gel	279.20	0.01	2.79	It is assumed to use the same value as for bodyshampoo/shower gel. The exposure appear from SCCS (2012), Table 3.
Sunscreens/ sun oils	46.15 or 23.08	1	46.15 or 23.08	An amount for sunscreens of 36 g/day is indicated. The exposure appear from SCCS (2012), Section 4-2. The sunscreen is not used daily, but is assumed to be used daily in 4 weeks per year.
Dandruff shampoo	150.49	0.1	15.05	The same values as for hair shampoo are used. The exposure appear from SCCS (2012), Table 3. As dandruff shampoo often has to stay in the hair and work for a while, an R_f value of 0.1 instead of

Product type	Relatively daily used amount (mg/kg bw/day)	R_f (no unit)	Calculated daily exposure in mg/kg bw/day	Comments
				0.01 is used.
Wet wipes	66.67 (103.77)	1	66.67 (103.77)	Adults: The same value as for cleansing wipes is used here. A weighing of a wet wipe has shown that it weighs about 5 g (4.99 g). After evaporation (drying) of the liquid in wet wipe, the wipe is weighed to 1.93 g. That is, the liquid on the wipe is measured to 3.06 g. 4 g is therefore used in the calculations as a worst case as for the cleansing wipes. Baby: SCCS/1446/11 has an amount of 550 mg/day for wet wipes by exposure of the baby's diaper area, i.e. 104 mg/kg bw/day for a baby of 3 months weighing 5.3 kg.
Eye creams	1.21	1	1.21	No specific amounts for eye creams are indicated. It is assumed to use an amount corresponding to 5 % of the amount of used facial cream.
Eye products	0.33	1	0.33	The value indicated by SCCS for eye shadow is used for eye products. The exposure appear from SCCS (2012), Table 3.

TABLE 18
DATA FOR DAILY USED AMOUNT, RETENTION FACTOR, AND EXPOSURE FOR THE DIFFERENT PRODUCT TYPES.

Data regarding absorption of the substances through the skin and by ingestion (dermal and oral absorption) are indicated in Table 19. Regarding oral absorption, this is only relevant to phenoxyethanol, which may be used in mouthwash, where a small portion is ingested directly. 100 % absorption (uptake) is assumed unless specific information exists regarding absorption of the specific substance.

Preservative	Dermal absorption	Oralt absorption / Diaper area of baby
DMDM Hydantoin	10 %	*Not relevant*
Imidazolidinyl urea	100 %	*Not relevant*
Zinc pyrithione		*Not relevant*

Preservative	Dermal absorption	Oralt absorption / Diaper area of baby
	1 %	
Thimerosal	100 %	*Not relevant*
Phenoxyethanol (Source: ANSM, 2012)	80 % / 48 % *	100

* A RISK OF DERMAL ABSORPTION OF 48% IS ALSO CALCULATED, SEE CHAPTER 9

TABLE 19
DERMAL AND ORAL ABSORPTION RATES USED IN THE EXPOSURE CALCULATIONS.

It should be noted that for phenoxyethanol the dermal absorption is indicated as a worst case of 40 % for rinse-off products and 80 % for leave-on products (ANSM, 2012). The values are based on a few *in vitro* data. An *in vivo* study with few test subjects indicates that absorption of the substance through the skin may be lower in humans. In the *in vivo* study with 4 volunteers was measured dermal absorption of between 8.5 and 48 % by application of 40 g of cream containing 1.2 % phenoxyethanol (ANSM, 2012).

In the REACH dossier on phenoxyethanol, data have been submitted on a study regarding dermal absorption (Roper et al., 1997). This study is based on *in vitro* test on human skin. An absorption of phenoxyethanol of 59.3 % ± 7.0 % is indicated here. Thus, a number of studies show a high absorption of phenoxyethanol. As a worst case, a dermal absorption of 80 % for phenoxyethanol is used. Based on *in vivo* data, the risk is also calculated by a dermal absorption of 48 % for phenoxyethanol for the total amount of daily used cosmetic products described in Section 8.4, see Chapter 9 below.

In the risk assessment based on the method indicated in SCCS Notes of Guidance (SCCS, 2012), a retention factor is used to take into account that some products are rinsed off after use or used in diluted form. In the calculations of this study, no distinction has therefore been made between rinse-off products and leave-on products in terms of dermal absorption, ie. different dermal absorption rates for rinse-off or leave-on products have not been used. A distinction, however, is made in the calculations by using the retention factor that is used to take into account that some products are rinsed off after use.

8.4 Results – exposure calculations

In this section, the results of the exposure calculations for the 5 selected preservatives are presented. The results are presented in the tables below for each of the product types in which the preservatives may occur (based on information from the survey).

The daily exposure dosage (SED) is calculated using the below formula:

$$SED\ (mg/kg\ bw/day) = \frac{AA\ (mg/day) \times Rf\ \times C\ (\%)/100\ \times\ DAp\ (\%)/100}{BW\ (kg)}$$

AA – applicated daily amount of the product (mg/dag)
R_f –retention factor that takes into account the rinse-off products, ei products that are not rinsed off have retention factor 1.
C – concentration of the substance in the product
DA_p – dermal absorption
BW – body weight (kg)

As an example, the daily exposure of phenoxyethanol is calculated from a facial cream using the concentration of 0.84 %, which was identified in the chemical analyses.

$$SED\ (mg/kg\ bw/day) = \frac{1540\ mg/day \times 1\ \times 0{,}84/100\ \times\ 80/100}{60\ kg}\ =\ 0{,}172\ mg/kg\ bw/day$$

As phenoxyethanol is used as a preservative in many different types of cosmetic products, the total exposure from daily use of different cosmetic products is also calculated. Similarly, the total daily exposure is calculated to DMDM Hydantoin and Imidazolidinyl urea, both of which also may be present in several types of cosmetic products. However, it is somewhat more likely that these preservatives will occur in all types of cosmetic products, but this is assumed to be worst case. The products included in the total calculations are indicated for adults (women) below.

SCCS indicate in their Notes of guidance (SCCS, 2012) that consumers may use several cosmetic products containing the same preservative corresponding to a total daily exposure (= daily amount used multiplied by the retention factor) of 17.4 g/day or 269 mg/kg bw/day. For some of the used products, recent studies show a slightly lower daily exposure when used frequently. This is reflected in the calculated relative exposure values indicated in SCCS (2012), Table 3, and are indicated in Table 18 above, and used in the following exposure calculations.

SCCS (2012) assumes that the following 14 cosmetic products are used daily. A similar assumption is used in the calculations of this report.

Facial cream	24.14 mg/kg bw/day
Bodylotion	123.20 mg/kg bw/day
Deodorant (roll-on)	22.08 mg/kg bw/day
Liquid hand soap	3.33 mg/kg bw/day
Foundation/BB creme	7.90 mg/kg bw/day
Hand cream	32.70 mg/kg bw/day
Hair conditioner	0.60 mg/kg bw/day
Hair shampoo	1.51 mg/kg bw/day
Hair styling products	5.74 mg/kg bw/day
Mascaras	0.42 mg/kg bw/day
Mouthwash	32.54 mg/kg bw/day
Cleanser (makeup remover)	8.33 mg/kg bw/day
Foam bath/bath gel	2.79 mg/kg bw/day
Eye products (eye makeup)	0.33 mg/kg bw/day

And especially for the summer scenario, is added the use of:

- Sunscreen — 46 mg/kg bw/day (recommended amount) or 23 mg/kg bw/day (if the use of sunscreen is only 18 g per day)

SCCS (2012) assumes that also toothpaste, lipstick and eyeliner are used, which, however, are not included in the calculations of this report, as these types of products have not been selected in the survey. However, this has no great impact on the results as these products (toothpaste, lipstick and eyeliner) only represent a daily use of 0.205 g per day or 3.14 mg/kg bw/day, and out of the daily use of 17.4 grams, they only constitute approximately 1.2 %.

The use of the above 14 different cosmetic products provides a total calculated daily exposure to cosmetic products of 266 mg/kg bw/day, ie. quite close to the 269 mg/kg bw/day stated in SCCS (2012). For the summer scenario that includes sunscreen, the result is thus a calculated daily exposure of up to 312 mg/kg bw/day.

For a few of the selected preservatives, a worst case scenario is also considered where it is conceivable that the same preservative is found in all cosmetic products used during a day. This situation is not inconceivable for the widely used preservative phenoxyethanol, but more unlikely for example for DMDM Hydantoin and Imidazolidinyl urea, which are observed in far fewer types of products in the survey, and quite unlikely for both Zinc pyrithione and Thimerosal, which are only allowed in rinse-off hair products and eye products, respectively.

The exposure to the preservatives appears in the following section.

8.4.1 Results – DMDM Hydantoin

DMDM hydantoin is observed in a number of different product types in the survey of this project. Exposure calculations have therefore been made for the following product types: hair conditioner, hair repair, hair shampoo, hair styling products, hairspray, and cleanser (face). The results appear from Table 20 below.

DMDM Hydantoin Product type	Calculated daily exposure (mg/kg bw/day) (refer to Table 18)	Max permitted concentration (%)	Dermal absorption (%) (refer to Table 19)	SED (mg/kg bw/day)
Hair conditioner	0.60	0.6	10	0.0004
Hair repair	6.03	0,6	10	0.004
Hair shampoo	1.51	0.6	10	0.001
Hair styling products	5.74	0.6	10	0.003
Hairspray	5.74	0.6	10	0.003
Cleanser (face)	8.33	0.6	10	0.005
Sum selected everyday products	**16.18**	**0.6**	10	**0.01**
Sum via all used products	**266**	**0.6**	10	**0.160**

TABLE 20
EXPOSURE CALCULATION FOR DMDM HYDANTOIN – CALCULATION OF SED.
THE DAILY USED PRODUCT TYPES ARE MARKED WITH GREEN BACKGROUND COLOUR.

8.4.2 Results – Imidazolidinyl urea

Imidazolidinyl urea has only been observed in a few products in the survey (totally 5), but in product types as facial masks, hair conditioners, mascaras and powders/blush. Therefore, exposure calculations have been made for these types of cosmetic products. The results are indicated for 100 % absorption through the skin in Table 21 below.

Imidazolidinyl urea **Product type**	**Calculated daily exposure (mg/kg bw/day)** **(refer to Table 18)**	**Max permitted concentration (%)**	**Dermal absorption (%)** **(refer to Table 19)**	**SED** **(mg/kg bw/day)**
Facial masks	2.41	0.6	100	0.014
Hair conditioner	0.60	0.6	100	0.004
Mascara	0.42	0.6	100	0.003
Powder/blush	1.67	0.6	100	0.010
Sum selected everyday products	**1.02**	**0.6**	**100**	**0.007**
Sum via all used products	**266**	**0.6**	**100**	**1.596**

TABLE 21
EXPOSURE CALCULATION FOR IMIDAZOLIDINYL UREA – CALCULATION OF SED.
THE DAILY USED PRODUCT TYPES ARE MARKED WITH GREEN BACKGROUND COLOUR.

8.4.3 Results – Phenoxyethanol

In the survey, phenoxyethanol has been observed in a wide variety of different types of cosmetic products. Exposure calculations have been made for selected types of cosmetic products (as described in Table 16). The results are indicated based on a worst case absorption through the skin of 80 %, and the max permitted concentration and concentrations measured in the analyses of this project, respectively (Table 22). However, the max permitted concentration of 1 % has been used for the selected product types, for which *no* analyses of the content condentration have been made.

The types of cosmetic products, which counts towards the total daily exposure (ie. the products assumed to be used every day by SCCS, 2012), are marked with green background colour.

Phenoxyethanol Product type	Calculated daily exposure (mg/kg bw/day) (refer to Table 18)	Measured concentration (%)	Dermal absorption (%) (refer to Table 19)	SED (mg/kg bw/day)
Facial creams	24.14	0.84	80	0.162
Bodylotion	123.20	0.85	80	0.838
Bodylotion/creams for "eczema skin"	123.20	0.50	80	0.493
Bodyscrub	1.30	0.87	80	0.009
Deodorants (roll-on)	22.08	0.51	80	0.090
Liquid hand soap	3.33	1*	80	0.027
Foot cream	24.14	0.56	80	0.115
Foundation/ BB cream	7.90	0.69	80	0.044
Hand cream	32.70	0.40	80	0.105
Hair conditioner	0.60	1*	80	0.005
Hair shampoo	1.51	1*	80	0.012
Hair styling products	5.74	1*	80	0.046
Intimate soap	0.78	0.61	80	0.004
Mascara	0.42	1*	80	0.003
Mouthwash	32.54	0.30	100	0.098
Cleanser (face)	8.33	0.80	80	0.053
Cleansing wipes	66.67	0.24	80	0.128

Phenoxyethanol Product type	Calculated daily exposure (mg/kg bw/day) (refer to Table 18)	Measured concentration (%)	Dermal absorption (%) (refer to Table 19)	SED (mg/kg bw/day)
Anti-wrinkle creams	24.14	0.62	80	0.120
Foambath/bath gel	2.79	1*	80	0.022
Sunscreens/sun oils	46.15 or 23.08	0.70	80	0.258 or 0.129
Wet wipes	66.67	0.86	80	0.459
Eye creams	1.21	0.89	80	0.009
Eye products	0.33	1*	80	0.0026
Sum selected everyday products	**265.61**	**Measured/1 %**	**80**	**1.508**
Sum selected everyday products + sunscreen	**312 (or 289)**	**Measured/1 %**	**80**	**1.766 (or 1.637)**

* THE CONCENTRATION IS NOT MEASURED HERE. THEREFORE THE MAX PERMITTED CONCENTRATION IS USED.

TABLE 22

EXPOSURE CALCULATION FOR PHENOXYETHANOL – CALCULATION OF SED FOR MEASURED CONCENTRATIONS (ANALYTICAL RESULTS). FOR THE SUNSCREENS EXPOSURE WHEN USING THE RECOMMENDED QUANTITY OF 36 G/DAY AND IN BRACKETS WHEN USING 18 G/DAY IS INDICATED. THE DAILY USED PRODUCT TYPES ARE MARKED WITH GREEN BACKGROUND COLOUR.

If all the mentioned cosmetic products contain the maximum permitted concentration of phenoxyethanol, the calculations are as follows:

Phenoxyethanol Product type	Calculated daily exposure (mg/kg bw/day) (refer to Table 18)	Max permitted concentration (%)	Dermal absorption (%) (refer to Table 19)	SED (mg/kg bw/day)
Aftersun lotion/spray	11.54	1	80	0.092
Facial masks	2.41	1	80	0.019
Facial creams	24.14	1	80	0.193
Bodylotion	123.20	1	80	0.986
Bodylotion/ creams for "eczema skin"	123.20	1	80	0.986
Bodyscrub	1.30	1	80	0.010
Deodorants (roll-on)	22.08	1	80	0.177
Liquid hand soap	3.33	1	80	0.027
Foot cream	24.14	1	80	0.205
Foundation/ BB cream	7.90	1	80	0.063
Hand cream	32.70	1	80	0.262
Hair conditioner	0.60	1	80	0.005
Hair repair	6.03	1	80	0.052
Hair shampoo	1.51	1	80	0.012
Hair styling products	5.74	1	80	0.046
Hairspray	5.74	1	80	0.046
Intimate soap	0.78	1	80	0.006
Mascara	0.42	1	80	0.003
Mouthwash	32.54	1	100	0.325
Powder/blush	1.67	1	80	0.013
Cleanser (face)	8.33	1	80	0.067

Phenoxyethanol Product type	Calculated daily exposure (mg/kg bw/day) (refer to Table 18)	Max permitted concentration (%)	Dermal absorption (%) (refer to Table 19)	SED (mg/kg bw/day)
Cleansing wipes	66.67	1	80	0.533
Anti-wrinkle creams	24.14	1	80	0.193
Foambath/bath gel	2.79	1	80	0.022
Sunscreens/ sun oils	46.15 or 23.08	1	80	0.369 or 0.184
Dandruff shampoo	15.05	1	80	0.139
Wet wipes	66.67	1	80	0.533
Eye creams	1.21	1	80	0.010
Eye product	0.33	1	80	0.003
Sum selected everyday products	**265.61**	**1**	**80**	**2.125**
Sum selected everyday products + sunscreen	**312 (or 289)**	**1**	**80**	**2.496 (or 2.312)**

TABLE 23
EXPOSURE CALCULATION FOR PHENOXYETHANOL – CALCULATION OF SED FOR MAX PERMITTED CONCENTRATIONS. FOR THE SUNSCREENS EXPOSURE WHEN USING THE RECOMMENDED QUANTITY OF 36 G/ DAY AND IN BRACKETS WHEN USING 18 G/DAY IS INDICATED.

8.4.4 Results – exposure of the diaper areas of babies

SCCS has assessed that there is no need for an additional safety factor in the assessment of children, and risk calculations for adults is so conservative that they also include children. However, there may be special cases where an exposure calculaton for children can be relevant, for example when assessing products for the diaper area of babies (SCCS 2012; SCCS/1446/11). In this project, the exposure of babies to wet wipes has therefore been calculated, as these products were selected in the project (see Table 24).

Phenoxyethanol Product type	Calculated daily exposure (mg/kg bw/day) (refer to Table 18)	Measured concentration (%)	Dermal absorption (%) (refer to Table 19)	SED Baby (mg/kg bw/day)
Wet wipes	103.77	0.86	100	0.89

TABLE 24
EXPOSURE CALCULATION FOR PHENOXYETHANOL – CALCULATION OF SED BABY FOR MEASURED CONCENTRATIONS (ANALYTICAL RESULTS).

If the exposure dose for children is calculated from the maximum permitted concentration of phenoxyethanol, the result is as follows (Table 25):

Phenoxyethanol Product type	Calculated daily exposure (mg/kg bw/day) (refer to Table 18)	Max permitted concentration (%)	Dermal absorption (%) (refer to Table 19)	SED Baby (mg/kg bw/day)
Wet wipes	103.77	1	100	1.038

TABLE 25
EXPOSURE CALCULATION FOR PHENOXYETHANOL – CALCULATION OF SED BABY FOR MAX PERMITTED CONCENTRATIONS.

8.4.5 Results – Thimerosal

Thimerosal has not been observed to be used in the studied products or used by the manufacturers. According to Cosing, Thiomeral is used in eye products[20], and according to WHO it is used worldwide in creams and soaps for bleaching the skin, and in eye makeup cleansing products and mascaras[21]. According to EU regulation on cosmetic products (EU regulation 1223, 2009), Thimerosal may only be used in eye products in the EU. Therefore, exposure calculations have been exclusively made on the use of Thimerosal in eye products. The results are indicated in Table 26 below.

Thimerosal Product type	Calculated daily exposure (mg/kg bw/day) (refer to Table 18)	Max permitted concentration (%)*	Dermal absorption (%) (refer to Table 19)	SED (mg/kg bw/day)
Eye products	0.33	0.007 for mercury	100	0.00023

TABLE 26
EXPOSURE CALCULATION FOR THIMEROSAL – CALCULATION OF SED.

8.4.6 Results – Zinc pyrithione

Zinc pyrithione has not been observed in any products in the survey, but 1 of the 8 manufacturers of cosmetic products contacted in the survey indicated that they use the preservative in dandruff shampoo. Therefore, exposure calculations have been exclusively made on the use of Zinc pyrithione in dandruff shampoo. The results are indicated in Table 27 below.

Zinc pyrithione Product type	Calculated daily exposure (mg/kg bw/day) (refer to Table 18)	Max permitted concentration (%)	Dermal absorption (%) (refer to Table 19)	SED (mg/kg bw/day)
Dandruff shampoo	15.05	1	1	0.0015

TABLE 27
EXPOSURE CALCULATION FOR ZPT USED IN DANDRUFF SHAMPOO – CALCULATION OF SED.

[20] Used in eye products acoording to Cosing (http://ec.europa.eu/consumers/cosmetics/cosing/index.cfm?fuseaction=search.details_v2&id=28141)

[21] http://www.who.int/ipcs/assessment/public_health/mercury_flyer.pdf?ua=1

9. Risk assessment

The risk assessment is carried out in accordance with the principles of SCCS Notes of Guidance, version 8 (SCCS, 2012). The principles are described below.

9.1 Method for calculation of risk

Possible health risks of exposure to the selected preservatives in selected cosmetic product types are evaluated by calculating a Margin of Safety (MoS). The calculation is based on NOAEL (No Observed Adverse Effect Level), possibly LOAEL (Lowest Observed Adverse Effect Level) determined based on the health profiles of the preservatives calculated in Chapter 7 "Hazard Assessment", and the estimated Systemic Exposure Dosage (SED) calculated in Chapter 8 "Exposure assessment". MoS is calculated as follows (SCCS, 2012):

$$MoS = \frac{NOAEL}{SED}$$

According to SCCS (2012), WHO recommends Mos to be at least 100, and it is generally accepted that MoS should be at least 100 to conclude that a substance is safe to use. This safety margin of 100 appears by including a safety factor of 10 for extrapolation of data from animals to humans and a safety factor of 10 for the difference between humans.

This MoS of at least 100 is according to SCCS (2012) also valid for children, and there is generally no need for an additional safety factor for children. This applies only as long as the skin is intact. That is for children (and adults) with eczema skin or for products used in the diaper area (such as wet wipes, which are calculated below), it might be necessary with an additional safety factor to conclude whether a substance is safe to use. The safety factor is however not indicated. SCCS (2012) writes directly that "cosmetic products are intended to be used on intact skin, therefore, a medical consultation is required in cases where there is genuinely damaged skin, and here pharmaceuticals and not cosmetics should be used ".

9.1.1 Method for calculation of overall risk

The overall risk by using several types of products containing the same preservative can be calculated by adding the estimated systemic exposure dose for each product type. The total systemic exposure dosage (SED_{total}) is finally compared to the NOAEL value based on the following formulas:

$$SED_{total} = SED_{product\ type\ 1} + SED_{product\ type\ 2} + \ldots + SED_{product\ type\ n}$$

$$MoS = \frac{NOAEL}{SED_{total}}$$

9.2 Used NOAEL values

The NOAEL values used in the risk assessment are indicated in Table 28 below. The NOAEL values for the four preservatives are taken from Chapter 7 "Hazard Assessment". It has not been included in this project to assess the NOAEL values for phenoxyethanol as the substance is currently under consideration by the EU. The assessment is expected to be completed by the SCCS in 2015.

This report therefore applies several NOAEL values, a NOAEL value from the French study (ANSM; 2012) and a newer NOAEL value from a REACH dossier. According to SPT, there are also newer studies that may be relevant. It has not been possible in the present study to closer review the mentioned studies on phenoxyethanol to examine whether, for example, the official guidelines for carrying out the studies have been followed. As a worst case will be used the lowest specified NOAEL for the calculation of the risk of phenoxyethanol, also, a risk assessment will be calculated with the specified higher NOAEL value. The lowest NOAEL value is derived from a 90-day study that showed hepatotoxic effects in rats by prolonged exposure.

Preservative	Applied NOAEL value (mg/kg bw/day)
DMDM Hydantoin	220
Imidazolidinyl urea	28
Zinc pyrithione	0.167
Thimerosal	0.04*
Phenoxyethanol	164 and 697

* BASED ON MERCURY

TABLE 28

APPLIED NOAEL (OTHER EFFECTS THAN ALLERGY) VALUES IN THE RISK ASSESSMENT.

9.3 Results – risk assessment

This section presents calculations of the MoS values for the 5 selected preservatives. The results appear from the tables below for the product types in which the preservatives may occur (based on the information from the survey).

For Phenoxyethanol, used as a preservative in many different types of cosmetic products, a calculation of the total use of several different cosmetic products in the same day has also been made. For DMDM Hydantoin and Imidazolidinyl, a calculation of the total use has been made as well, as these preservatives may also occur in a variety of cosmetic products. The products included in this overall calculation are listed in the previous chapter (Chapter 8 "Exposure Calculations").

SCCS indicates in their Notes of guidance (SCCS, 2012) that consumers may use several cosmetic products containing the same preservative corresponding to a total calculated daily external exposure (= daily applied amount times the retention factor) of 17.4 g/day or 269 mg/kg bw/day.

9.3.1 Results – DMDM Hydantoin

DMDM Hydantoin has been observed in a number of product types in the survey of this project, but only in 13 of the total of 639 products investigated in the survey. Exposure calculations and risk assessment have been made for other effects besides allergies for the following product types: hair conditioners, hair repair, hair shampoos, hair styling products, hairsprays and cleaners (face). The results are given in Table 29 below.

DMDM Hydantoin Product type	SED (mg/kg bw/day) (refer to Table 20)	NOAEL (mg/kg bw/day) (refer to Table 28)	MoS
Hair conditioner	0.0004	220	550 000
Hair repair	0.004	220	55 000
Hair shampoo	0.001	220	220 000
Hairstyling products	0.003	220	73 333
Hairspray	0.003	220	73 333
Cleansers (face)	0.005	220	44 000
Sum selected everyday products	**0.01**	**220**	**2000**
Sum via all used products	**0.160**	**220**	**1375**

TABLE 29
RISK ASSESSMENT OF DMDM HYDANTOIN– CALCULATION OF MOS FOR OTHER EFFECTS BESIDES ALLERGIES. THE SELECTED PRODUCT TYPES (SUM VIA THE 14 SCCS SELECTED EVERYDAY PRODUCTS) ARE MARKED WITH GREEN BACKGROUND COLOUR.

As can be seen, the calculated MoS values are well above 100, both for the individual cosmetic product types, and also for the hypothetical worst case scenario that DMDM Hydantoin should be contained in *all* cosmetic products that might be used during a day (a calculated daily exposure of 17.4 g/day). Ie. DMDM Hydantoin is assessed to be safe for use in cosmetic products in the currently maximum permitted concentration of 0.6 % compared to other health effects besides allergies.

DMDM Hydantoin may release formaldehyde and the substance may cause contact allergy, which is also observed in several patch tests with humans (see Section 7.1). It has not been possible to establish a limit value for the sensitising effects based on the available data, and therefore a MoS calculation on this basis has not been possible.

9.3.2 Results – Imidazolidinyl urea

Imidazolidinyl urea has only been observed in a few products in the survey (5 in total), but in four different product types as facial masks, hair conditioners, mascaras and powder/blush. Exposure calculations and risk assessment have been made for other effects besides allergies for these types of cosmetic products. The results are presented in Table 30 below.

Imidazolidinyl urea Product type	SED (mg/kg bw/day) (refer to Table 21)	NOAEL (mg/kg bw/day) (refer to Table 28)	MoS
Facial masks	0.014	28	2000
Hair conditioner	0.004	28	7143
Mascara	0.003	28	11 200
Powder/blush	0.010	28	2800
Sum selected everyday products	**0.007**	28	**4000**
Sum via all used products	**1.596**	28	**17.5**

TABLE 30
RISK ASSESSMENT OF IMIDAZOLIDINYL UREA – CALCULATION OF MOS FOR OTHER EFFECTS BESIDES ALLERGIES. THE SELECTED PRODUCT TYPES (SUM VIA THE 14 SCCS SELECTED EVERYDAY PRODUCTS) ARE MARKED WITH GREEN BACKGROUND COLOUR.

As can be seen, the calculated MoS values are well above 100 when the individual cosmetics products are assessed. For the hypothetical worst case scenario that Imidazolidinyl urea should be contained in *all* cosmetic products that might be used during a day (a calculated daily exposure of 17 g/day), the calculated total MoS is, however, far below 100 (MoS value 17.5). It should be noted, however, that Imidazolidinyl urea has only been observed in 5 different products out of the 639 products investigated in the survey. It is therefore considered unlikely that *all* the 14 different cosmetic products, that may be used during a day, should contain the preservative Imidazolidinyl urea.

Although the MoS value is above 100 for the individual products, it does not take many cosmetic products per day before the use of multiple products simultaneously will result in an overall MoS below 100, as also indicated in the hypothetical worst case scenario. However, the calculations are based on 100 % skin absorption, as there are no data for dermal absorption of Imidazolidinyl urea. The actual skin absorption will probably be somewhat lower, which means a higher safety margin.

Imidazolidinyl urea may release formaldehyde and the substance may cause contact allergy, which is also observed in several patch tests with humans. It has not been possible to establish a limit value for the sensitising effects based on the available data, and therefore a MoS calculation on this basis has not been possible.

9.3.3 Results – Phenoxyethanol

9.3.3.1 Phenoxyethanol and risk assessment with a NOAEL of 164 mg/kg bw/day

Phenoxyethanol has been observed in a wide range of different types of cosmetics in the survey. Exposure calculations and risk assessment of selected types of cosmetic products have been made (as described in Table 16). The results are indicated in the tables below at concentrations measured by the analyses in this project and maximum permitted concentrations (see Table 31 to Table 36). The maximum permitted concentration of 1 % is used for the selected product types for which there have been *no* analyses of content concentration.

Phenoxyethanol Product type	SED (mg/kg bw/day) (refer to Table 22)	NOAEL (mg/kg bw/day) (refer to Table 28)	MoS
Facial creams	0.162	164	1012
Bodylotion	0.838	164	196
Bodylotion/ creams for "eczema skin"	0.493	164	332
Bodyscrub	0.0090	164	18 222
Deodorants (roll-on)	0.090	164	1822
Liquid hand soap*	0.027	164	607
Foot cream	0.115	164	1426
Foundation/BB cream	0.044	164	3727
Hand cream	0.105	164	1562
Hair conditioner*	0.005	164	32 800
Hair shampoo*	0.012	164	13 667
Hairstyling products*	0.046	164	3565
Intimate soap	0.004	164	43 201
Mascara*	0.003	164	49 200
Mouthwash	0.098	164	1673
Cleansers (face)	0.053	164	3075
Cleansing wipes	0.128	164	1281
Anti-wrinkle creams	0.1	164	1367
Foambath/bath gel*	0,022	164	7.455
Sunscreens/sun oils	0.258 (or 0.129)	164	635 (or 1271)
Wet wipes	0.459	164	357
Eye creams	0.009	164	17 948
Eye products*	0.0026	164	63 076
Sum selected everyday products	**1.508**	**164**	**109**

Phenoxyethanol Product type	SED (mg/kg bw/day) (refer to Table 22)	NOAEL (mg/kg bw/day) (refer to Table 28)	MoS
Sum selected everyday products + sunscreen	1.766 (or 1.637)	164	93 (or 100)

* The concentrationen has not been measured here. Therefore maximum permitted concentratin is used.

TABLE 31
RISK ASSESSMENT OF PHENOXYETHANOL – CALCULATION OF MOS FOR MEASURED CONCENTRATIONS (ANALYTICAL RESULTS). FOR THE SUNSCREENS, MOS WHEN USING THE RECOMMENDED AMOUNT OF 36 G/DAY AND IN BRACKET MOS WHEN USING 18 G/DAY ARE INDICATED. THE SELECTED PRODUCT TYPES (SUM VIA THE 14 SCCS SELECTED EVERYDAY PRODUCTS) ARE MARKED WITH GREEN BACKGROUND COLOUR.

As can be seen from the calculated MoS values for cosmetic products with the actually measured concentrations (identified by the chemical analyses in this project), all values for each type of products are above 100 for adults. It should be noted that for some of the selected products (with green background colour) the maximum permitted concentration of 1 % has been used for the calculation, as these product types were not analysed. These products are marked with * in the table above (Table 31). Thus, the individual products do not pose a risk with a skin absorption of 80 % and with the selection of a NOAEL of 164 mg/kg bw/day.

If all 14 selected cosmetic products are used in one day (product types marked with green background colour), the calculated MoS is 108.8. If sunscreen is used in the recommended amount of 36 g/day in addition to the 14 selected cosmetic products in one day (as SCCS indicates for being realistic in Notes of guidance (SCCS, 2012)), the MoS is less than 100, ie. 93 for the analysed products, including skin absorption of 80 % and with the selection of a NOAEL of 164 mg/kg bw/day.

Often less sunscreen is used in reality than the recommended 36 g/day. An amount of 18 g/day is recommended for use in risk assessments by SCCS (SCCS, 2012). With this amount included, MoS is above 100. The calculation is based on the actually measured concentrations. This means that there may be products with both higher and lower concentrations of Phenoxyethanol, as some products contained Phenoxyethanol in concentrations lower than the maximum permitted concentration of 1 %, for example 0.3 % (measured in mouthwash) or 0.4 % (measured in the hand cream).

Calculation of MoS from the maximum permitted amount of Phenoxyethanol in the products gives the following result (Table 32):

Phenoxyethanol Product type	SED (mg/kg bw/day) (refer to Table 23)	NOAEL (mg/kg bw/day) (refer to Table 28)	MoS
Sum selected everyday products	2.125	164	77
Sum selected everyday products + sunscreen	2.496 (or 2.312)	164	66 (or 71)

TABLE 32
RISK ASSESSMENT OF PHENOXYETHANOL – CALCULATION OF MOS FOR MAXIMUM PERMITTED CONCENTRATIONS. FOR THE SUNSCREENS, MOS WHEN USING THE RECOMMENDED AMOUNT OF 36 G/DAY AND IN

BRACKET MOS WHEN USING 18 G/DAY ARE INDICATED. THE SELECTED PRODUCT TYPES (SUM VIA THE 14 SCCS SELECTED EVERYDAY PRODUCTS) ARE MARKED WITH GREEN BACKGROUND COLOUR.

If all 14 selected cosmetic products are used in one day, and they all contain the maximum permitted concentration of Phenoxyethanol, the calculated MoS is 77, and is now below 100. If more than the 14 selected cosmetic products are used in one day, MoS is even lower, and with exposure to sunscreen in the recommended amount of 36 g/day, MoS ends up being down to 66 with a skin absorption of 80 % and with the selection of a NOAEL of 164 mg/kg bw/day. With the reduced amount of sunscreen per day, MoS will be 71.

That is, if a NOAEL = 164 mg/kg bw/day is used, and at the same time assuming a high skin absorption (80 %), the use of Phenoxyethanol is not considered to be safe when taking into account that several cosmetic products containing Phenoxyethanol may be used every day. The survey has shown that Phenoxyethanol is currently the most widely used preservative, and therefore 14 cosmetic products may theoretically be used on the same day, all containing Phenoxyethanol.

The calculation is made on the maximum permitted concentrations for all products, so the calculation is thus a worst case scenario with highest permitted concentration for all the used products.

9.3.3.2 Phenoxyethanol and risk assessment with a NOAEL of 697 mg/kg bw/day

If another NOAEL of 697 mg/kg bw/day based on a recent study is selected, MoS is more than 4 times higher, and there is no risk in daily use of all 14 selected products with the measured concentrations and with a dermal absorption of 80 % (Table 33 and Table 34).

Phenoxyethanol Product type	SED (mg/kg bw/day) (refer to Table 22)	NOAEL (mg/kg bw/day) (refer to Table 28)	MoS
Sum selected everyday products	1.508	697	462.2
Sum selected everyday products + sunscreen	1.766	697	394.6

TABLE 33
RISK ASSESSMENT OF PHENOXYETHANOL – CALCULATION OF MOS FOR ADULTS FOR MEASURED CONCENTRATIONS (ANALYTICAL RESULTS). FOR THE SUNSCREENS, MOS USING THE RECOMMENDED AMOUNT OF 36 G/DAY IS INDICATED.

Phenoxyethanol Produkttype	SED (mg/kg lgv/dag) (jf.tabel 23)	NOAEL (mg/kg lgv/dag) (jf. tabel 28)	MoS
Sum udvalgte hverdagsprodukter	2,125	697	328
Sum udvalgte hverdagsprodukter + solcreme	2,496	697	279

TABEL 34
RISK ASSESSMENT OF PHENOXYETHANOL – CALCULATION OF MOS FOR ADULTS FOR MAXIMUM PERMITTED CONCENTRATIONS. FOR THE SUNSCREENS, MOS USING THE RECOMMENDED AMOUNT OF 36 G/DAY IS INDICATED.

9.3.3.3 Phenoxyethanol and risk assessment with dermal absorption of 48 %

The skin absorption of Phenoxyethanol of 80 % used in the previous risk assessments also influences the result of the risk calculation. This absorption rate is based on few *in vitro* data. Other studies (*in vivo*) with few test subjects suggest that the dermal absorption may be lower. In *in vivo* studies with four volunteers, skin absorption of between 8.5 and 48 % was measured by application of 40 g of cream containing 1.2 % Phenoxyethanol (ANSM, 2012). The REACH dossier on Phenoxyethanol indicates a dermal absorption of 59.3 % ± 7.0 %. Therefore, a number of studies are showing a high absorption of Phenoxyethanol. The value used for skin absorption of 80 % for Phenoxyethanol is thus a worst case. It is obvious that a difference between the used 80 % and the 48 % as specified here gives a reduction in the exposure of about 40 % and thus a correspondingly higher margin of safety (MoS value). Therefore, a calculation of the MoS with a skin absorption of 48 % has been made. These MoS values are indicated in brackets in Table 35.

Phenoxyethanol	MoS at measured conc.	MoS at max conc.
Sum udvalgte hverdagsprodukter	109 (181)	77 (115)
Sum udvalgte hverdagsprodukter + solcreme	93 or 100 (154 or 167)	66 or 71 (107 or 115)

TABLE 35
RISK ASSESSMENTS OF PHENOXYETHANOL AT A NOAEL OF 164 MG/KG BW/DAY – CALCULATION OF MOS. THE VALUES IN BRACKETS INDICATE MOS VALUES BY USE OF A DERMAL ABSORPTION OF 48 % INSTEAD OF THE 80 % USED IN TABLES 31 AND 32. FOR THE SUNSCREENS, THE MOS BY USE OF THE RECOMMENDED AMOUNTS OF 36/DAY AND 18 G/DAY ARE INDICATED.

As the table shows, a lower dermal absorption of 48 % changes the conclusion for Phenoxyethanol at the the lowest NOAEL of 164 mg/kg bw/day, as the total MoS for use of several products in the same day then is above 100 by use of products including sunscreen and when calculating on the maximum permitted concentration of 1 %.

9.3.3.4 Phenoxyethanol and risk calculation of baby (diaper area)

The skin in the baby's diaper area can be particularly vulnerable, because it has a higher pH value and increased hydration than other skin areas. Based on the exposure data provided by SCCS on exposure of a baby's diaper area, the risk calculations for babies' exposure to wet wipes with Phenoxyethanol are indicated below (Table 36). The calculation for the diaper area of babies has been made on the actually measured concentrations in the wet wipes. This means that there may be products with a higher or lower concentration of Phenoxyethanol.

Phenoxyethanol Product type	SED Baby (mg/kg bw/day) (refer to Table 24)	NOAEL (mg/kg bw/day) (refer to Table 28)	MoS Baby
Wet wipes	0.89	164	184

TABLE 36
RISK ASSESSMENT OF PHENOXYETHANOL – CALCULATION OF MOS BABY FOR MEASURED CONCENTRATIONS (ANALYTICAL RESULTS). THE SELECTED PRODUCT TYPES MENTIONED EARLIER ARE MARKED WITH GREEN BACKGROUND COLOUR.

The calculations show that there is no risk at the concentrations measured in the selected products at a NOAEL of 164 mg/kg bw/day and a skin absorption of 100 %. The skin absorption is set to 100 % as skin absorption in that skin area may be high.

In the following Table 37, Mos is calculated from the maximum permitted concentration of Phenoxyethanol in wet wipes.

Phenoxyethanol Product type	SED Baby (mg/kg bw/day) (refer to Table 25)	NOAEL (mg/kg bw/day) (refer to Table 28)	MoS Baby
Wet wipes	1.038	164	158

TABLE 37
RISK ASSESSMENT OF PHENOXYETHANOL – CALCULATON OF MOS FOR BABY FOR MAXIMUM PERMITTED CONCENTRATIONS (USED DERMAL ABSORPTION: 100 %)

No risk is seen when using wet wipes containing the maximum permitted concentration of Phenoxyethanol and with a skin absorption of 100 % and a NOAEL of 164 mg/kg bw/day.

9.3.4 Results – Thimerosal

Thimerosal was not found in any of the surveyed products, but is allowed in eye products in the EU.

Therefore, exposure calculations and risk assessment have been made exclusively on the use of Thimerosal in eye products. The results are presented in Table 38 below.

Thimerosal Product type	SED Adults (mg/kg bw/day) (refer to Table 26)	NOAEL (mg/kg bw/day) (refer to Table 28)	MoS Adults
Eye products	0.00023	0.04	174

TABLE 38
RISK ASSESSMENT OF THIMEROSAL FOR ADULTS USED IN EYE PRODUCTS – CALCULATION OF MOS

As can be seen, the calculated MoS for eye products is above 100, which is the recommended minimum MoS value to conclude that a substance is safe to use. This means that Thimerosal based on this calculation is estimated safe to use in eye products in the currently maximum permitted concentration of 0.007 % in the form of mercury (according to Annex V of the Cosmetics Regulation). It is assessed that allergies are also a critical effect of the substance, but a limit value for this effect was not possible to determine based on the available data.

The hazard assessment of Thimerosal showed a lack of data on the health effects of the substance, and a NOAEL for calculating the MoS is therefore not available for the substance. The MoS calculation for other effects besides allergies is therefore based on a tolerable weekly exposure to mercury. This tolerable dose is determined by reference to the use of pharmaceuticals, where the limits are sometimes more flexible than by use of other products, because side effects of pharmaceuticals are sometimes accepted. In this case, the tolerable weekly exposure, however, is determined using Thimerosal in vaccines, where massive side effects are unwanted. It is therefore considered acceptable to use this limit value to calculate a MoS for Thimerosal.

9.3.5 Results – Zinc pyrithione

Zinc pyrithione (ZPT) was not observed in any products in the survey, but 1 of the 8 manufacturers of cosmetic products contacted in the survey indicated that they use the preservative in dandruff shampoo. Therefore, exposure calculations and risk assessment are made exclusively on the use of ZPT in dandruff shampoo. The result is given in Table 39 below and shows safe use of ZPT in a concentration of up to 2 % in dandruff shampoo.

Zink pyrithione Product type	SED Adults (mg/kg bw/day) (refer to Table 27)	NOAEL (mg/kg bw/day) (refer to Table 28)	MoS Adults (no unit)
Dandruff shampoo	0.0015	0.167	111

TABLE 39
RISK ASSESSMENT OF ZPT FOR ADULTS USED IN DANDRUFF SHAMPOO – CALCULATION OF MOS

Based on the calculated MoS of 111 for ZPT by use in dandruff shampoo, it is concluded that the substance is safe to use in the currently maximum permitted concentration of 1 % (in rinse-off products).

9.4 Discussion

Generally, the underlying data for the selected preservatives are limited. Many of the available data are older (back from the 80s – 90s), and literature studies showed that only very few new data have been generated on the substances. It was impossible for the project team to access documents from DMDM Hydantoin's re-evaluation as a biocidal active substance.

9.4.1 Other effects besides allergies

The general picture is that no individual cosmetic product in which the five investigated preservatives DMDM hydantoin, Imidazolidinyl urea, Zinc pyrithione, Thimerosal and Phenoxyethanol are used, in itself constitutes a risk for other health effects besides allergies, as all calculated MoS values are above 100.

Regarding DMDM Hydantoin, this substance is assessed to be safe to use in cosmetic products in the currently maximum permitted concentration of 0.6 % compared to other health effects besides allergies.

For Imidazolidinyl urea and the hypothetical worst case scenario that all cosmetic products used by an adult in one day contain Imidazolidinyl urea, the calculated overall MoS is far below 100 (MoS value is 17.5). Imidazolidinyl urea was observed only in 5 different products of the 639 products investigated in the survey. As Imidazolidinyl urea is relatively rarely used, the substance is expected not to pose a risk when used in the currently maximum permitted concentration of 0.6 % compared to other health effects besides allergies. It is therefore considered unlikely that adults will use 14 different cosmetic products in one day, *all* containing the preservative Imidazolidinyl urea. It should however be noted that although the MoS value is above 100 for the individual products, it does not take many cosmetic products per day before the use of these would imply a MoS below 100, which the worst case scenario indicates.

Zinc pyrithione and Thimerosal are only allowed in a few product types, and therefore a risk calculation using several products on the same day has not been made for these two substances. The risk calculation for Zinc pyrithione shows safe use in a concentration of up to 2 % in dandruff shampoo.

The limited use of Thimerosal in cosmetic products is considered to be safe in the maximum permitted concentration of 0.014 % (0.007 % for mercury) considering other health effects besides allergies; however, Thimerosal may also be sensitising.

A variety of risk calculations have been made for Phenoxyethanol. Below the different conditions and assumptions are described and discussed:

- No cosmetic product in itself constitutes a risk as all calculated MoS values are above 100, calculated with a NOAEL of 164 mg/kg bw/day and a skin absorption of 80 %.
- By exposure of baby's diaper area to wet wipes, calculations of MoS showed that the products posed no risk at a skin absorption of 100 % and a NOAEL of 164 mg/kg bw/day.
- When the daily exposure is added for the 14 daily used cosmetic products, it gives a MoS of above 100 (109), calculated from the measured concentrations of Phenoxyethanol in this study. If sunscreen is used simultaneously in the recommended amount of 36 g/day, it gives a MoS below 100 (93), but the more realistic amount of sunscreen of 18 g/day gives a MoS of 100 from calculations with measured concentrations in the products, NOAEL at 164 mg/kg bw/day and skin absorption of 80 %. Thus, in a worst case scenario with the recommended quantity of 36 g/day, there is a very small margin of safety for health effects.
- There is also a calculated risk in daily use of the 14 everyday products from the maximum permitted concentration of Phenoxyethanol, NOAEL of 164 mg/kg bw/day and skin absorption of 80 %, both with and without the use of sunscreen (MoS 66 and 77, respectively).
- As the applied skin absorption for Phenoxyethanol affects the result of the risk calculation, it is assessed whether the applied skin absorption of 80 % is realistic for skin absorption in humans. The used 80 % skin absorption of Phenoxyethanol was derived from *in vitro* studies with the substance, investigating the size of the amount of substance penetrating a skin membrane set up in a diffusion cell (test vessel for the measurement of skin permeability). In studies on a few individuals, a somewhat lower absorption was seen (between 8.5 and 48%), but due to the very low number of test subjects it may be unsafe to use a significantly lower skin absorption in the risk calculations, although data may suggest that skin absorption of Phenoxyethanol in humans is somewhat lower than seen in the available *in vitro* studies. By using 48 % instead of the applied worst case of 80 %, there will be a reduction in the exposure of just under 40 % and thus a correspondingly higher margin of safety (MoS value). When using 48 % skin absorption and a NOAEL of 164 mg/kg bw/day, the total MoS for use of several products on the same day is above 100 when using products including sunscreen in the recommended amount of 36 g/day and calculating on the maximum permitted concentration of 1 %. When calculating with the lower skin absorption, the use may therefore be considered safe.
- The applied NOAEL used in the worst case risk calculations for Phenoxyethanol is derived from a study from 1996. Different parties have argued in favour of using a NOAEL for Phenoxyethanol of 697 mg/kg bw/day, which was found in a recent study, or to use NOAELs from other recent studies in the risk assessment. Using this higher NOAEL gives a MoS for all exposure scenarios above 100, and thus there is no risk in daily use of 14 everyday products.

Thus, it can be seen that skin absorption and NOAEL can change the risk calculations significantly. The choice of NOAEL for health effects of Phenoxyethanol must be made from the quality of data submitted for the relevant studies, ie. the most reliable study.

It has not been possible to make a robust risk assessment of the data available in this project. Based on of a mandate from 22 April 2014 prepared by the Commission, SCCS is currently assessing the safe use of Phenoxyethanol in cosmetics. In the mandate, SCCS is asked to assess whether a concentration of 1 % is safe for all age groups (SCCS, 2013b). In connection with this assessment of Phenoxyethanol, the trade association Cosmetics Europe has submitted a safety dossier to defend the use of Phenoxyethanol in up to 1 % in cosmetic products.

9.4.2 Contact allergy

Regardarding contact allergy to preservatives in general, this is well described in the literature, and is one of the major causes of contact allergy to cosmetic products. Risk assessment for skin sensitisation was traditionally carried out from a hazard assessment with the simple purpose to classify and label chemicals, which are either sensitising or non-sensitising, ie. there has been nothing in between (RIVM, 2008).

Sensitisation usually refers to an induction of an immunological (hypersensitive) state followed by exposure to a chemical, so that subsequent exposure to the chemical (or cross-reactive chemicals) will cause an allergic reaction (elicitation). Both induction and elicitation exhibit a dose-response relationship and have threshold values. The threshold value for induction can be defined as the highest exposure value not to cause sensitisation. The threshold value for elicitation can be defined as the highest exposure value that does not elicitate a reaction in an already sensitised individual (ECHA R.8, 2008).

Limit values are set in the chemical legislation for a number of allergenic substances contained in products, but these are not based on a quantitative risk assessment. In order to do so, it must be possible to determine the dose that can induce an allergic reaction. Knowledge of this critical dose is crucial to be able to set safe limit values for sensitisers in a particular product (RIVM, 2008).

For several of the selected preservatives in this project, the critical effect is assessed to be allergy. Unfortunately, the available data are not sufficient to determine a threshold value and thus calculate a risk using the permitted concentration of the substance, nor has it been possible in this project to obtain precise numbers on the actual exposure for released formaldehyde from the formaldehyde releasing preservatives. Generally, in patch tests with humans there is an incidence of allergy up to 2 % to formaldehyde releasers (de Groot et al. 2010a), and for Thimerosal an incidence of up to 4.7 % (Allergy Research Centre, 2014).

Lundov et al (2010) found that patients who are allergic to a formaldehyde releaser, often have contact allergy to formaldehyde. Other combinations were also commonly seen. In patients who reacted to more than two formaldehyde releasers, almost all reacted to formaldehyde as well. Furthermore, it was found that contact allergy to one formaldehyde releaser almost always goes with contact allergy to another formaldehyde releaser. Seventyfive percent of formaldehyde allergic patients were using a product containing formaldehyde. It is not clear whether products preserved with formaldehyde releasers may contain enough free formaldehyde to pose a risk to individuals with contact allergy to formaldehyde. There are only fragmented data on the amount of free formaldehyde in cosmetics preserved with formaldehyde. However, all formaldehyde releasers (with the exception of 2-bromo-2-nitropropane-1,3-diol, for which no sufficient data exist) can under the right circumstances with respect to concentration and product composition release > 200 ppm formaldehyde, which may result in allergic contact dermatitis. Whether this is actually the case in a particular product can not be determined from the list of ingredients. Therefore, patients who are allergic to Formaldehyde are recommended to avoid leave-on cosmetics preserved with Quaternium-15, Diazolidinyl urea, DMDM Hydantoin or Imidazolidinyl urea, in the realisation that many probably would still tolerate the products.

In Australia, a total of 6845 patients were patch tested in the period from 1993 to 2006, and during this period the five most common preservative sensitisers were Formaldehyde (4.6 %), Euxyl K400 (containing Methyldibromo glutaronitrile and Phenoxyethanol) (3.3 %), Quaternium-15 (2.9 %), Diazolidinyl urea (2.4 %) and Methylchloroisothiazolinone/Methylisothiazolinone (2.3 %). These were followed by DMDM Hydantoin (2.1 %), and Imidazolidinyl urea (1.9 %) (Chow et al., 2013). The use of preservatives in Australia may be different than in the EU, but the figures only show the sensitising potential of several preservatives. In Europe, frequencies of sensitisation have been observed for: 2-Bromo-2-nitropropane-1,3-diol (0.4 to 1.2 %), Diazolidinyl urea (0.5-1.4 %), Imidazolidinyl urea (0.3 to 1.4 %) and Quaternium-15 (0.6 -1.9 %) (de Groot et al. 2010a).

Based on results from the patch tests conducted in humans, it can be concluded that there is a serious risk of allergy from preservatives used in cosmetics. The phased out use of parabens has led to use of the other, from an allergy point of view, more worrying preservatives. Especially the use of formaldehyde releasers seems to cause more cases of allergies and are therefore more risky, and the release of formaldehyde from these substances and derived carcinogenic and mutagenic considerations should be included in the overall assessment of the substances. An approved analytical method for measurement of released formaldehyde has not yet been developed, and therefore it has not been possible in this study to analyse on the actual levels of formaldehyde released from the selected formaldehyde releasing preservatives. The classification of Formaldehyde as carcinogen 1B (effective from 26 September 2015) may eventually lead to a possible restriction of formaldehyde releasers in cosmetic products, and is expected in the near future to trigger a reassessment of the formaldehyde releasing preservatives.

10. Conclusion

In the present study there has been a selection of 639 cosmetic products, and an investigation of the preservatives used in these products in Denmark today. In the survey, a total of 53 preservatives was identified used in cosmetic products on the Danish market. The survey has shown that Phenoxyethanol is the most widely used preservative today, so it is not unrealistic to use several cosmetic products daily, all of which contain Phenoxyethanol.

Of the many permitted preservatives, the vast majority is assessed to be safe for use in cosmetic products. Some of the permitted preservatives are already subject to various studies/assessments in the EU for their known health effects, and even though they are interesting for the purpose of this project, they were not considered further in the project (eg. MI, Formaldehyde). Five preservatives were selected for further analyses based on environmental and health screenings: DMDM Hydantoin, Imidazolidinyl urea, Zinc pyrithione alcohol, Thimerosal and Phenoxyethanol.

It can be concluded that there is an allergy risk by using cosmetic products containing 3 of the 5 preservatives further investigated in this project: DMDM Hydantoin, Imidazolidinyl urea and Thimerosal. Contact allergy to preservatives is well described in the literature, and is one of the major causes of contact allergy to cosmetic products. Unfortunately, the available data are not sufficient to determine a threshold value and calculate a risk by using the permitted concentrations of the substances. Especially the use of formaldehyde releasing preservatives is assessed to be risky in terms of allergies, and the release of Formaldehyde from these substances and derived CMR considerations should be included in an overall assessment of the substances. It has not been possible in this project to measure the amount of Formaldehyde released from the cosmetic products. Generally, patch tests in humans show an incidence of allergy to formaldehyde releasing substances at levels of up to 2 %, and for Thimerosal an allergy incidence of up to 4.7 %, which seems high considering that the substance is only permitted in eye cosmetics. Other uses of the substance than in cosmetics may also occur (vaccines), and allergy incidence of this use can not be excluded.

Disregarding the allergy risk of preservatives, the risk assessment of the five selected preservatives shows that the use of these is safe when the assessment is made on a *single* product containing the maximum permitted amount of the preservative. The risk assessment is based on all calculated MoS values being above 100, which is generally the lowest MoS value a substance may have in order to be considered acceptable for safe use in a product.

A risk assessment was carried out for the daily exposure to the sum of the 14 cosmetic products considered realistic to use per day, both with and without the use of sunscreen. If the risk of Phenoxyethanol is calculated as worst-case from the maximum permitted concentration, a high skin permeability of 80 % and a NOAEL of 164 mg/kg bw/day, the calculated MoS value is below 100. If the risk is calculated from the measured concentrations of the analyses of the products, MoS stays above 100, and there is no risk.

Skin absorption of Phenoxyethanol has implications for the result of the risk calculation. The used skin absorption of 80 % originates from *in vitro* studies with the substance. A study in few humans shows an absorption which is somewhat lower (between 8.5 and 48 %). Using 48 % skin absorption and a NOAEL of 164 mg/kg bw/day show a MoS for use of several products and sunscreen on the same day above 100. With the calculation with the lower skin absorption of 48 %, the use may therefore be considered safe.

The NOAEL used in worst-case risk calculations for Phenoxyethanol originates from a study from 1996. Various parties have argued for the use of a NOAEL for Phenoxyethanol of 697 mg/kg bw/day, which was found in a recent study, or to use NOAELs from other recent studies in the risk assessment. Using this higher NOAEL, MoS for all exposure scenarios is above 100, and thus there is no risk in a daily use of 14 everyday products and sunscreen.

The values for skin absorption and NOAEL thus can change the risk calculations significantly. The selection of NOAEL for health effects of Phenoxyethanol should be made based on the quality of the data presented in the studies in question, ie. the most reliable of the studies. It has not been possible to make a robust risk assessment with the available data in this project. Based on a mandate from 22 April 2014 prepared by the Commission, SCCS is currently assessing the safe use of Phenoxyethanol in cosmetics. The mandate asks SCCS to assess whether a concentration of 1 % is safe for all age groups (SCCS, 2013b). In connection with the assessment of Phenoxyethanol, the trade association Cosmetics Europe has submitted a safety dossier to defend the use of Phenoxyethanol in up to 1 % in cosmetic products.

Overall, this study shows that most preservatives are safe for use in cosmetic products in the permitted concentrations - both by exposure to a single product or by daily use of several products containing the same preservative. However, there is a risk of induction of allergy by use of some of the permitted preservatives. The study has not been able to substantiate this allergy risk further due to lack of data on the individual substances.

Most formaldehyde releasers release Formaldehyde under the right circumstances, which may result in allergic contact dermatitis. Therefore, persons who are allergic to Formaldehyde are recommended to avoid leave-on cosmetics preserved with the formaldehyde releasers Quaternium-15, Diazolidinyl urea, DMDM Hydantoin or Imidazolidinyl urea, in the realisation that many probably would still tolerate the products.

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Appendix 1: List of preservatives permitted in cosmetic products (Annex V of the Cosmetics Regulation)

This table, which is an extract from Annex V of the Cosmetics Regulation, indicates chemical name, INCI name, CAS no., maximum permitted concentration, substance status relative to the Biocides Regulation, whether it is registered under REACH and its classificaton (harmonised and notified).

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
1	Benzoic acid and its sodium salt	SODIUM BENZOATE	532-32-1			Yes, Annex 1 1451/2007 Nej, Commission Decision 2008/809/EC phased out 25/10/2009 PT1, PT2, PT6 Nej, Commission Decision 2010/675/EU phased out 01/11/2011 PT11, PT20	Yes	No	Not Classified (Eye Irrit. 2 H319)
1	Benzoic acid and its sodium salt	BENZOIC ACID; SODIUM BENZOATE	65-85-0 532-32-1	a) Rinse-off products, except oral care products b) Oral care products c) Leave-on products	a) 2.5% (acid) b) 1.7% (acid) c) 0.5% (acid)	Yes, Annex 1 1451/2007			
1	Benzoic acid and its sodium salt	BENZOIC ACID	65-85-0			Yes, Annex 1 1451/2007 No, Commission Decision 2008/809/EC phased out 25/10/2009 PT1, PT2, PT6 No, Commission Decision 2010/72/EU phased out 09/02/2011 PT11 No, Commission Decision 2010/675/EU phased out 01/11/2011 PT20	Yes	No	Acute Tox. 4 H302 Skin Irrit. 2 H315 Eye Irrit. 2 H319
2	Propionic acid and its salts	PROPIONIC ACID	79-09-4			Yes, Annex 1 1451/2007	Yes	Skin Corr. 1B H314	
2	Propionic acid and its salts	PROPIONIC ACID / AMMONIUM PROPIONATE / CALCIUM PROPIONATE / MAGNESIUM PROPIONATE / POTASSIUM PROPIONATE / SODIUM	79-09-4 17496-08-1 4075-81-4 557-27-7 327-62-8 137-40-6		2% (acid)				

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
		PROPIONATE							
2	Propionic acid and its salts	AMMONIUM PROPIONATE	17496-08-1			No, Annex 1 1451/2007	No	No	Skin Irrit. 2 H315 Eye Irrit. 2 H319 STOT SE 3 H335
2	Propionic acid and its salts	CALCIUM PROPIONATE (Calcium Dipropionate)	4075-81-4			No, Annex 1 1451/2007	Yes	No	Not Classified
2	Propionic acid and its salts	MAGNESIUM PROPIONATE (Magnesium dipropionate)	557-27-7			No, Annex 1 1451/2007	No	No	Not Classified
2	Propionic acid and its salts	POTASSIUM PROPIONATE	327-62-8			No, Annex 1 1451/2007	No	No	Not Classified
2	Propionic acid and its salts	SODIUM PROPIONATE	137-40-6			Yes, Annex 1 1451/2007	No	No	Not Classified
3	Salicylic acid (1) and its salts	SALICYLIC ACID	69-72-7			Yes, Annex 1 1451/2007 Yes, but phased out 01/02/2014, no descision reference PT1	Yes	No	Acute Tox. 4 H302 Acute Tox. 4 H312 Eye Irrit. 2 H319
3	Salicylic acid (1) and its salts	SODIUM SALICYLATE	54-21-7			Yes, Annex 1 1451/2007	Yes	No	Acute Tox. 4 H302 Eye Irrit. 2 H319
3	Salicylic acid (1) and its salts	SALICYLIC ACID / CALCIUM SALICYLATE / MAGNESIUM SALICYLATE / MEA-SALICYLATE / SODIUM SALICYLATE / POTASSIUM	69-72-7 824-35-1 18917-89-0 59866-70-5 54-21-7 578-36-9 2174-16-5		0.5% (acid)				

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
		SALICYLATE / TEA-SALICYLATE							
3	Salicylic acid (1) and its salts	CALCIUM SALICYLATE (Calcium disalicylate)	824-35-1			No, Annex 1 1451/2007	No	No	Not Classified
3	Salicylic acid (1) and its salts	MAGNESIUM SALICYLATE (Magnesium disalicylate)	18917-89-0			No, Annex 1 1451/2007	No	No	Not Classified
3	Salicylic acid (1) and its salts	MEA-SALICYLATE (Salicylic acid, compound with 2-aminoethanol (1:1))	59866-70-5			No, Annex 1 1451/2007	No	No	Not Classified
3	Salicylic acid (1) and its salts	POTASSIUM SALICYLATE	578-36-9			No, Annex 1 1451/2007	No	No	Acute Tox. 4 H302 Eye Dam. 1 H318
3	Salicylic acid (1) and its salts	TEA-SALICYLATE (Salicylic acid, compound with 2,2',2''-nitrilotriethanol (1:1))	578-36-9			No, Annex 1 1451/2007	No	No	Acute Tox. 4 H302 Skin Irrit. 2 H315 Eye Irrit. 2 H319 STOT SE 3 H335
4	Hexa-2,4-dienoic acid and its salts	SORBIC ACID (Hexa-2,4-dienoic acid)	110-44-1			Yes, Annex 1 1451/2007 No, Commission Decision 2008/809/EC phased out 25/10/2009 PT1, PT2, PT3, PT4, PT5 No, Commission Decision 2010/72/EU phased out 09/02/2011 PT7, PT9, PT10 No, Commission Decision 2008/681/EC phased out 21/08/2009 PT8	Yes	No	Skin Irrit. 2 H315 Eye Irrit. 2 H319
4	Hexa-2,4-dienoic acid and its salts	SODIUM SORBATE (Sodium (E,E)-hexa-	7757-81-5			No, Annex 1 1451/2007	No	No	Not Classified

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
		2,4-dienoate)							
4	Hexa-2,4-dienoic acid and its salts	POTASSIUM SORBATE (Potassium (E,E)-hexa-2,4-dienoate)	24634-61-5			Yes, Annex 1 1451/2007 No, Commission Decision 2008/809/EC phased out 25/10/2009 PT1, PT2, PT3, PT4, PT5 No, Commission Decision 2010/72/EU phased out 09/02/2011 PT7, PT9, PT10	Yes	No	Skin Irrit. 2 H315 Eye Irrit. 2 H319 STOT SE 3 H335
4	Hexa-2,4-dienoic acid and its salts	SORBIC ACID / CALCIUM SORBATE / SODIUM SORBATE / POTASSIUM SORBATE	110-44-1 7492-55-9 7757-81-5 24634-61-5		0.6% (acid)				
4	Hexa-2,4-dienoic acid and its salts	CALCIUM SORBATE (Calcium dihexa-2,4-dienoate)	7492-55-9			Yes, Annex 1 1451/2007 No, Commission Decision 2008/809/EC phased out 25/10/2009 PT1, PT3, PT6 No, Commission Decision 2010/72/EU phased out 09/02/2011 PT7, PT9, PT20 No, Commission Regulation (EC) 1048/2005 phased out 01/09/2006 PT8	No	No	Not Classified (Eye Irrit. 2, H319)
5	Formaldehyde, paraformaldehyde (3)	FORMALDEHYDE	50-00-0			Yes, Annex 1 1451/2007 No, Commission Decision 2011/391/EU phased out 01/07/2012 PT1, PT5, , PT9, PT23 No, Commission Decision 2010/675/EU phased out 01/11/2011 PT4, PT6 No, Commission Decision 2008/681/EC phased out 21/08/2009 PT11, PT12, PT13 No, Commission Regulation (EC) 1849/2006 phased out 03/01/2008 PT18, PT21	Yes	Acute Tox. 3 * H301 Acute Tox. 3 * H311 Skin Corr. 1B H314 Skin Sens. 1 H317 Acute Tox. 3 * H331 Carc. 2 H351	

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
5	Formaldehyde, paraformaldehyde (3)	FORMALDEHYDE / PARAFORMALDEHYDE	50-00-0 30525-89-4	a) Oral products b) Other products	a) 0.1% (free formaldehyde) b) 0.2% (free formaldehyde)				
5	Formaldehyde, paraformaldehyde (3)	PARAFORMALDEHYDE	30525-89-4			Yes, Annex 1 1451/2007	No	No	Flam. Sol. 2 H228 Acute Tox. 4 H302 Skin Irrit. 2 H315 Skin Sens. 1 H317 Eye Dam. 1 H318 Acute Tox. 4 H332 Resp. Sens. 1 H334
6	*Moved or deleted*								
7	Biphenyl-2-ol, and its salts	O-PHENYLPHENOL / MEA O-PHENYLPHENATE /POTASSIUM O-PHENYLPHENATE / SODIUM O-PHENYLPHENATE	90-43-7 84145-04-0 13707-65-8 132-27-4		0.2% (as the phenol)				
7	Biphenyl-2-ol, and its salts	O-PHENYLPHENOL (Biphenyl-2-ol / 2-phenylphenol (ISO) / 2-hydroxybiphenyl)	90-43-7			Yes, Annex 1 1451/2007	Yes	Skin Irrit. 2 H315 Eye Irrit. 2 H319 STOT SE 3 H335 Aquatic Acute 1 H400	
7	Biphenyl-2-ol, and its salts	MEA O-PHENYLPHENATE ([1,1'-biphenyl]-2-ol, compound with 2-aminoethanol (1:1))	84145-04-0			No, Annex 1 1451/2007	No	No	Not Classified
7	Biphenyl-2-ol, and its salts	POTASSIUM O-PHENYLPHENATE (Potassium 2-	13707-65-8			Yes, Annex 1 1451/2007	No	No	Acute Tox. 4 H302 Skin Corr. 1B H314

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
		biphenylate)							
7	Biphenyl-2-ol, and its salts	SODIUM O-PHENYLPHENATE (Sodium 2-biphenylate / 2-phenylphenol, sodium salt)	132-27-4			Yes, Annex 1 1451/2007	No	Acute Tox. 4 * H302 Skin Irrit. 2 H315 Eye Dam. 1 H318 STOT SE 3 H335 Aquatic Acute 1 H400	
8	Pyrithione zinc (4)	ZINC PYRITHIONE	13463-41-7	a) Hair products b) Other products	a) 1.0% b) 0.5%	Yes, Annex 1 1451/2007 No, Commission Decision 2008/809/EC phased out 25/10/2009 PT13	Yes	No	Acute Tox. 3 H301 Eye Dam. 1 H318 Acute Tox. 4 H332 Aquatic Acute 1 H400
9	Inorganic sulphites and hydrogensulphites (5)	SODIUM SULFITE (Sodium sulphite)	7757-83-7			Yes, Annex 1 1451/2007 No, Commission Decision 2008/809/EC phased out 25/10/2009 PT1, PT2, PT4, PT5, PT6, PT13 No, Commission Decision 2010/72/EU phased out 09/02/2011 PT9, PT11, PT12, PT20, PT22 No, Commission Regulation (EC) 1849/2006 phased out 03/01/2008 PT21	Yes	No	Skin Corr. 1B H314
9	Inorganic sulphites and hydrogensulphites (5)	SODIUM METABISULFITE (Disodium disulphite / Sodium metabisulphite)	7681-57-4			Yes, Annex 1 1451/2007 Nej, Commission Decision 2008/809/EC phased out 25/10/2009 PT1, PT2, PT4, PT5, PT6, PT13 No, Commission Decision 2010/72/EU phased out 09/02/2011 PT9, PT11, PT12, PT20, PT22 No, Commission Regulation (EC)	Yes	Acute Tox. 4 * H302 Eye Dam. 1 H318	

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
						1849/2006 phased out 03/01/2008 PT21			
9	Inorganic sulphites and hydrogensulphites (5)	SODIUM BISULFITE (Sodium hydrogensulfite)	7631-90-5			Yes, Annex 1 1451/2007 No, Commission Decision 2008/809/EC phased out 25/10/2009 PT1, PT2, PT4, PT5, PT6, PT13 No, Commission Decision 2010/72/EU phased out 09/02/2011 PT9, PT11, PT12, PT20, PT22 No, Commission Regulation (EC) 1849/2006 phased out 03/01/2008 PT21	Yes	Acute Tox. 4 * H302	
9	Inorganic sulphites and hydrogensulphites (5)	SODIUM SULFITE / AMMONIUM BISULFITE / AMMONIUM SULFITE / POTASSIUM SULFITE / POTASSIUM HYDROGEN SULFITE / SODIUM BISULFITE / SODIUM METABISULFITE / POTASSIUM METABISULFITE	7757-83-7 10192-30-0 10196-04-0 10117-38-1 7773-03-7 7631-90-5 7681-57-4 16731-55-8		0.2% (as free SO2)				
9	Inorganic sulphites and hydrogensulphites (5)	AMMONIUM BISULFITE (Ammonium hydrogensulphite)	10192-30-0			No, Annex 1 1451/2007	Yes	No	Eye Irrit. 2 H319
9	Inorganic sulphites and hydrogensulphites	AMMONIUM SULFITE (Ammonium	10196-04-0			No, Annex 1 1451/2007	No	No	Skin Corr. 1B H314

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
	(5)	sulphite)							
9	Inorganic sulphites and hydrogensulphites (5)	POTASSIUM SULFITE (Potassium sulphite)	10117-38-1			Yes, Annex 1 1451/2007 No, Commission Decision 2008/809/EC phased out 25/10/2009 PT1, PT2, PT4, PT5, PT6, PT13 No, Commission Decision 2010/72/EU phased out 09/02/2011 PT9, PT11, PT12, PT20, PT22 No, Commission Regulation (EC) 1849/2006 phased out 03/01/2008 PT21	Yes	No	Not Classified
9	Inorganic sulphites and hydrogensulphites (5)	POTASSIUM HYDROGEN SULFITE (Potassium hydrogen sulphite)	7773-03-7			No, Annex 1 1451/2007	No	No	Eye Irrit. 2 H319 STOT SE 3 H335
9	Inorganic sulphites and hydrogensulphites (5)	POTASSIUM METABISULFITE (Dipotassium disulphite)	16731-55-8			Yes, Annex 1 1451/2007 No, Commission Decision 2008/809/EC phased out 25/10/2009 PT1, PT2, PT4, PT5, PT6, PT13 No, Commission Decision 2010/72/EU phased out 09/02/2011 PT9, PT11, PT12, PT20, PT22 No, Commission Regulation (EC) 1849/2006 phased out 03/01/2008 PT21	Yes	No	Skin Irrit. 2 H315 STOT SE 3 H335
10	*Moved or deleted*								
11	Chlorobutanol	CHLOROBUTANOL	57-15-8		0.5%	No, Annex 1 1451/2007	No	No	Acute Tox. 4 H302

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
12	4-hydroxybenzoic acid and its salts and esters	METHYLPARABEN	99-76-3			Yes, Annex 1 1451/2007	Yes	No	Not Classified (Skin Irrit. 2 H315 Eye Irrit. 2 H319 STOT SE 3 H335)
12	4-hydroxybenzoic acid and its salts and esters	PROPYLPARABEN	94-13-3			Yes, Annex 1 1451/2007	Yes	No	Skin Irrit. 2 H315 Eye Irrit. 2 H319 STOT SE 3 H335
12	4-hydroxybenzoic acid and its salts and esters	BUTYLPARABEN	94-26-8			Yes, Annex 1 1451/2007	No	No	Skin Irrit. 2 H315 Eye Irrit. 2 H319 STOT SE 3 H335
12	4-hydroxybenzoic acid and its salts and esters	ETHYLPARABEN	120-47-8			Yes, Annex 1 1451/2007	Yes	No	Not Classified (Asp. Tox. 1 H304 Skin Irrit. 2 H315 Skin Sens. 1 H317 Eye Irrit. 2 H319)
12	4-hydroxybenzoic acid and its salts and esters	ISOBUTYLPARABEN	4247-02-3			Yes, Annex 1 1451/2007	No	No	Not Classified
12	4-hydroxybenzoic acid and its salts and esters	ISOPROPYLPARABEN	4191-73-5			No, Annex 1 1451/2007	No	No	Eye Irrit. 2 H319
12	4-hydroxybenzoic acid and its salts and esters	SODIUM METHYLPARABEN	5026-62-0			Yes, Annex 1 1451/2007	Yes	No	Acute Tox. 4 H302 Eye Dam. 1 H318
12	4-hydroxybenzoic acid and its salts and esters	SODIUM PROPYLPARABEN	35285-69-9			Ja, Annex 1 1451/2007	No	No	Eye Dam. 1 H318

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
12	4-hydroxybenzoic acid and its salts and esters	4-HYDROXYBENZOIC ACID / BUTYLPARABEN / CALCIUM PARABEN / ETHYLPARABEN/ ISOBUTYLPARABEN / ISOPROPYLPARABEN / METHYLPARABEN / PHENYLPARABEN / POTASSIUM BUTYLPARABEN / POTASSIUM ETHYLPARABEN/ POTASSIUM METHYLPARABEN / POTASSIUM PARABEN / POTASSIUM PROPYLPARABEN / PROPYLPARABEN / SODIUM BUTYLPARABEN / SODIUM ETHYLPARABEN / SODIUM ISOBUTYLPARABEN / SODIUM ISOPROPYLPARABEN / SODIUM METHYLPARABEN / SODIUM PARABEN /	99-96-7 99-76-3 94-26-8 36457-19-9 16782-08-4 94-13-3 4247-02-3 5026-62-0 35285-68-8 36457-20-0 84930-15-4 - 120-47-8 114-63-6 4191-73-5 2611-07-2 38566-94-8 84930-17-4 35285-69-9 69959-44-0 17696-62-7		0.4% (as acid) for single ester 0.8% (as acid) for mixtures of esters				

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
		SODIUM PROPYLPARABEN							
12	4-hydroxybenzoic acid and its salts and esters	4-HYDROXYBENZOIC ACID	99-96-7			No, Annex 1 1451/2007	Yes	No	Eye Dam. 1 H318
12	4-hydroxybenzoic acid and its salts and esters	CALCIUM PARABEN	69959-44-0			No, Annex 1 1451/2007	No	No	Not available in ECHA database
12	4-hydroxybenzoic acid and its salts and esters	PHENYLPARABEN	17696-62-7			No, Annex 1 1451/2007	No	No	Not Classified (Skin Irrit. 2 H315 Eye Irrit. 2 H319)

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
12	4-hydroxybenzoic acid and its salts and esters	POTASSIUM BUTYLPARABEN	38566-94-8			No, Annex 1 1451/2007	No	No	Not Classified
12	4-hydroxybenzoic acid and its salts and esters	POTASSIUM ETHYLPARABEN	36457-19-9			No, Annex 1 1451/2007	No	No	Not Classified
12	4-hydroxybenzoic acid and its salts and esters	POTASSIUM METHYLPARABEN	26112-07-2			No, Annex 1 1451/2007	No	No	Not available in ECHA database
12	4-hydroxybenzoic acid and its salts and esters	POTASSIUM PARABEN	16782-08-4			No, Annex 1 1451/2007	No	No	Not Classified
12	4-hydroxybenzoic acid and its salts and esters	POTASSIUM PROPYLPARABEN	84930-16-5			No, Annex 1 1451/2007	No	No	Not Classified
12	4-hydroxybenzoic acid and its salts and esters	SODIUM BUTYLPARABEN	36457-20-2			No, Annex 1 1451/2007	No	No	Acute Tox. 4 H302 Eye Dam. 1 H318
12	4-hydroxybenzoic acid and its salts and esters	SODIUM ETHYLPARABEN	35285-68-8			Yes, Annex 1 1451/2007	No	No	Eye Dam. 1 H318
12	4-hydroxybenzoic acid and its salts and esters	SODIUM ISOBUTYLPARABEN	84930-15-4			No, Annex 1 1451/2007	No	Nej	Not available in ECHA database
12	4-hydroxybenzoic acid and its salts and esters	SODIUM ISOPROPYLPARABEN	No CAS available			No, Annex 1 1451/2007	No	No	Not available in ECHA database
12	4-hydroxybenzoic acid and its salts and esters	SODIUM PARABEN	114-63-6			No, Annex 1 1451/2007	No	No	Skin Irrit. 2 H315 Eye Irrit. 2 H319 STOT SE 3 H335
13		DEHYDROACETIC ACID	520-45-6		0.6% (as acid)	Yes, Annex 1 1451/2007	No	Acute Tox. 4 H302	
13		SODIUM DEHYDROACETATE	4418-26-2		0.6% (as acid)	Yes, Annex 1 1451/2007	No	Acute Tox. 4 H302	
13	3-Acetyl-6-methylpyran-2,4(3H)-dione and its salts	DEHYDROACETIC ACID / SODIUM DEHYDROACETATE	520-45-6 4418-26-2		0.6% (as acid)		No		

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
14	Formic acid and its sodium salt	FORMIC ACID	64-18-6		0.5% (as acid)	Yes, Annex 1 1451/2007 No, Commission Decision 2007/565/EC phased out 22/08/2008 PT18 No, Commission Decision 2008/809/EC phased out 25/10/2009 PT1, PT13 No, Commission Regulation (EC) 1048/2005 phased out 01/09/2006 PT8 No, Commission Decision 2010/72/EU phased out 09/02/2011 PT9	Yes	Skin Corr. 1A H314	
14	Formic acid and its sodium salt	FORMIC ACID / SODIUM FORMATE	64-18-6 141-53-7		0.5% (as acid)				
14	Formic acid and its sodium salt	SODIUM FORMATE	141-53-7		0.5% (as acid)	Ja, Annex 1 1451/2007	Yes		Not Classified
15	3,3'-Dibromo-4,4'-hexamethylene dioxydibenzamidine and its salts (including isethionate)	DIBROMOHEXAMIDINE ISETHIONATE	93856-83-8		0.1%	No, Annex 1 1451/2007	No	No	Not Classified
16	Thiomersal	THIOMERSAL	54-64-8	Eye products	0.007% (of Hg) If mixed with other mercurial compounds authorized by this Regulation, the maximum concentration of Hg remains fixed at 0.007%	No, Annex 1 1451/2007	No	No	Acute Tox. 2 H300 Acute Tox. 1 H310 Acute Tox. 2 H330 STOT RE 2 H373 Aquatic Acute 1 H400 Aquatic Chronic 1 H410

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
17	Phenylmercuric salts (including borate)	PHENYL MERCURIC ACETATE	62-38-4			No, Annex 1 1451/2007	No	Acute Tox. 3 * H301 Skin Corr. 1B H314 STOT RE 1 H372 ** Aquatic Acute 1 H400 Aquatic Chronic 1 H410	
17	Phenylmercuric salts (including borate)	PHENYL MERCURIC ACETATE / PHENYL MERCURIC BENZOATE	62-38-4 94-43-9	Eye products	0.007% (of Hg) If mixed with other mercurial compounds authorized by this Directive, the maximum concentration of Hg remains fixed at 0.007%				
17	Phenylmercuric salts (including borate)	PHENYL MERCURIC BENZOATE	94-43-9			No, Annex 1 1451/2007	No	No	Not Classified
18	Undec-10-enoic acid and its salts	UNDECYLENIC ACID / POTASSIUM UNDECYLENATE / SODIUM UNDECYLENATE / CALCIUM UNDECYLENATE / MEA-UNDECYLENATE / TEA-UNDECYLENATE	112-38-9 6159-41-7 3398-33-2 1322-14-1 84471-25-0 56532-40-2		0.2% (as acid)				

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
18	Undec-10-enoic acid and its salts	UNDECYLENIC ACID	112-38-9			Yes, Annex 1 1451/2007	Yes	No	Skin Irrit. 2 H315 Eye Irrit. 2 H319 Aquatic Chronic 3 H412
18	Undec-10-enoic acid and its salts	POTASSIUM UNDECYLENATE	6159-41-7			No, Annex 1 1451/2007	No	No	Aquatic Chronic 3 H412
18	Undec-10-enoic acid and its salts	SODIUM UNDECYLENATE	3398-33-2			No, Annex 1 1451/2007	No	No	Not Classified (Skin Irrit. 2 H315 Eye Irrit. 2 H319)
18	Undec-10-enoic acid and its salts	CALCIUM UNDECYLENATE	1322-14-1			No, Annex 1 1451/2007	No	No	Not Classified
18	Undec-10-enoic acid and its salts	MEA-UNDECYLENATE	56532-40-2			No, Annex 1 1451/2007	No		Not Classified (Skin Irrit. 2 H315 Eye Irrit. 2 H319)
18	Undec-10-enoic acid and its salts	TEA-UNDECYLENATE	84471-25-0			No, Annex 1 1451/2007	No	No	Not available in ECHA database
19	5-Pyrimidinamine, 1,3-bis(2-ethylhexyl)hexahydro-5- methyl-	HEXETIDINE	141-94-6		0.1%	No, Annex 1 1451/2007	No	No	Skin Irrit. 2 H315 Eye Irrit. 2 H319 STOT SE 3 H335
20	5-Bromo-5-nitro-1,3-dioxane	5-BROMO-5-NITRO-1,3-DIOXANE	30007-47-7	Rinse-off products	0.1%	Yes, Annex 1 1451/2007	No	No	Acute Tox. 4 H302 Skin Irrit. 2 H315

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
21	Bronopol	2-BROMO-2-NITROPROPANE-1,3-DIOL	52-51-7		0.1%	Yes, Annex 1 1451/2007 No, Commission Decision 2008/809/EC phased out 25/10/2009 PT1, PT3, PT4, PT13 No, Commission Decision 2010/72/EU phased out 09/02/2011 PT7, PT10	Yes	Acute Tox. 4 * H302 Acute Tox. 4 * H312 Skin Irrit. 2 H315 Eye Dam. 1 H318 STOT SE 3 H335 Aquatic Acute 1 H400	
22	2,4-Dichlorobenzyl alcohol	DICHLOROBENZYL ALCOHOL	1777-82-8		0.15%	Yes, Annex 1 1451/2007 No, Commission Decision 2008/809/EC phased out 25/10/2009 PT2, PT6, PT13 No, Commission Decision 2010/72/EU phased out 09/02/2011 PT7, PT9, PT10, PT12	No	No	Aquatic Chronic 3 H412
23	1-(4-Chlorophenyl)-3-(3,4-dichlorophenyl)urea (6)	TRICLOCARBAN	101-20-2		0.2%	Yes, Annex 1 1451/2007 No, Commission Decision 2008/809/EC phased out 25/10/2009 PT1, PT2, PT4	Yes	No	Aquatic Acute 1 H400 Aquatic Chronic 1 H410
24	Chlorocresol	P-CHLORO-M-CRESOL	59-50-7	Not to be used in products applied on mucous membranes	0.2%	Yes, Annex 1 1451/2007 No, Commission Decision 2010/72/EU phased out 09/02/2011 PT10 No, Commission Decision 2008/809/EC phased out 25/10/2009 PT4, PT10	Yes	Acute Tox. 4 * H302 Acute Tox. 4 * H312 Skin Sens. 1 H317 Eye Dam. 1 H318 Aquatic Acute 1 H400	

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
25	5-Chloro-2-(2,4-dichlorophenoxy) phenol	TRICLOSAN	3380-34-5		0.3%	Yes, Annex 1 1451/2007 No, Commission Decision 2010/675/EU phased out 01/11/2011 PT3	Yes	Skin Irrit. 2 H315 Eye Irrit. 2 H319 Aquatic Acute 1 H400 Aquatic Chronic 1 H410	
26	Chloroxylenol	Chloroxylenol	1321-23-9			No, Annex 1 1451/2007	No	Acute Tox. 4 * H302 Skin Irrit. 2 H315 Skin Sens. 1 H317 Eye Irrit. 2 H319	
26	Chloroxylenol	CHLOROXYLENOL	88-04-0 1321-23-9		0.5%				
26	Chloroxylenol	4-chloro-3,5-dimethylphenol	88-04-0			Yes, Annex 1 1451/2007 No, Commission Decision 2008/809/EC phased out 25/10/2009 PT1, PT2, PT3, PT4, PT5, PT6	No	Acute Tox. 4 * H302 Skin Irrit. 2 H315 Skin Sens. 1 H317 Eye Irrit. 2 H319	
27	N,N''-Methylenebis[N'-[3-(hydroxymethyl)-2,5-dioxoimidazolidin-4-yl]urea]	IMIDAZOLIDINYL UREA	39236-46-9		0.6%	Yes, Annex 1 1451/2007	Yes	No	Not Classified

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
28	Poly(methylene), .alpha.,.omega.-bis[[[(aminoiminomethyl)amino]iminomethyl]amino]-, dihydrochloride	POLYAMINOPROPYL BIGUANIDE	28757-47-3			No, Annex 1 1451/2007	No information in ECHA DB	No information in ECHA DB	No information in ECHA DB
28	Poly(methylene), .alpha.,.omega.-bis[[[(aminoiminomethyl)amino]iminomethyl]amino]-, dihydrochloride	POLYAMINOPROPYL BIGUANIDE	133029-32-0			No, Annex 1 1451/2007	No information in ECHA DB	No information in ECHA DB	No information in ECHA DB
28	Poly(methylene), .alpha.,.omega.-bis[[[(aminoiminomethyl)amino]iminomethyl]amino]-, dihydrochloride	POLYAMINOPROPYL BIGUANIDE	70170-61-5 28757-47-3 133029-32-0 32289-58-0		0.3%		No		
28	Poly(methylene), .alpha.,.omega.-bis[[[(aminoiminomethyl)amino]iminomethyl]amino]-, dihydrochloride	4-[(4-Nitrophenyl)azo]aniline (CAS No 730-40-5) (Disperse Orange 3) and its salts, when used as a substance in hair dye products	70170-61-5			No, Annex 1 1451/2007	No information in ECHA DB	No information in ECHA DB	No information in ECHA DB
28	Poly(methylene), .alpha.,.omega.-bis[[[(aminoiminomethyl)amino]iminomethyl]amino]-, dihydrochloride	Poly(hexamethylene biguanide) hydrochloride	32289-58-0			Yes, Annex 1 1451/2007	No	No	Skin Irrit. 2 H315 Skin Sens. 1 H317 Eye Irrit. 2 H319
29	2-Phenoxyethanol	PHENOXYETHANOL	122-99-6		1.0%	Yes, Annex 1 1451/2007 No, Commission Decision 2010/72/EU phased out 09/02/2011 PT7, PT10, PT11	Yes	Acute Tox. 4 H302 Eye Irrit. 2 H319	

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
30	Methenamine	METHENAMINE	100-97-0		0.15%	Yes, Annex 1 1451/2007	Yes	Flam. Sol. 2 H228 Skin Sens. 1 H317	
31	Methenamine 3-chloroallylochloride	QUATERNIUM-15	4080-31-3 51229-78-8		0.2%	Yes, Annex 1 1451/2007 No, Commission Decision 2010/72/EU phased out 09/02/2011 PT9 (applies to both CAS nos)	No	No	Acute Tox. 3 H301 Acute Tox. 3 H311 Skin Irrit. 2 H315 Eye Irrit. 2 H319
32	1-(4-Chlorophenoxy)-1-(imidazol-1-yl)-3,3-dimethylbutan-2-one	CLIMBAZOLE	38083-17-9		0.5%	No, Annex 1 1451/2007	Yes	No	Acute Tox. 4 H302 Aquatic Chronic 3 H412
33	1,3-Bis(hydroxymethyl)-5,5-dimethylimidazolidine-2,4-dione	DMDM HYDANTOIN	6440-58-0		0.6%	Yes, Annex 1 1451/2007 No, Commission Decision 2010/72/EU phased out 09/02/2011 PT11, PT12 No, Commission Decision 2008/809/EC phased out 25/10/2009 PT2	Yes	No	Not Classified (Acute Tox. 4 H302) (Acute Tox. 4 H302 Eye Irrit. 2 H319 Resp. Sens. 1 H334)
34	Benzyl alcohol (7)	BENZYL ALCOHOL	100-51-6		1.0%	Yes, Annex 1 1451/2007	Yes	Acute Tox. 4 * H302 Acute Tox. 4 * H332	
35	1-Hydroxy-4-methyl-6-(2,4,4-trimethylpentyl)-2 pyridon and its monoethanolamine salt	1-HYDROXY-4-METHYL-6-(2,4,4-TRIMETHYLPENTYL)-2 PYRIDON, PIROCTONE OLAMINE	68890-66-4			Yes, Annex 1 1451/2007	Yes	No	Skin Irrit. 2 H315 Eye Dam. 1 H318 STOT SE 3 H335 Aquatic Acute 1 H400 Aquatic Chronic 1 H410

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
35	1-Hydroxy-4-methyl-6-(2,4,4-trim ethylpentyl)-2 pyridon and its monoethanolamine salt	1-HYDROXY-4-METHYL-6-(2,4,4-TRIMETHYLPENTYL)-2 PYRIDON, PIROCTONE OLAMINE	50650-76-5 68890-66-4	a) Rinse-off products b) Other products	a) 1.0% b) 0.5%		Yes	No	Skin Irrit. 2 H315 Eye Dam. 1 H318 STOT SE 3 H335 Aquatic Acute 1 H400 Aquatic Chronic 1 H410
35	1-Hydroxy-4-methyl-6-(2,4,4-trim ethylpentyl)-2 pyridon and its monoethanolamine salt		50650-76-5			No, Annex 1 1451/2007	No information in ECHA DB nor in COSING DB	No information in ECHA DB nor in COSING DB	No information in ECHA DB nor in COSING DB
36	*Moved or deleted*								
37	2,2'-Methylenebis(6-bromo-4-chlorophenol)	BROMOCHLOROPHENE	15435-29-7		0.1%	Yes, Annex 1 1451/2007	No	No	Not Classified (Skin Irrit. 2 H315 Eye Irrit. 2 H319)
38	4-Isopropyl-m-cresol	O-CYMEN-5-OL	3228-02-2		0.1%	Yes, Annex 1 1451/2007	No	No	Not Classified (Acute Tox. 4 H302 Skin Corr. 1B H314)

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
39	Mixture of 5-Chloro-2-methyl-isothiazol-3(2H)-one and 2-Methylisothiazol-3(2H)-one with magnesium chloride and magnesium nitrate	Mixture of 5-Chloro-2-methyl-isothiazol-3(2H)-one and 2-Methylisothiazol-3(2H)-one with magnesium chloride and magnesium nitrate	55965-84-9		0.0015% (of a mixture in the ratio 3:1 of 5-Chloro-2-methyl-isothiazol-3(2H)-o ne and 2-Methylisothiazol-3(2H)-one	Yes, Annex 1 1451/2007 No, Commission Decision 2010/72/EU phased out 09/02/2011 PT7, PT9, PT10 No, Commission Decision 2008/809/EC phased out 25/10/2009 PT3	No	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	
39	Mixture of 5-Chloro-2-methyl-isothiazol-3(2H)-one and 2-Methylisothiazol-3(2H)-one with magnesium chloride and magnesium nitrate	METHYLCHLOROISOTHIAZOLINONE	26172-55-4		0.0015% (of a mixture in the ratio 3:1 of 5-Chloro-2-methyl-isothiazol-3(2H)-o ne and 2-Methylisothiazol-3(2H)-one	Yes, Annex 1 1451/2007	No	No	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
39	Mixture of 5-Chloro-2-methyl-isothiazol-3(2H)-one and 2-Methylisothiazol-3(2H)-one with magnesium chloride and magnesium nitrate	METHYLCHLOROISOTHIAZOLINONE AND METHYLISOTHIAZOLINONE	2682-20-4		0.0015% (of a mixture in the ratio 3:1 of 5-Chloro-2-methyl-isothiazol-3(2H)-o ne and 2-Methylisothiazol-3(2H)-one	Yes, Annex 1 1451/2007 No, Commission Decision 2010/72/EU phased out 09/02/2011 PT7, PT9, PT10, PT22 No, Commission Decision 2008/809/EC phased out 25/10/2009 PT2, PT4	No	No	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

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
39	Mixture of 5-Chloro-2-methyl-isothiazol-3(2H)-one and 2-Methylisothiazol-3(2H)-one with magnesium chloride and magnesium nitrate	METHYLCHLOROISOTHIAZOLINONE AND METHYLISOTHIAZOLINONE	55965-84-9 26172-55-4 2682-20-4		0.0015% (of a mixture in the ratio 3:1 of 5-Chloro-2-methyl-isothiazol-3(2H)-one and 2-Methylisothiazol-3(2H)-one				
40	2-Benzyl-4-chlorophenol	CHLOROPHENE	120-32-1		0.2%	Yes, Annex 1 1451/2007 No, Commission Decision 2008/809/EC phased out 25/10/2009 PT1, PT4, PT6	No	No	Skin Irrit. 2 H315 Eye Dam. 1 H318 Aquatic Acute 1 H400 Aquatic Chronic 1 H410
41	2-Chloroacetamide	CHLOROACETAMIDE	79-07-2		0.3%	Yes, Annex 1 1451/2007 No, Commission Decision 2011/391/EU phased out 01/07/2012 PT3, PT6, PT13 No, Commission Decision 2010/72/EU phased out 09/02/2011 PT7, PT9, PT10, PT11	Yes	Acute Tox. 3 * H301 Skin Sens. 1 H317 Repr. 2 H361f ***	
42	N,N'-bis(4-chlorophenyl)-3,12-diimino-2,4,11,13-tetraazatetradecanediamidine and its digluconate, diacetate and dihydrochloride	CHLORHEXIDINE	55-56-1			No, Annex 1 1451/2007	Yes	No	Skin Irrit. 2 H315 Eye Irrit. 2 H319 Resp. Sens. 1 H334 STOT SE 3 H335 Aquatic Acute 1 H400 Aquatic Chronic 1 H410

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
42	N,N'-bis(4-chlorophenyl)-3,12-dii mino-2,4,11,13-tetraazatetradecanediamidine and its digluconate, diacetate and dihydrochloride	CHLORHEXIDINE DIACETATE	56-95-1			Yes, Annex 1 1451/2007	No	No	Eye Irrit. 2 H319 Aquatic Chronic 2 H411 (Acute Tox. 4 H302 Aquatic Acute 1 H400 Aquatic Chronic 1 H410)
42	N,N'-bis(4-chlorophenyl)-3,12-dii mino-2,4,11,13-tetraazatetradecanediamidine and its digluconate, diacetate and dihydrochloride	CHLORHEXIDINE DIGLUCONATE	18472-51-0			Yes, Annex 1 1451/2007 No, Commission Decision 2008/809/EC phased out 25/10/2009 PT4, PT6	Yes	No	Eye Dam. 1 H318 Aquatic Acute 1 H400
42	N,N'-bis(4-chlorophenyl)-3,12-dii mino-2,4,11,13-tetraazatetradecanediamidine and its digluconate, diacetate and dihydrochloride	CHLORHEXIDINE DIHYDROCHLORIDE	3697-42-5			Yes, Annex 1 1451/2007	No	No	Skin Irrit. 2 H315 Eye Irrit. 2 H319 STOT SE 3 H335
42	N,N'-bis(4-chlorophenyl)-3,12-dii mino-2,4,11,13-tetraazatetradecanediamidine and its digluconate, diacetate and dihydrochloride	CHLORHEXIDINE / CHLORHEXIDINE DIACETATE / CHLORHEXIDINE DIGLUCONATE / CHLORHEXIDINE DIHYDROCHLORIDE	55-56-1 56-95-1 18472-51-0 3697-42-5		0.3% (as chlorhexidine)	55-56-1 No, Annex 1 1451/2007 56-95-1 Yes, Annex 1 1451/2007 18472-51-0 Yes, Annex 1 1451/2007 3697-42-5 Yes, Annex 1 1451/2007			
43	1-Phenoxypropan-2-ol (8)	PHENOXYISOPROPANOL	770-35-4	Only for rinse-off products	1.0%	No, Annex 1 1451/2007	Yes	No	Eye Irrit. 2 H319

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
44	Alkyl (C12-C22) trimethyl ammonium bromide and chloride	CETRIMONIUM CHLORIDE	112-02-7			Yes, Annex 1 1451/2007	Yes	No	Acute Tox. 3 H301 Skin Irrit. 2 H315 Eye Dam. 1 H318 STOT SE 3 H335 Aquatic Acute 1 H400
44	Alkyl (C12-C22) trimethyl ammonium bromide and chloride	BEHENTRIMONIUM CHLORIDE	17301-53-0			No, Annex 1 1451/2007	No	No	Skin Irrit. 2 H315 Eye Irrit. 2 H319 Aquatic Acute 1 H400 Aquatic Chronic 1 H410
44	Alkyl (C12-C22) trimethyl ammonium bromide and chloride	LAURTRIMONIUM BROMIDE	1119-94-4			Yes, Annex 1 1451/2007	No	No	Acute Tox. 3 H301 Skin Irrit. 2 H315 Eye Irrit. 2 H319 STOT SE 3 H335 Aquatic Acute 1 H400 Aquatic Chronic 1 H410
44	Alkyl (C12-C22) trimethyl ammonium bromide and chloride	STEARTRIMONIUM CHLORIDE	112-03-8			No, Annex 1 1451/2007	No	No	Acute Tox. 4 H302 Skin Corr. 1C H314 Eye Dam. 1 H318 Aquatic Acute 1 H400 Aquatic Chronic 1 H410
44	Alkyl (C12-C22) trimethyl ammonium bromide and chloride	BEHENTRIMONIUM CHLORIDE / CETRIMONIUM BROMIDE / CETRIMONIUM CHLORIDE / LAURTRIMONIUM BROMIDE / LAURTRIMONIUM CHLORIDE / STEARTRIMONIUM BROMIDE / STEARTRIMONIU	17301-53-0 57-09-0 112-02-7 1119-94-4 112-00-5 1120-02-1 112-03-8		0.1%				

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
		M CHLORIDE							
44	Alkyl (C12-C22) trimethyl ammonium bromide and chloride	CETRIMONIUM BROMIDE	57-09-0			Yes, Annex 1 1451/2007	Yes	No	Acute Tox. 4 H302 Aquatic Acute 1 H400 Aquatic Chronic 1 H410
44	Alkyl (C12-C22) trimethyl ammonium bromide and chloride	LAURTRIMONIUM CHLORIDE	112-00-5			No, Annex 1 1451/2007	No	No	Acute Tox. 4 H302 Skin Corr. 1C H314 Eye Dam. 1 H318 Aquatic Acute 1 H400
44	Alkyl (C12-C22) trimethyl ammonium bromide and chloride	STEARTRIMONIUM BROMIDE	1120-02-1			No, Annex 1 1451/2007	No	No	Skin Irrit. 2 H315 Eye Irrit. 2 H319 STOT SE 3 H335
45	4,4-Dimethyl-1,3-oxazolidine	DIMETHYL OXAZOLIDINE	51200-87-4		0.1%	Yes, Annex 1 1451/2007 No, Commission Decision 2010/72/EU 09/02/2011 PT11	No	No	Flam. Liq. 3 H226 Acute Tox. 4 H302 Skin Irrit. 2 H315 Eye Dam. 1 H318 Acute Tox. 4 H332
46	N-(Hydroxymethyl)-N-(dihydroxymethyl-1,3-dioxo-2,5-imidazolidinyl-4)-N'-(hydroxymethyl)ur	DIAZOLIDINYL UREA	78491-02-8		0.5%	Yes, Annex 1 1451/2007 No, Commission Decision 2008/809/EC phased out 25/10/2009 PT6, PT7	Yes	No	Skin Sens. 1 H317

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
	ea								
47	Benzenecarboximidamide, 4,4'-(1,6-hexanediylbis(oxy))bis-, and its salts (including isothionate and p-hydroxybenzoate)	HEXAMIDINE / HEXAMIDINE DIISETHIONATE / HEXAMIDINE DIPARABEN / HEXAMIDINE PARABEN	3811-75-4 659-40-5 93841-83-9 -		0.1%				
47	Benzenecarboximidamide, 4,4'-(1,6-hexanediylbis(oxy))bis-, and its salts (including isothionate and p-hydroxybenzoate)	HEXAMIDINE	3811-75-4			No, Annex 1 1451/2007	No	No	Not available in ECHA database
47	Benzenecarboximidamide, 4,4'-(1,6-hexanediylbis(oxy))bis-, and its salts (including isothionate and p-hydroxybenzoate)	HEXAMIDINE DIISETHIONATE	659-40-5			Yes, Annex 1 1451/2007	No	No	Not Classified

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
47	Benzenecarboximidamide, 4,4'-(1,6-hexanediylbis(oxy))bis-, and its salts (including isothionate and p-hydroxybenzoate)	HEXAMIDINE DIPARABEN	93841-83-9			No, Annex 1 1451/2007	No	No	Not Classified
47	Benzenecarboximidamide, 4,4'-(1,6-hexanediylbis(oxy))bis-, and its salts (including isothionate and p-hydroxybenzoate)	HEXAMIDINE PARABEN	not available				not available	not available	not available
48	Glutaraldehyde (Pentane-1,5-dial)	GLUTARAL	111-30-8		0.1%	Yes, Annex 1 1451/2007 No, Commission Decision 2010/72/EU phased out 09/02/2011 PT7, PT9, PT10, PT22 Yes, but phased out 01/02/2014 no decision reference PT5	Yes	Acute Tox. 3 * H301 Skin Corr. 1B H314 Skin Sens. 1 H317 Acute Tox. 3 * H331 Resp. Sens. 1 H334 Aquatic Acute 1 H400	
49	5-Ethyl-3,7-dioxa-1-azabicyclo[3.3.0] octane	7-ETHYLBICYCLOOXAZOLIDINE	7747-35-5		0.3%	Yes, Annex 1 1451/2007 No, Commission Decision 2010/72/EU phased out 09/02/2011 PT11, PT12	Yes	No	Acute Tox. 4 H312 Skin Irrit. 2 H315 Skin Sens. 1 H317 Eye Irrit. 2 H319 Acute Tox. 4 H332 Aquatic Chronic 3 H412

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
50	3-(p-Chlorophenoxy)-propane-1,2 -diol	CHLORPHENESIN	104-29-0		0.3%	Yes, Annex 1 1451/2007	No	No	Acute Tox. 4 H302 Acute Tox. 4 H312 Skin Irrit. 2 H315 Eye Irrit. 2 H319 Acute Tox. 4 H332 STOT SE 3 H335
51	Sodium hydroxymethylamino acetate	SODIUM HYDROXYMETHYL GLYCINA TE	70161-44-3		0.5%	Yes, Annex 1 1451/2007 No, Commission Decision 2010/72/EU phased out 09/02/2011 PT7	No	No	Skin Sens. 1 H317 Eye Irrit. 2 H319
52	Silver chloride deposited on titanium dioxide	SILVER CHLORIDE	7783-90-6		0.004% (as AgCl)	Yes, Annex 1 1451/2007	Yes	No	Not Classified (STOT SE 2 H335 Aquatic Acute 1 H400)
53	Benzenemethanaminium, N,N-dimethyl-N-[2-[2-[4-(1,1,3,3,-tetramethylbutyl)phenoxy]ethoxy]ethyl]-, chloride	BENZETHONIUM CHLORIDE	121-54-0	a) Rinse-off products b) Leave-on products other than oral products	0.1%	Yes, Annex 1 1451/2007 No, Commission Decision 2008/809/EC phased out 25/10/2009 PT1	No	No	Acute Tox. 3 H301 Skin Corr. 1B H314 Aquatic Acute 1 H400 Aquatic Chronic 1 H410

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
54	Benzalkonium chloride, bromide and saccharinate (10)	Benzalkonium Chlorid Benzalkonium chloride N-alkyl(C8-C16)dimethylbenzyl ammonium chloride Quaternary ammonium compounds, alkylbenzyldimethyl, chlorides ammonium, alkylbenzyldimethyl-,chloride benzalkonium chloride benzyl-dimethyl-tetradecylazanium chloride benzyl-dodecyl-dimethylazanium chloride benzyl-dodecyl-dimethylazanium chloride	8001-54-5			Yes, Annex 1 1451/2007	No	No	Acute Tox. 4 H302 Acute Tox. 4 H312 Skin Corr. 1B H314 Acute Tox. 4 H332
54	Benzalkonium chloride, bromide and saccharinate (10)	BENZALKONIUM CHLORIDE / BENZALKONIUM BROMIDE / BENZALKONIUM SACCHARINATE	8001-54-5 85409-22-9 68424-85-1 68391-01-5 63449-41-2/ 91080-29-4 68989-01-5 61789-71-7		0.1% (as benzalkonium chloride)	Yes, Annex 1 1451/2007			

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
54	Benzalkonium chloride, bromide and saccharinate (10)	Benzyl-C12-14-alkyldimethylammonium chlorides	85409-22-9			Yes, Annex 1 1451/2007 No, Commission Decision 2010/72/EU phased out 09/02/2011 PT7, PT9, PT17 No, Commission Decision 2007/565/EC phased out 22/08/2008 PT16, PT18, PT19, PT21 No, Commission Decision 2008/809/EC phased out 25/10/2009 PT5, PT6, PT13 No, Commission Regulation (EC) 1048/2005 phased out 01/09/2006 PT8	Yes	No	Acute Tox. 4 H302 Skin Corr. 1B H314 Aquatic Acute 1 H400
54	Benzalkonium chloride, bromide and saccharinate (10)	Quaternary ammonium compounds, benzyl-C12-16-alkyldimethyl, chlorides	68424-85-1			Yes, Annex 1 1451/2007 No, Commission Regulation (EC) 1849/2006 phased out 03/01/2008 PT18, PT19, PT21 No, Commission Decision 2008/809/EC phased out 25/10/2009 PT6, PT13 No, Commission Decision 2010/72/EU phased out 09/02/2011 PT7, PT9	No	No	Acute Tox. 4 H302 Skin Corr. 1B H314
54	Benzalkonium chloride, bromide and saccharinate (10)	Quaternary ammonium compounds, benzyl-C12-18-alkyldimethyl, chlorides	68391-01-5			Yes, Annex 1 1451/2007 No, Commission Decision 2008/809/EC phased out 25/10/2009 PT 5, PT6, PT13 No, Commission Decision 2010/72/EU phased out 09/02/2011 PT7 , PT9, PT17 No, Commission Regulation (EC) 1048/2005 phased out 01/09/2006 PT8 No, Commission Decision 2007/565/EC phased out 22/08/2008 PT16	No	No	Acute Tox. 4 H302 Skin Corr. 1B H314 Aquatic Acute 1 H400

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
54	Benzalkonium chloride, bromide and saccharinate (10)	Quaternary ammonium compounds, benzyl-C8-18-alkyldimethyl, chlorides	63449-41-2			Yes, Annex 1 1451/2007	Yes	Acute Tox. 4 * H302 Acute Tox. 4 * H312 Skin Corr. 1B H314 Aquatic Acute 1 H400	
54	Benzalkonium chloride, bromide and saccharinate (10)	BENZALKONIUM BROMIDE	91080-29-4			Yes, Annex 1 1451/2007	No	No	Not Classified (Acute Tox. 3 H301 Acute Tox. 4 H312 Skin Corr. 1B H314 Aquatic Acute 1 H400)
54	Benzalkonium chloride, bromide and saccharinate (10)	BENZALKONIUM SACCHARINATE	68989-01-5			Yes, Annex 1 1451/2007 No, Commission Decision 2010/72/EU phased out 09/02/2011 PT11, PT12	No	No	Not Classified (Acute Tox. 4 H302 Acute Tox. 4 H312 Skin Corr. 1C H314 Aquatic Acute 1 H400)
54	Benzalkonium chloride, bromide and saccharinate (10)	COCOALKONIUM CHLORIDE	61789-71-7			Yes, Annex 1 1451/2007	No	No	Acute Tox. 4 H302 Acute Tox. 4 H312 Skin Corr. 1B H314 Aquatic Acute 1 H400
55	Methanol, (phenylmethoxy)-	BENZYLHEMIFORMAL	14548-60-8	Rinse-off products	0.15%	Yes, Annex 1 1451/2007, No, Commission Decision 2010/72/EU phased out 09/02/2011 PR9, PT10 og PT 11, Commission Decision 2008/809/EC phased out 25/10/2009 PT2	No	No	Acute Tox. 4 H302 Acute Tox. 4 H312 Skin Irrit. 2 H315 Skin Sens. 1 H317 Eye Dam. 1 H318 STOT SE 3 H335

Ref No.	Chemical name / INN	Name of Common Ingredients Glossary	CAS Number	Product Type, body parts	Maximum concentration in ready for use preparation	Biocidal active substance	Registered acc. to REACH (yes/no)	Harmonised classification	Notified classification
56	3-Iodo-2-propynylbutylcarbamate	IODOPROPYNYL BUTYLCARBAMATE	55406-53-6	a) Rinse-off products b) Leave-on products c) Deodorants/antiperspirants	a) 0.02% b) 0.01% c) 0.0075%	Yes, Annex 1 1451/2007, No, Commission Decision 2010/72/EU phased out 09/02/2011 PT11, Commission Decision 2007/565/EC phased out 22/08/2008 PT18	No	No	Acute Tox. 4 H302 Skin Sens. 1 H317 Eye Dam. 1 H318 Acute Tox. 4 H332 STOT SE 3 H335 Aquatic Acute 1 H400
57	2-Methyl-2H-isothiazol-3-one	METHYLISOTHIAZOLINONE	2682-20-4		0.01%	Yes, Annex 1 1451/2007, No, Commission Decision 2008/809/EC PT 2, PT4, phased out 25/10/2009, PT7, PT9, PT10, PT22 Commission Decision 2010/72/EU phased out 09/02/2011	No	No	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

Appendix 2: Extract from Statistics Denmark on the imports and exports of cosmetic products

Table 40 below shows imports and exports in kilos for the 29 product codes for 2012. In addition to this the amounts produced in Denmark, but these are not indicated (partly because manufactured amounts are stated in values and not in amounts, whereas import and export are stated in both amounts and values, and partly because the value of the manufactured products is insignificant compared to the value of the imported products).

Note that for two product codes ("34012090 Soap ..." and "33069000 Preparations for oral or dental hygiene ..."), exports are larger than imports, which may be explained by the fact that there is a significant production in Denmark, which is exported - despite the fact that the production figures in Denmark for cosmetic products are generally low compared to the quantities imported.

Table below is sorted with the largest import volumes for 2012 listed first.

The table also indicates in which of the five categories used by the SPT in their statistics (hair care, skin care, perfumes and fragrances, toiletries and decorative cosmetics) the product code is assumed to be included. These categories are used to obtain a total and more overall picture of the amounts of these five types of cosmetic products in the report (see Section 1.7 “Distribution of cosmetic products on the Danish market”).

Some product codes are indicated with”0” corresponding to no import. It seems that there has been a shift in the use of the product codes, as these product codes have significant imports in previous years, whereas other product codes here are indicated with "0".

Product code	Category as used by the SPT (see Figure 1)	Import 2012 (kg)	Export 2012 (kg)
33059000 Hair care products (excluding shampoos, preparations for permanent waving and hair spray)	Hair care	10.070.212	5.228.846
33061000 Dentifrices, including those used by dentists	Toiletries	9.841.729	7.532.869
34013000 Organic surface active substances and preparations for washing the skin, in liquid form or as cream, in packings for retail sale, also with content of soap	Skin care	8.711.675	5.224.042
33049900 Prepared beauty or make-up products and preparations for skin care, including sunscreen and sun tan (excluding pharmaceuticals and cosmetics for the lips, make-up for the eyes, manicure or pedicure preparations and powders, including powder in solid form)	Decorative cosmetics	8.283.097	4.862.098
33051000 Shampoos	Hair care	8.259.059	6.375.156

Product code	Category as used by the SPT (see Figure 1)	Import 2012 (kg)	Export 2012 (kg)
34012090 Soap in the form of pasta soft soap, in aqueous solution liquid soapor in other forms nes (not elsewhere specified)	Skin care	7.403.987	10.200.704
34011900 Soap and organic surface active substances and preparations for use as soap, in the form of bars, blocks or molded pieces or shapes, and paper, wadding, felt and fibre cloth, impregnated or coated with soap or detergent (excluding toilet use, including medical use)	Skin care	4.744.113	280.177
33073000 Perfumed bath salts and other bath preparations	Toiletries	3.316.566	1.854.218
34011100 Soap and organic surface active substances and preparations for use as soap, in the form of bars, blocks or molded pieces or shapes, and paper, wadding, felt and fibre cloth, impregnated or coated with soap or detergent, for toilet purposes including for medical	Skin care	3.221.791	1.319.993
33079000 Depilatories and other perfumery, cosmetics or toilet preparations, nes	Skin care	2.644.599	1.637.619
33072000 Deodorants and antiperspirants for personal use	Perfumes and fragrances	2.592.110	1.344.010
33074900 Preparations for perfuming or deodorising rooms, including odoriferous preparations used during religious ceremonies (except agarbatti and other odoriferous preparations operating by burning)	Perfumes and fragrances	1.691.870	1.163.448
33053000 Hair spray	Hair care	1.507.292	353.696
34012010 Soap in the form of flakes, granules or powders	Skin care	1.498.112	128.798
33069000 Preparations for oral or dental hygiene, including powder and cream for attaching dentures (excluding dentifrices and dental floss)	Toiletries	1.016.468	2.045.123
33071000 Preparations for use before, during and after shaving	Toiletries	911.409	98.760
33043000 Manicure and pedicure preparations	Decorative cosmetics	768.598	299.229

Product code	Category as used by the SPT (see Figure 1)	Import 2012 (kg)	Export 2012 (kg)
33042000 Eye make-up	Decorative cosmetics	420.495	271.280
33030090 Toilet water (excluding aftershave lotions and deodorants for personal use)	Perfumes and fragrances	384.182	162.770
33030010 Perfumes (excluding aftershave lotions and deodorants for personal use)	Perfumes and fragrances	221.674	83.766
33041000 Lip make-up	Decorative cosmetics	198.730	83.348
33062000 Dental floss, i packings for retail sale	Toiletries	198.458	17.955
33049100 Powder for make-up or skin care, including baby powder and solid powder (excluding medical products)	Decorative cosmetics	192.098	118.872
33052000 Preparations for permanent waving	Hair care	65.941	26.023
33074100 Agarbatti and other odoriferous preparations operating by burning	Perfumes and fragrances	36.631	534
33049910 Skin cream and skin oil	Skin care	0	0
33049990 Beauty Products for make-up and skin care, excluding lip preparations, eye make-up preparations, manicure and pedicure preparations, powders, skin care products	Skin care	0	0
33059010 Hair lotions	Hair care	0	0
33059090 Hair care products, excluding hair shampoos, hair spray, hair lotions and preparations for permanent waving	Hair care	0	0

TABLE 40
EXTRACT FROM STATISTICS BANK. NUMBER OF KILOS IMPORTED/EXPORTED IN 2012 (SOURCE: STATISTICS BANK).

Appendix 3: Previous surveys of cosmetic products

The Environmental Protection Agency has made a number of previous surveys dealing with cosmetic products:

- Hair dyes (365 products, 2011), (Poulsen & Strandesen, 2013).
- Non-preserved cosmetics (89 products, 2009) – here the use of a few preservatives from Annex V of the Cosmetics Regulation was seen, as a group of "naturally" preserved products were also included in the study (Poulsen & Strandesen, 2011).
- Sunscreens and creams for children in the project on exposure of 2-year old children to chemical substances (60 products, 2008), (Tønning *et al*, 2009).
- Cosmetic products for children (208 products, 2007) (Poulsen & Schmidt, 2007).
- Hair styling products (328 products, 2001), (Poulsen *et al*, 2002).

In the following, the preservatives registered by the EPA's previous studies of cosmetic products are reviewed (in tabular form). The oldest of the studies are more than 10 years old, and a lot may have happened in the use of preservatives since then. The information from these previous studies is therefore used in this report only as a historical background and to provide a picture of the fact that certain types of cosmetic products are probably non-preserved (ie. contains no preservatives as specified in Annex V of the Cosmetics Regulation). It should be noted that cosmetic products are often reformulated, and therefore studies that are several years old can only be used as a snapshot from the time they were made.

Previous survey of hair dyes

In 2011, the full lists of ingredients were entered on a total of 365 hair dyes in this study (Poulsen & Strandesen, 2013). Of these, 159 products were hair dyes for private use, ie. products that could be purchased by consumers on the Danish market. Of these, 107 hair dyes contained preservatives from Annex V of the Cosmetics Regulation corresponding to 67 % of the products containing preservatives. Table 41 below indicates the preservatives found, and in which number of products.

Preservative	Regulation Annex V	In number of products of 159	In products of 159 (%)
SODIUM SULFITE	Ref. no. 9	58	54%
SODIUM METABISULFITE	Ref. no. 9	41	38%
PHENOXYETHANOL	Ref. no. 29	11	10%
CETRIMONIUM CHLORIDE	Ref. no. 44	11	10%
BENZYL ALCOHOL	Ref. no. 34	10	9%
SODIUM BENZOATE	Ref. no. 1	9	8%
SALICYLIC ACID	Ref. no. 3	7	7%
POTASSIUM SORBATE	Ref. no. 4	6	6%
SORBIC ACID	Ref. no. 4	5	5%
PROPYLPARABEN	Ref. no. 12	5	5%
METHYLPARABEN	Ref. no. 12	5	5%

Preservative	Regulation Annex V	In number of products of 159	In products of 159 (%)
ETHYLPARABEN	Ref. no. 12	4	4%
METHYLISOTHIAZOLINONE	Ref. nos. 39 and 57	2	2%
METHYLCHLOROISOTHIAZOLINONE	Ref. no. 39	2	2%
BUTYLPARABEN	Ref. no. 12	2	2%

TABLE 40
CONTENTS OF PRESERVATIVES IN HAIR DYES (POULSEN & STRANDESEN, 2013).

Previous survey of non-preserved cosmetics

In autumn 2009, the full lists of ingredients were entered in this study on a total of 89 cosmetic products marketed as “non-preserved” or “naturally preserved”. That is, some of the products contained preservatives described by the manufacturers as "natural". A total of 12 of the 89 studied cosmetic products contained preservatives from Annex V of the Cosmetics Regulation corresponding to 13 % of the products containing preservatives. The used preservatives are indicated in Table 42 below.

Preservative	Regulation Annex V	In number of products of 89	In products of 89 (%)
SODIUM BENZOATE	Ref. no. 1	5	6%
POTASSIUM SORBATE	Ref. no. 4	4	4%
PHENOXYETHANOL	Ref. no. 29	2	2%
METHYLISOTHIAZOLINONE	Ref. nos. 39 and 57	2	2%
BENZYL ALCOHOL	Ref. no. 34	2	2%
SORBIC ACID	Ref. no. 4	1	1%
SODIUM HYDROXYMETHYLGLYCINATE	Ref. no. 51	1	1%
SODIUM DEHYDROACETATE	Ref. no. 13	1	1%
METHYLCHLOROISOTHIAZOLINONE	Ref. no. 39	1	1%
CETRIMONIUM CHLORIDE	Ref. no. 44	1	1%

TABLE 41
CONTENTS OF PRESERVATIVES IN ”NON-PRESERVED” AND ”NATURALLY PRESERVED” COSMETIC PRODUCTS (POULSEN & STRANDESEN, 2011).

Previous survey of sunscreens and creams for children

In 2008, the full lists of ingredients were entered in this study on a total of 32 creams/bodylotions and 28 sunscreens. The study was conducted under the project on exposure of 2-year old children to chemical substances, and all sunscreens and creams were therefore marketed/aimed at children. 19 creams and 19 sunscreens contained preservatives from Annex V of the Cosmetics Regulation corresponding to 59 % of the creams and 68 % of the sunscreens containing preservatives. The preservatives used in the creams and sunscreens are indicated in Table 43 and Table 44 below.

Preservative	Regulation AnnexV	In number of products of 32	In products of 32 (%)
PHENOXYETHANOL	Ref. no. 29	16	50%
METHYLPARABEN	Ref. no. 12	7	22%
SODIUM BENZOATE	Ref. no. 1	6	19%
PROPYLPARABEN	Ref. no. 12	6	19%
BENZOIC ACID	Ref. no. 1	6	19%
ETHYLPARABEN	Ref. no. 12	4	13%
DEHYDROACETIC ACID	Ref. no. 13	4	13%
POTASSIUM SORBATE	Ref. no. 4	3	9%
CHLORPHENESIN	Ref. no. 50	2	6%
BENZYL ALCOHOL	Ref. no. 34	2	6%
SORBIC ACID	Ref. no. 4	1	3%
ISOBUTYLPARABEN	Ref. no. 12	1	3%
IMIDAZOLIDINYL UREA	Ref. no. 27	1	3%
BUTYLPARABEN	Ref. no. 12	1	3%

TABLE 42
CONTENTS OF PRESERVATIVES IN CREAMS/BODYLOTIONS MARKETED FOR CHILDREN (TØNNING *ET AL*, 2009).

Preservative	Regulation AnnexV	In number of products of 28	In products of 28 (%)

Preservative	Regulation AnnexV	In number of products of 28	In products of 28 (%)
PHENOXYETHANOL	Ref. no. 29	17	61%
SODIUM BENZOATE	Ref. no. 1	8	29%
METHYLPARABEN	Ref. no. 12	7	25%
PROPYLPARABEN	Ref. no. 12	5	18%
SODIUM DEHYDROACETATE	Ref. no. 13	3	11%
POTASSIUM SORBATE	Ref. no. 4	2	7%
ETHYLPARABEN	Ref. no. 12	2	7%
DEHYDROACETIC ACID	Ref. no. 13	2	7%
BENZOIC ACID	Ref. no. 1	2	7%
SORBIC ACID	Ref. no. 4	1	4%
SODIUM SULFITE	Ref. no. 9	1	4%
o-CYMEN-5-OL	Ref. no. 38	1	4%
BUTYLPARABEN	Ref. no. 12	1	4%

TABLE 43
CONTENTS OF PRESERVATIVES IN SUNSCREENS MARKETED FOR CHILDREN (TØNNING *ET AL*, 2009).

Previous survey of cosmetic products for children

In 2006, the full lists of ingredients were entered in this study on a total of 208 different cosmetic products for children. A total of 131 of the 208 cosmetic products contained preservatives from Annex V of of the Cosmetics Regulation corresponding to 63 % of all studied cosmetic products for children containing preservatives. The preservatives used in cosmetic products for children are indicated in Table 45 below. The project studied several different types of cosmetic products for children. Table 46 show the number of products containing preservatives spread over the different types of cosmetic products.

Preservative	Regulation AnnexV	In number of products of 208	In products of 208 (%)
METHYLPARABEN	Ref. no. 12	79	38%
PROPYLPARABEN	Ref. no. 12	70	34%
PHENOXYETHANOL	Ref. no. 29	50	24%
BUTYLPARABEN	Ref. no. 12	48	23%

Preservative	Regulation AnnexV	In number of products of 208	In products of 208 (%)
ETHYLPARABEN	Ref. no. 12	46	22%
ISOBUTYLPARABEN	Ref. no. 12	39	19%
BENZYL ALCOHOL	Ref. no. 34	20	10%
METHYLISOTHIAZOLINONE	Ref. nos. 39 and 57	15	7%
5-BROMO-5-NITRO-1,3-DIOXANE	Ref. no. 20	15	7%
METHYLCHLOROISOTHIAZOLINONE	Ref. no. 39	15	7%
SODIUM BENZOATE	Ref. no. 1	13	6%
DMDM HYDANTOIN	Ref. no. 33	11	5%
CETRIMONIUM CHLORIDE	Ref. no. 44	9	4%
BEHENTRIMONIUM CHLORIDE	Ref. no. 44	7	3%
IMIDAZOLIDINYL UREA	Ref. no. 27	7	3%
2-BROMO-2-NITROPROPANE-1,3-DIOL	Ref. no. 21	6	3%
DIAZOLIDINYL UREA	Ref. no. 46	4	2%
ISOPROPYLPARABEN	Ref. no. 12	4	2%
LAURTRIMONIUM CHLORIDE	Ref. no. 44	2	1%
QUATERNIUM-15	Ref. no. 31	2	1%
SODIUM METHYLPARABEN	Ref. no. 12	1	0,5%
POTASSIUM SORBATE	Ref. no. 4	1	0,5%
IODOPROPYNYL BUTYLCARBAMATE	Ref. no. 56	1	0,5%

TABLE 44
CONTENTS OF PRESERVATIVES IN COSMETIC PRODUCTS FOR CHILDREN (POULSEN & SCHMIDT, 2007).

Product type	Number of products of 208	Number of products containing preservative (%)
Bath confetti/caviar/fizzle salt[22]	29	21 (72%)
Bath oil	8	0 (0%)
Conditioner	5	3 (60%)
Bodylotion/cream	17	11 (65%)
Bodyshampoo/shower gel	43	41 (95%)
Deodorant	1	0 (0%)
Eau de toilette - perfume	9	1 (11%)
Hair dye (rinsing colour)	7	7 (100%)
Hair styling products	2	2 (100%)
Massage oil	1	0 (0%)
Shampoo	26	19 (73%)
Foam bath	21	13 (62%)
Soap - solid	11	1 (9%)
Soap - liquid	1	1 (100%)
Toothpaste	19	7 (37%)
Other	8	4 (50%)

TABLE 45
THE PROPORTION OF PRODUCTS CONTAINING PRESERVATIVES SPREAD OVER DIFFERENT TYPES OF STUDIED COSMETIC PRODUCTS FOR CHILDREN (POULSEN & SCHMIDT, 2007).

Previous survey of hair styling products

In 2001, the full lists of ingredients were entered in this study on a total of 328 different hair styling products. Of these, 161 hair styling products contained preservatives from Annex V of the Cosmetics Regulation corresponding to 49 % containing preservatives. The preservatives used in the hair styling products are indicated in Table 47 below, and Table 48 states contents of preservatives in the different types of hair styling products.

[22] Bath salt, flakes of bath soap for use in the bath tub, where they will slowly dissolve

Preservative	Regulation Annex V	In number of products of 328	In products of 328 (%)
METHYLPARABEN	Ref. no. 12	75	23%
PHENOXYETHANOL	Ref. no. 29	58	18%
PROPYLPARABEN	Ref. no. 12	52	16%
BUTYLPARABEN	Ref. no. 12	28	9%
CETRIMONIUM CHLORIDE	Ref. no. 44	28	9%
DMDM HYDANTOIN	Ref. no. 33	27	8%
ETHYLPARABEN	Ref. no. 12	27	8%
BENZYL ALCOHOL	Ref. no. 34	14	4%
ISOBUTYLPARABEN	Ref. no. 12	14	4%
DIAZOLIDINYL UREA	Ref. no. 46	13	4%
SODIUM BENZOATE	Ref. no. 1	10	3%
METHYLISOTHIAZOLINONE	Ref. nos. 39 and 57	8	2%
METHYLCHLOROISOTHIAZOLINONE	Ref. no. 39	8	2%
POTASSIUM SORBATE	Ref. no. 4	8	2%
IODOPROPYNYL BUTYLCARBAMATE	Ref. no. 56	6	2%
SORBIC ACID	Ref. no. 4	5	2%
BENZOIC ACID	Ref. no. 1	4	1%
SODIUM METHYLPARABEN	Ref. no. 12	3	0,9%
AMMONIUM BENZOATE	Ref. no. 1a	3	0,9%
BEHENTRIMONIUM CHLORIDE	Ref. no. 44	3	0,9%
ISOPROPYLPARABEN	Ref. no. 12	2	0,6%
2-BROMO-2-NITROPROPANE-1,3-DIOL	Ref. no. 21	2	0,6%
SODIUM	Ref. no. 51	2	0,6%

Preservative	Regulation Annex V	In number of products of 328	In products of 328 (%)
HYDROXYMETHYLGLYCINATE			
BENZALKONIUM CHLORIDE	Ref. no. 54	1	0,3%
STEARALKONIUM CHLORIDE	Ref. no. 54	1	0,3%
IMIDAZOLIDINYL UREA	Ref. no. 27	1	0,3%
CHLOROACETAMIDE	Ref. no. 41	1	0,3%
CHLORPHENESIN	Ref. no. 50	1	0,3%
SODIUM METABISULFITE	Ref. no. 9	1	0,3%
SODIUM BISULFITE	Ref. no. 9	1	0,3%
HEXAMIDINE PARABEN	Ref. no. 47	1	0,3%
CETRIMONIUM BROMIDE	Ref. no. 44	1	0,3%

TABLE 46
CONTENTS OF PRESERVATIVES IN HAIR STYLING PRODUCTS (POULSEN *ET AL*, 2002).

Product type	Number of products of 328	Number of products containing preservatives (%)
Cream	18	15 (83%)
Gel	74	42 (57%)
Gel spray	16	7 (44%)
Hair spray	98	20 (20%)
Hair straightener	10	8 (80%)
Foam	59	37 (63%)
Wax	48	29 (60%)
Other	5	3 (60%)

TABLE 48
THE PROPORTION OF HAIR STYLING PRODUCTS CONTAINING PRESERVATIVES SPREAD OVER DIFFERENT TYPES OF STUDIED HAIR STYLING PRODUCTS (POULSEN *ET AL*, 2002).

Appendix 4: Indicative list of products considered to be cosmetic products

This is the indicative list of products considered to be cosmetic products, which can be found in Annex I of the previous Cosmetics Regulation (Regulation 422, 2006).

Cream, emulsion, lotion, gel and oil for the skin (hands, face, feet, etc.),
Facial mask,
Coloured foundation (in liquid and solid form, and powder),
Facial powder, bath powder, talcum powder, etc.,
Toilet soap, deodorant soap, etc.,
Perfume, »eau de toilette«, »eau de Cologne«,
Bath products (salt, foam bath, oil, gel, etc.),
Depilatories,
Deodorants and antiperspirants,
Preparations for hair care:

- Hair dyes and bleaching products,
- permanent and extraction fluids, and hair styling products,
- water ondulation fluids,
- hair shampoos (lotion, dry shampoo and shampoo),
- various hair care products (lotion, cream, oil),
- hairdressing products (lotion, spray, brillantine),

Shaving products (soap, shaving cream, lotion, etc.),
Facial make-up and eye make-up, and associated cleansing products,
Lip make-up, lip balm, etc.,
Dental and dental hygiene products,
Nail care products and nail polish,
Products for external intimate hygiene,
Sun oils, etc.,
Tanning products without sun,
Skin-bleaching products,
Anti wrinkle products.

Appendix 5: Number of products for each of the 55 product types

This appendix contains an overview of the number of products studied for the contents of preservatives in this project, ie. the number of products included in this survey. The information is based on the lists of ingredients of the individual products found in the retail trade and in internet shops.

Product type	Comments (the product type also includes)	Number of products in the survey
After shave products		9
Aftersun lotions/sprays	And sun rash products which are not pharmaceuticals	12
Other mouth products	Such as antiplaque tablets	2
Facial creams (day and night)		16
Facial masks	And moisture masks, clay masks, facial peeling, exfoliating cream	10
Facial products for spotty skin	Ie facial wash or scrub for spotty skin, spot pin for spotty skin, wipes, powder for spotty skin, make-up/foundation for spotty skin	11
Facial soap		9
Bath oils		4
Shaving products men/women		11
Bodylotion/creams	Abdominal creams and body gel	20
Bodylotion/creams for "eczema skin"	Or for very dry or sensitive skin, eg fatty creams	9
Body scrubs		6
Body shampoos		17
Deodorants	In the form of sticks, spray, roll-on or cream	35
Various other products*	In the form of skin-bleaching products, fix spray (making make-up last)	0
Various foot products	In the form of foot cream/ointment, heel cream, foot	11

Product type	Comments (the product type also includes)	Number of products in the survey
	bath salt and foot bath oil	
Solid hand soap		9
Liquid hand soap		15
Foundation, BB cream, concealer	BB cream (blemish base) and CC cream (colour corrector). Also contains cover sticks, primers and the like.	17
Hand cream		12
Hair conditioner		20
Hair bleaches	Including bleaching creams for body hair	3
Hair dyes		10
Depilatories	Including wax strips for depilation	5
Hair care products	Such as hair repair, hair serum, hair oil, hair conditioner, shine spray, hair treatment	16
Hair shampoo		31
Hair styling products - various		1
Hair styling products – hair spray		23
Hair styling products - foam/mousse		16
Hair styling products - aqueous hair spray		4
Hair styling products - wax/gel/paste		21
Intimate care products	Such as intimate soap, intimate gel	3
Body oils/massage oils		10
Lip balm/lip gloss		18
Lipstick/lip liner		11

Product type	Comments (the product type also includes)	Number of products in the survey
Make-up remover and cleansers	And cleansing milk, cleansing lotion, facial cleanser and face wash	21
Mascara		15
Mouth rinse liquid		10
Nail polish	And nail glitter	10
Nail polish remover		7
Nail care products or other nail products	Ie. nail creams, nail serum, cuticle agent, cuticle oil, nail polish hardeners, nail pen	9
Perfumes/eau de toilette	Including body scents (body spray)	13
Powder/blush		8
Wipes		13
Anti wrinkle cream and serum		10
Ointment		5
Self-tanning products for face and body		10
Skin tonic		16
Bath foams/shower gels		3
Sunscreens/sun oils	And sun sticks	14
Toothpaste		12
Wipes	Primarily for babies	12
Eye pencils	And eyebrow pencils, eye liner, eye definer	6
Eye creams	And eye gels	8
Eye shadow		10
In total		**639 products**

*THESE OTHER PRODUCTS HAVE NOT BEEN SURVEYED BECAUSE THE PRELIMINARY SURVEY DID NOT INDICATE THESE PRODUCTS TO BE SOLD TO A LARGE EXTENT.

TABLE 49
OVERVIEW OF THE NUMBER OF COSMETIC PRODUCTS STUDIED FOR CONTENTS OF PRESERVATIVES – SPREAD OVER THE 55 PRODUCT TYPES USED IN THIS PROJECT.

Appendix 6: Preservatives used in different groups of cosmetic products

This appendix lists the preservatives used in the five different overall groups of cosmetic products used by the SPT:

- Perfumes and fragrances
- Decorative cosmetics
- Skin care
- Hair care
- Toiletries

The preservatives are indicated in the next five tables - one table for each of the five groups mentioned above.

Preservative	In number of products of 58	As a percentage of the 58 products	As a percentage of the 29 products containing preservatives
Benzyl alcohol	18	31%	62%
Phenoxyethanol	8	14%	28%
Benzoic acid	4	7%	14%
Dehydroacetic acid	3	5%	10%
Methylparaben	3	5%	10%
Ethylparaben	2	3%	7%
Sodium benzoate	2	3%	7%
Triclosan	2	3%	7%
Butylparaben	1	2%	3%
Chlorphenesin	1	2%	3%
Isobutylparaben	1	2%	3%
Potassium sorbate	1	2%	3%
Propylparaben	1	2%	3%
Sodium bisulfite	1	2%	3%
Sorbic acid	1	2%	3%

TABLE 47
PRESERVATIVES IN PERFUMES AND FRAGRANCES – A TOTAL OF 15 DIFFERENT PRESERVATIVES. 29 PRODUCTS OF 58, IE. 50 % DID NOT CONTAIN PRESERVATIVES.

Preservative	In number of products of 97	As a percentage of the 97 products	As a percentage of the 63 products containing preservatives
Phenoxyethanol	42	43%	67%
Methylparaben	22	23%	35%
Propylparaben	15	15%	24%
Chlorphenesin	10	10%	16%
Potassium sorbate	10	10%	16%
Ethylparaben	9	9%	14%
Butylparaben	8	8%	13%
Isobutylparaben	7	7%	11%
Benzyl alcohol	6	6%	10%
Sodium dehydroacetate	6	6%	10%
Sorbic acid	5	5%	8%
Salicylic acid	3	3%	5%
Sodium benzoate	3	3%	5%
Imidazolidinyl urea	2	2%	3%
Isopropylparaben	2	2%	3%
Methylisothiazolinone	2	2%	3%
Benzoic acid	1	1%	2%
Chloroxylenol	1	1%	2%
Formaldehyde	1	1%	2%
Sodium propylparaben	1	1%	2%

TABLE 48
PRESERVATIVES IN DECORATIVE COSMETICS – A TOTAL OF 20 DIFFERENT PRESERVATIVES. 34 PRODUCTS OF 97, IE. 35% DID NOT CONTAIN PRESERVATIVES.

Preservative	In number of products of 241	As a percentage of the 241 products	As a percentage of the 184 products containing preservatives
Phenoxyethanol	130	54%	71%
Sodium benzoate	58	24%	32%
Methylparaben	50	21%	27%
Benzyl alcohol	36	15%	20%
Potassium sorbate	34	14%	18%
Propylparaben	24	10%	13%
Benzoic acid	19	8%	10%
Ethylparaben	16	7%	9%
Dehydroacetic acid	15	6%	8%
Methylisothiazolinone	11	5%	6%
Salicylic acid	11	5%	6%
Sorbic acid	10	4%	5%
Chlorphenesin	9	4%	5%
Butylparaben	8	3%	4%
Sodium dehydroacetate	7	3%	4%
Methylchloroisothiazolinone	6	2%	3%
Isobutylparaben	5	2%	3%
Quaternium-15	3	1,2%	2%
Cetrimonium chloride	2	0,8%	1.1%
Imidazolidinyl urea	2	0,8%	1.1%
Sodium metabisulfite	2	0,8%	1.1%
Benzalkonium chloride	1	0,4%	0.5%
Chlorhexidine dihydrochloride	1	0,4%	0.5%

Preservative	In number of products of 241	As a percentage of the 241 products	As a percentage of the 184 products containing preservatives
Diazolidinyl urea	1	0,4%	0.5%
DMDM Hydantoin	1	0,4%	0.5%
Myrtrimonium bromide	1	0,4%	0.5%
Polyaminopropyl biguanide	1	0,4%	0.5%
Potassium benzoate	1	0,4%	0.5%
Propionic acid	1	0,4%	0.5%
Sodium bisulfite	1	0,4%	0.5%
Sodium hydroxymethylglycinate	1	0,4%	0.5%
Sodium salicylate	1	0,4%	0.5%
Sodium sorbate	1	0,4%	0.5%
Sodium sulfite	1	0,4%	0.5%

TABLE 49
PRESERVATIVES IN SKIN CARE PRODUCTS – A TOTAL OF 35 DIFFERENT PRESERVATIVES. 57 PRODUCTS OF 241, IE. 24% DID NOT CONTAIN PRESERVATIVES.

Preservative	In number of products of 145	As a percentage of the 145 products	As a percentage of the 98 products containing preservatives
Phenoxyethanol	56	39%	57%
Benzyl alcohol	39	27%	40%
Sodium benzoate	36	25%	37%
Cetrimonium chloride	27	19%	28%
Methylparaben	26	18%	27%
Methylisothiazolinone	20	14%	20%
Benzoic acid	18	12%	18%
Methylchloroisothiazolinone	17	12%	17%
Potassium sorbate	16	11%	16%
Behentrimonium chloride	12	8%	12%
DMDM Hydantoin	12	8%	12%
Dehydroacetic acid	11	8%	11%
Ethylparaben	11	8%	11%
Propylparaben	9	6%	9%
Sodium sulfite	7	5%	7%
Sodium methylparaben	5	3%	5%
Butylparaben	3	2%	3%
Formic acid	3	2%	3%
Polyaminopropyl biguanide	3	2%	3%
Sodium metabisulfite	3	2%	3%
Chlorhexidine	2	1.4%	2%
Isobutylparaben	2	1.4%	2%
Quaternium-15	2	1.4%	2%
Salicylic acid	2	1.4%	2%

Preservative	In number of products of 145	As a percentage of the 145 products	As a percentage of the 98 products containing preservatives
Sodium salicylate	2	1.4%	2%
Chlorhexidine digluconate	1	0.7%	1.0%
Chloroacetamide	1	0.7%	1.0%
Diazolidinyl urea	1	0.7%	1.0%
Imidazolidinyl urea	1	0.7%	1.0%
Piroctone olamine	1	0.7%	1.0%
Sorbic acid	1	0.7%	1.0%
Stearalkonium chloride	1	0.7%	1.0%
Steartrimonium chloride	1	0,7%	1,0%

TABLE 50
PRESERVATIVES IN HAIR CARE PRODUCTS – A TOTAL OF 33 DIFFERENT PRESERVATIVES. 47 PRODUCTS OF 145, IE. 32% DID NOT CONTAIN PRESERVATIVES.

Preservative	In number of products of 98	As a percentage of the 98 products	As a percentage of the 32 products containing preservatives
Sodium benzoate	43	44%	63%
Phenoxyethanol	24	24%	35%
Benzoic acid	18	18%	26%
Benzyl alcohol	9	9%	13%
Dehydroacetic acid	9	9%	13%
Potassium sorbate	8	8%	12%
Methylisothiazolinone	7	7%	10%
Methylparaben	4	4%	6%
Sodium salicylate	4	4%	6%
Methylchloroisothiazolinone	3	3%	4%
2-bromo-2-nitropropane-1,3-diol	2	2%	3%
Sorbic acid	2	2%	3%
Benzalkonium chloride	1	1%	1%
Cetrimonium chloride	1	1%	1%
Chlorhexidine diacetate	1	1%	1%
Formic acid	1	1%	1%
Methyl benzoate	1	1%	1%
Quaternium-15	1	1%	1%
Sodium methylparaben	1	1%	1%
Sodium propylparaben	1	1%	1%

TABLE 51
PRESERVATIVES IN TOILETRIES – A TOTAL OF 20 DIFFERENT PRESERVATIVES. 32 PRODUCTS OF 98, IE. 33% DID NOT CONTAIN PRESERVATIVES.

Appendix 7: Classification of biocidal product types

Number	Product type	Description
Main group 1: Disinfectants These product types exclude cleaning products that are not intended to have a biocidal effect, including washing liquids, powders and similar products.		
PT 1	Human hygiene	Products in this group are biocidal products used for human hygiene purposes, applied on or in contact with human skin or scalps for the primary purpose of disinfecting the skin or scalp.
PT 2	Disinfectants and algaecides not intended for direct application to humans or animals	Used for the disinfection of surfaces, materials, equipment and furniture which are not used for direct contact with food or feeding stuffs. Usage areas include, inter alia, swimming pools, aquariums, bathing and other waters; air conditioning systems; and walls and floors in private, public, and industrial areas and in other areas for professional activities. Used for disinfection of air, water not used for human or animal consumption, chemical toilets, waste water, hospital waste and soil. Used as algaecides for treatment of swimming pools, aquariums and other waters and for remedial treatment of construction materials. Used to be incorporated in textiles, tissues, masks, paints and other articles or materials with the purpose of producing treated articles with disinfecting properties.
PT 3	Veterinary hygiene	Used for veterinary hygiene purposes such as disinfectants, disinfecting soaps, oral or corporal hygiene products or with anti-microbial function. Used to disinfect the materials and surfaces associated with the housing or transportation of animals.
PT 4	Food and feed area	Used for the disinfection of equipment, containers, consumption utensils, surfaces or pipework associated with the production, transport, storage or consumption of food or feed (including drinking water) for humans and animals. Used to impregnate materials which may enter into contact with food.
PT 5	Drinking water	Used for the disinfection of drinking water for both humans and animals.
Main group 2: Preservatives Unless otherwise stated these product-types include only products to prevent microbial and algal development.		
PT 6	Preservatives for products during storage	Used for the preservation of manufactured products, other than foodstuffs, feeding stuffs, cosmetics or medicinal products or medical devices by the control of microbial deterioration to ensure their shelf life. Used as preservatives for the storage or use of rodenticide, insecticide or other baits.
PT 7	Film preservatives	Used for the preservation of films or coatings by the control of microbial deterioration or algal growth in order to protect the initial properties of the surface of

Number	Product type	Description
		materials or objects such as paints, plastics, sealants, wall adhesives, binders, papers, art works.
PT 8	Wood preservatives	Used for the preservation of wood, from and including the saw-mill stage, or wood products by the control of wood-destroying or wood-disfiguring organisms, including insects. This product type includes both preventive and curative products.
PT 9	Fibre, leather, rubber and polymerised materials preservatives	Used for the preservation of fibrous or polymerised materials, such as leather, rubber or paper or textile products by the control of microbiological deterioration. This product type includes biocidal products which antagonise the settlement of micro-organisms on the surface of materials and therefore hamper or prevent the development of odour and/or offer other kinds of benefits.
PT 10	Construction material preservatives	Used for the preservation of masonry, composite materials, or other construction materials other than wood by the control of microbiological and algal attack.
PT 11	Preservatives for liquid-cooling and processing systems	Used for the preservation of water or other liquids used in cooling and processing systems by the control of harmful organisms such as microbes, algae and mussels. Products used for the disinfection of drinking water or of water for swimming pools are not included in this product type.
PT 12	Slimicides	Used for the prevention or control of slime growth on materials, equipment and structures, used in industrial processes, e.g. on wood and paper pulp, porous sand strata in oil extraction.
PT 13	Working or cutting fluid preservatives	Products to control microbial deterioration in fluids used for working or cutting metal, glass or other materials.
Main group 3: Pest control		
PT 14	Rodenticides	Used for the control of mice, rats or other rodents, by means other than repulsion or attraction.
PT 15	Avicides	Used for the control of birds, by means other than repulsion or attraction.
PT 16	Molluscicides, vermicides and products to control other invertebrates	Used for the control of molluscs, worms and invertebrates not covered by other product types, by means other than repulsion or attraction.
PT 17	Piscicides	Used for the control of fish, by means other than repulsion or attraction.
PT 18	Insecticides, acaricides and products to control other arthropods	Used for the control of arthropods (e.g. insects, arachnids and crustaceans), by means other than repulsion or attraction.
PT 19	Repellents and attractants	Used to control harmful organisms (invertebrates such as fleas, vertebrates such as birds, fish, rodents), by repelling or attracting, including those that are used for human or veterinary hygiene either directly on the skin or indirectly in the environment of humans or animals.
PT 20	Control of other vertebrates	Used for the control of vertebrates other than those already covered by the other product types of this main

Number	Product type	Description
		group, by means other than repulsion or attraction.
Main group 4: Other biocidal products		
PT 21	Antifouling products	Used to control the growth and settlement of fouling organisms (microbes and higher forms of plant or animal species) on vessels, aquaculture equipment or other structures used in water.
PT 22	Embalming and taxidermist fluids	Used for the disinfection and preservation of human or animal corpses, or parts thereof.

Survey and health and environmental assessment of preservatives in cosmetic products

The survey of more than 600 cosmetic products identified a total of 53 preservatives. Based on the environmental and health screenings the following 5 were investigated: DMDM hydantoin, imidazolidinyl urea, zinc pyrithione, thimerosal and phenoxyethanol. The study showed risk of allergy using: DMDM hydantoin, imidazolidinyl urea and thimerosal, but because of insufficient data for the substances it was impossible to set a maximum concentration limit value and to calculate a risk by the allowed concentration. Furthermore the risk assessment showed that use of the products is safe, at the maximum allowed concentration of the 5 preservatives too. The survey showed that phenoxyethanol is the most widely used preservative. Therefore use of many cosmetic products is not unrealistic, all containing phenoxyethanol. To get more knowledge about the specific content of various types of cosmetic products, 30 products were selected for analysis of phenoxyethanol. The literature search showed more values for skin absorption and NOAEL for phenoxyethanol, and it was demonstrated that these can significantly change the risk calculation. At the most critical values and with the measured concentrations of phenoxyethanol a risk calculation showed no risk by daily exposure to phenoxyethanol from 14 everyday cosmetic products. However based on the maximum allowed concentration of phenoxyethanol in all 14 products, there is a risk by daily use of them. EU focus already on phenoxyethanol and the SCCP is currently assessing the safety of the substance in cosmetic products and if the maximum concentration of 1% is safe for all ages.

Ministry of Environment and Food
The Danish Environmental Protection Agency

Strandgade 29
DK-1401 Copenhagen K
Tel.: (+45) 72 54 40 00

www. mst.dk