



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

Cosmetovigilance in The Netherlands
Trend report 2012 - 2013

RIVM Letter Report 090128001/2013
L. de Wit-Bos et al.



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Colophon

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Rapport in het kort

Huidklachten door cosmetische producten

Tendrapportage 2012 – 2013

Cosmetica zijn in principe veilig, maar kunnen soms huidklachten veroorzaken, zoals roodheid en jeuk. Het RIVM beheert een systeem waarin deze klachten en andere overgevoeligheidsreacties na gebruik van cosmetica kunnen worden geregistreerd (CESES, Consumer Exposure Skin Effects and Surveillance).

Net als in voorgaande jaren zijn dergelijke klachten in 2012-2013 vooral gemeld na het gebruik van haarproducten, huidverzorgingsproducten en make-up. De klachten doen zich vooral voor bij producten die bedoeld zijn voor gebruik op of rond de ogen. Daarnaast hebben relatief veel kappers contacteczeem op de handen na het gebruik van haarproducten op hun werk.

Isothiazolinonen, gebruikt als conserveringsmiddel in cosmetica, en geurstoffen blijven de ingrediënten die het vaakst allergische reacties veroorzaken. Extra aandacht voor isothiazolinonen, zowel wat betreft regelgeving als onderzoek, is van belang, omdat deze stoffen ook in andere consumenten- en industriële producten gebruikt worden. Dit maakt het voor consumenten die overgevoelig zijn voor isothiazolinonen lastig om deze stoffen te vermijden. Voor kappers blijven ammoniumpersulfaat en PPD de belangrijkste veroorzakers van contacteczeem. Net als in voorgaande jaren zijn in 2012 en 2013 allergische reacties gemeld op het UV-filter octocryleen, dat in zonnebrandcrème zit, en op co-/crosspolymeren, die ook in bepaalde crèmes gebruikt worden.

CESES wordt gebruikt om na te gaan of Europese wetgeving en handhaving de consument voldoende beschermt. Ook kunnen risico's voor werknemers worden geïdentificeerd. Consumenten kunnen zelf hun klacht melden via de website www.cosmeticaklachten.nl. Daarnaast registreren deelnemende dermatologen huidklachten van patiënten waarbij cosmetica de mogelijke oorzaak zijn. Bij deze patiënten wordt vervolgens een allergieonderzoek uitgevoerd om vast te stellen welk(e) productingrediënt(en) de klacht veroorzaakt.

Abstract

Cosmetovigilance in The Netherlands

Trend report 2012 - 2013

Cosmetics are in principle safe to use. In some cases however, cosmetic products may lead to undesirable reactions, such as itching and erythema. RIVM has set up a monitoring system in which undesirable reactions as well as other allergic reactions caused by cosmetics can be registered (CESES, Consumer Exposure Skin Effects and Surveillance).

As in previous years, such reactions are mainly reported after the use of hair products, skin products and make-up, including primarily those products intended to use on or around the eyes. In addition, relatively many hairdressers reported contact dermatitis located on the hands after the use of hair products at their work.

Isothiazolinones, a preservative in cosmetics, and fragrances remain the cosmetic ingredients relatively most responsible for allergic reactions. More attention to isothiazolinones is especially important, because these ingredients are also widely used in other consumer and industrial products. As a result, it is difficult for consumers, who are allergic to isothiazolinones, to avoid these ingredients. Ammonium persulfates and PPD remain the most important causative agents for contact dermatitis in hairdressers. As in previous years, allergic reactions to the UV filter octocrylene, which is used in sunscreens, and co/cross polymers, which are used in several creams, were reported.

The goal of CESES is to monitor undesirable reactions attributable to cosmetics and cosmetic ingredients to assess whether current EU legislation on cosmetics provides adequate consumer protection. Also, risks for workers can be identified. Consumers can report allergic reactions on the website www.cosmeticaklachten.nl. In addition, participating dermatologists report cases of contact dermatitis to the system when cosmetics are expected to be the cause. Dermatologists also carried out patch tests and, where necessary, tests with specific batch ingredients of the associated cosmetic product.

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Summary

Since 2009, the CESES project, aiming at collecting data on undesirable reactions attributed to cosmetic products, is in operation. So far, almost 2500 reports have been received. In the current trend report, reports from consumers and dermatologists in the period October 2012 – October 2013 were analysed.

In this period, 244 consumers reported relevant cases of undesirable reactions. The reactions were mainly localised on or around the eyes/eyelashes, the face, the neck or on the scalp, and symptoms primarily included erythema, itching and a burning sensation. Reported cosmetic products were mainly facial care products, make-up and hair products. This is well in line with the location where most of the cosmetic products, allegedly responsible for the reaction, are used. A large part of the consumers applied self-treatment and did not visit a general practitioner and subsequently, a dermatologist.

Dermatologists reported 66 new cases of undesirable reactions in the period October 2012 – October 2013. Occupational exposure to allergens was probably related to the development of the undesirable reaction in about a quarter of the patients. The undesirable reactions were primarily located on the hands and face. Reported symptoms included mainly erythema, itching and scaling, in a few cases pain and in one case breathing problems. The most frequently reported product categories were hair products, skin products, make-up and sunscreen/tanning products.

In the clinical route, the causative allergen was confirmed by conducting diagnostic patch testing. When all results obtained since the start of the CESES project are included, it is shown the most prevalent allergens in patients were methyl(chloro)isothiazolinone (26%), fragrance mix I (25%), nickel sulphate (22%) and fragrance mix II (18%). Of the hairdressers, 60% tested positive for ammonium persulfate, 33% for p-phenylenediamine (PPD), and 19% for methyl(chloro)isothiazolinone. Patch testing with the batch-specific ingredients of the cosmetic product(s) showed that 55% of the 46 patients with a positive response developed a reaction to surfactants and/or emulsifying agents, 21% to preservatives, and 19% to fragrances. Furthermore, regarding cosmetic ingredients that received special attention the past years, one patient showed a positive response to acrylates/C10-30 alkyl acrylate crosspolymer in a sunscreen and one patient showed a positive response to the UV-filter octocrylene.

Compared to the previous trend report (2011-2012), the same observations were generally made regarding the persons who experienced an undesirable reaction, the description of the reaction and the cosmetic product(s) involved. With respect to the reports from dermatologists, the cases reported by the Centrum voor Huid en Arbeid concerned occupational exposure-related cases, mainly hairdressers, with a different pattern of symptoms, location, cosmetic products and patch test results than the other patients seen by dermatologists.

Based on the CESES reports published so far, the most important cosmetic allergens in The Netherlands remain isothiazolinones and fragrances. These ingredients should be closely monitored, which will be facilitated when methylisothiazolinone is included in the European baseline patch test series as used by dermatologists. It is important to consider that besides cosmetics, household and industrial products also largely contribute to the exposure to isothiazolinones and isothiazolinone-related cases of contact dermatitis, and a

combined approach when reassessing the safety of isothiazolinones is needed. Isothiazolinones are not yet regulated in those areas. Persulfates, especially ammonium persulfate, and PPD remain the most important allergens for hairdressers. Awareness, avoidance and the use of protective measures (gloves) may help to prevent the development of reactions to these cosmetic ingredients. For successful monitoring of these allergens within CESES, awareness among consumers by continuous communication to the public about the possibility to report undesirable reactions is essential.

1 Introduction

In 2009, RIVM initiated, on request of NVWA and VWS, the CESES project, aiming at monitoring undesirable reactions attributed to cosmetic products. These monitoring data could contribute to the assessment of whether current EU legislation on cosmetics provides adequate protection. In addition, other goals are to gain insight in the incidence and prevalence of undesirable reactions to cosmetics and assist in the identification of cosmetic products and product ingredients responsible for undesirable reactions. A complete overview of the background of the CESES project can be found in previous reports (Salverda-Nijhof et al., 2011; de Wit-Bos et al., 2012).

Under the European Cosmetic Products Regulation, the cosmetic industry is obliged to have an own cosmetovigilance system (EC No 1223/2009). According to this Regulation, the cosmetic industry is obliged to notify Competent Authorities (CAs) in case of serious undesirable effects (SUEs). Based on this obligation extreme severe reactions will be registered and notified, i.e. in case of temporary or permanent functional incapacity, disability, hospitalisation, congenital anomalies or an immediate vital risk or death. Many undesirable reactions, as described in this report, will not meet these criteria and will therefore not be notified to CAs. Furthermore, trends in undesirable reactions due to occupational exposure and the prevalence of undesirable reactions attributed to specific allergens are not reported by industry. A cosmetovigilance system such as CESES is therefore a valuable addition to the Cosmetics Products Regulation.

In the current report, consumer and dermatologist reports received in the period 1 October 2012 – 1 October 2013 are analysed and discussed (see Chapters 3 and 4). An overall summary and discussion of the results is presented in Chapter 5. Conclusions and recommendations based on the reported cases of on undesirable reactions attributed to cosmetic products can be found in Chapter 6.

2 Goal and set-up of the CESES project

The goal and set-up are extensively described in a previous report of the CESES project and in a scientific paper (Salverda-Nijhof et al., 2011; Salverda et al., 2013).

Consumer reports were collected via the online questionnaire on the website www.cosmeticaklachten.nl. Dermatologists who reported undesirable reactions the past year were part of eight participating dermatological centres. These dermatological centres included academic hospitals (UMCU, VUmc, LUMC and UMCG), peripheral hospitals (Deventer Hospital, Reinier de Graaf Hospital and St. Antonius Hospital), and a referral centre for occupational skin diseases (Centrum voor Huid en Arbeid).

Within the CESES project, an undesirable reaction is defined as any adverse effect attributed to the use of cosmetics under reasonably foreseeable conditions.

3 Overview of consumer reports

In the period 1 October 2012 – 1 October 2013, 246 consumers reported an undesirable reaction via de website www.cosmeticaklachten.nl. In two cases (1%) however, no detailed information on the cosmetic product was available or the product did not concern a cosmetic product and therefore these cases were excluded.

3.1 General description of the consumer reports

Figure 3-1 provides an overview of the number of consumer reports registered per month. The number of reported cases shows a rather erratic course with a minimum of three reported cases per month and a maximum of 55 cases per month. The increases in the number of reported undesirable reactions are directly linked to moments of media attention. For example, in December 2012 an interview with RIVM about CESES was published on www.gezondheidsplein.nl for the December theme 'Beauty during the holidays' (see Appendix I).

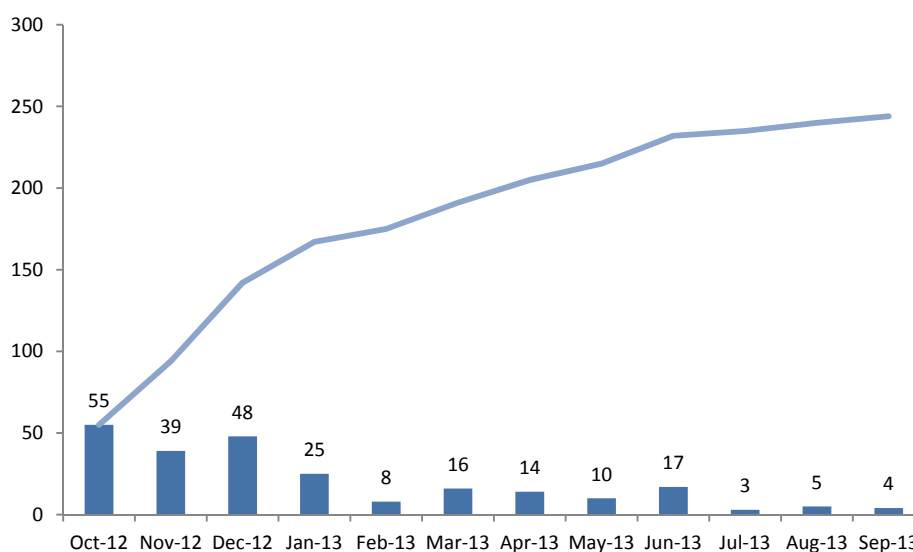


Figure 3-1 Number of usable reports per month and cumulative number between 1 October 2012 and 1 October 2013.

As observed previously, most undesirable reactions were reported by women (96%, n=235). Approximately three-quarter of the consumers with an undesirable reaction was between 20 and 50 years of age. Twenty-one reports (8%) concerned children or young adults (0-19 years). The average age of the consumer population reporting an undesirable reaction in CESES is 39 years of age.

3.2 Description of the undesirable reaction

The undesirable reactions could be characterised by several symptoms, of which erythema (18%, n=181), itching (17%, n=177), and a burning sensation (16%, n=164) were the most reported symptoms (Appendix II, Figure II-1). Severe

reactions, including pain, nausea, breathing problems, blistering, dizziness, burns and hair loss, were responsible for 11% (n=114) of the symptoms mentioned. These severe reactions concerned in most cases pain (n=83).

Most of the undesirable reactions occurred around the eyes or on the eyelashes (32%, n=150) and on the face (26%, n=124) (Appendix II, Figure II-2). In addition, the neck and scalp were relatively often mentioned as the location where the undesirable reaction occurred. This is in line with what was observed in previous reports that most of the undesirable reactions attributed to cosmetics use occur on or close to the head region. This is well in line with the location where most of the cosmetic products, allegedly responsible for the reaction, are used. The reported cosmetic products were primarily used on the face (39%, n=110) followed by on/around the eyes and eyelashes (23%, n=63) (Appendix II, Figure II-3). Also, hair (10%, n=27), neck (9%, n=24), and scalp (6%, n=17) were relatively often mentioned.

For a large part of the consumers who reported an undesirable reaction (73%, n=177), it was the first time they experienced an adverse effect after using the cosmetic product. For the majority (58%, n=37) of the consumers who had experienced a reaction before, the current reaction was equally severe.

Most consumers (70%, n=172) stated that the undesirable reaction began on the same day as the cosmetic product was applied. For about a third of these consumers (n=53) the undesirable reaction developed within 30 minutes. At the time of completing the CESES questionnaire, 76% (n=186) reported to still suffer from the undesirable reaction.

3.3 Cosmetic products

Of the consumers, 90% (n=220) was able to report the cosmetic product(s) that probably caused the undesirable reaction. In total, 254 cosmetic products were mentioned. Figure 3-2 shows to which product categories the reported products belong.

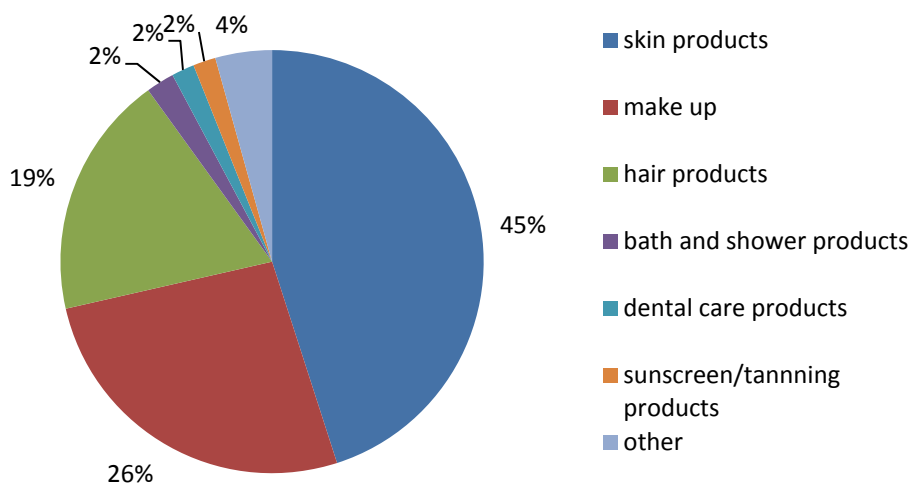


Figure 3-3 Reported product categories that probably caused undesirable reaction in % (n=231). The category other includes perfumes and deodorants and some other products.

Approximately half of the cosmetic products probably responsible for the undesirable reactions were skin products (45%, n=104). These concerned mainly facial care products (80%, n=83), and more specifically leave-on day and night creams (84%, n=70). Products for the delicate eye area, i.e. for example eye-contour creams, were mentioned less often than in previous years. Facial cleaning products were held responsible for the undesirable reaction in 16% (n=17) of the cases. Make-up (26%, n=61) is the second largest product category reported by consumers as the probable cause. Reported products within this product category were generally designed for application on or around the eyes (77%, n=47), such as mascara, eyeliner and eye shadow. Hair products (19%, n=43) complete the top three most-reported product categories. Within this product category, reports concerned mainly (permanent) hair dyes (60%, n=26) followed by hair care products (40%, n=17). Other product categories, such as perfumes and child care products, were only seldom mentioned.

Table 3-1 provides an overview of the market shares of the different product categories and the percentage of undesirable reactions per product category, as reported by consumers, when corrected for their market share. In previous years, the correction for market share led to a different top three with respect to which product categories were primarily responsible for the undesirable reactions. The current reports do not lead to a shift, and the top three remains: 1) Skin products, 2) Make-up, and 3) Hair products.

Table 3-1 Relative contribution of product categories when corrected for market share (Source: NCV, 2012).

Product category	Market share (%)	Number of undesirable reactions CESES	Corrected for market share	
Skin products	19	104	547	35.4%
Make-up	15	61	412	26.7%
Hair products	16	43	270	17.5%
Sunscreen/tanning products	3	4	138	8.9%
Bath and shower products	7	5	68	4.4%
Dental care products	7	4	55	3.5%
Deodorant	7	3	45	2.9%
Perfumes	19	2	11	0.7%
Shaving products	1	0	0	0%
Soap	2	0	0	0%

3.4 Factors possibly related to the undesirable reaction

Around a quarter of the consumer population (23%, n=55) reporting an undesirable reaction probably attributed to cosmetics suffers from other skin problems, including irritant or allergic contact dermatitis (42%, n=23) and atopic dermatitis (18%, n=10). Underlying allergies (38%, n=92) were also reported, and included mainly allergies for pollen (51%, n=47), drugs (11%, n=28), metals, like nickel (11%, n=27), and food products (11%, n=26).

By far the majority of the consumers (95%, n=232) did not expect their occupation to be related to the undesirable reaction. In addition, as no specific details on the occupation were given by consumers, occupational exposure is not further addressed here.

3.5 Diagnosis and treatment

A large part of the consumers (61%, n=142) applied self-treatment. This self-treatment consisted of applying a soothing (fatty) cream, washing or cooling the location where the undesirable reaction occurred, stopping the use of the cosmetic product and starting the use of an alternative product or not, or a combination of these measures. However, after refraining from using the cosmetic product, 25% (n=62) of the consumers still suffered from the undesirable reaction. Several reasons may be the responsible for this. It may be that either it takes some time before the reaction has completely disappeared, that the cosmetic product was not responsible for the development of the undesirable reaction, or that the cosmetic product(s) that was used as an alternative resulted in the same kind of undesirable reactions.

The undesirable reaction was for 29% (n=70) of the consumers a reason to visit the general practitioner (GP). In 93% of the cases (n=65), the GP advised treatment which mainly consisted of a prescription for medication (78%, n=51), such as a corticosteroid cream or antihistamines or a combination of both. Twenty consumers (8%) were redirected to a dermatologist and received treatment in 85% of the cases (n=17). Treatment entailed the application of a (corticosteroid) cream or undergoing a patch test. Medication was prescribed in 50% of the cases (n=10) and a patch test in 70% (n=14). Nine of the consumers that underwent a patch test were tested positive for one or more allergens, being for example methylisothiazolinone (MI), colophonium or specific cosmetic products.

3.6 Contact to manufacturer or retailer

As observed in previous years, consumers are not inclined to contact the manufacturer or retailer of the cosmetic product(s) they hold responsible for the undesirable reaction. Around 18% of the consumers (n=43) went back to the shop where they bought the cosmetic product and 12% (n=30) of the consumers contacted the manufacturer.

4 Overview of reports from dermatologists

The reports from dermatologists were analysed in different ways in order to allow a trend comparison between the current report and the previous CESES reports. Also a general overview of all data gathered in the period 2009 – 2013 is provided in this overview. As a result, the following set-up is used:

- For the general analysis (i.e. demographics, occupation, description of the undesirable reaction, product information) it was decided to include those reports that were initiated and finalised in the period between 1 October 2012 and 1 October 2013 for trend comparison.
- For analysis of the patch tests with the European Baseline series and for the patch test with batch-specific ingredients of the cosmetic products, including the causality assessment, all reports of undesirable reactions received since the start of the CESES project until 1 October 2013 were included.

4.1 Number of undesirable reactions

In the period between 1 October 2012 and 1 October 2013, dermatologists initiated and finalised 66 reports of undesirable reactions. Figure 4-1 shows the number of reports received by dermatologists per month. On average, five reports were received each month but actual numbers varied between 1 and 12 reports.

Figure 4-2 shows the number of reports per participating dermatological centre in a certain period. In the period between 1 October 2012 and 1 October 2013, most reports were received from the Centrum voor Huid en Arbeid. On the other hand, in total, most reports were received from VUmc.

4.2 General description of the reports from dermatologists

Of the 66 reports received in the period October 2012 – October 2013, 82% (n=54) concerned women. Most patients were between 20 and 70 years of age, with a quarter of the patient population being in their twenties. The average age of the patients was 40 years.

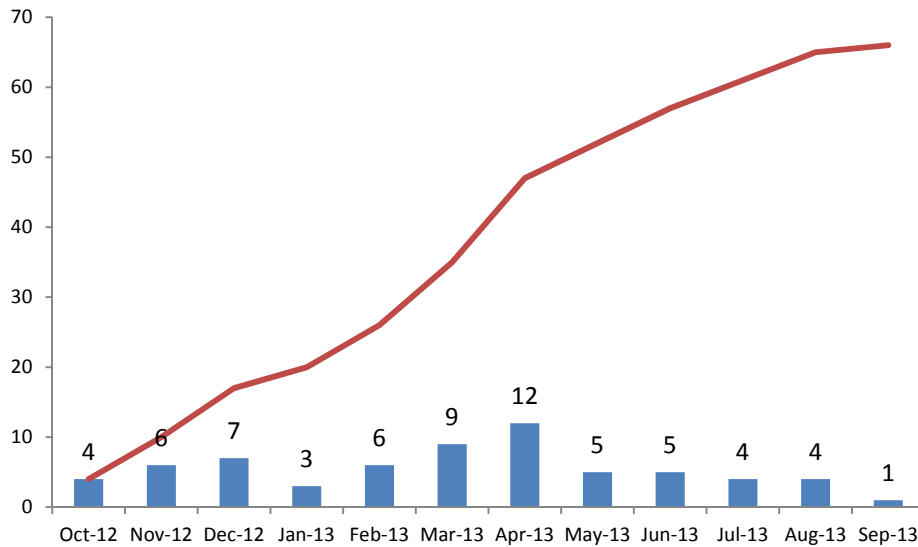


Figure 4-1 Number of usable reports per month and cumulative numbers between 1 October 2012 and 1 October 2013.

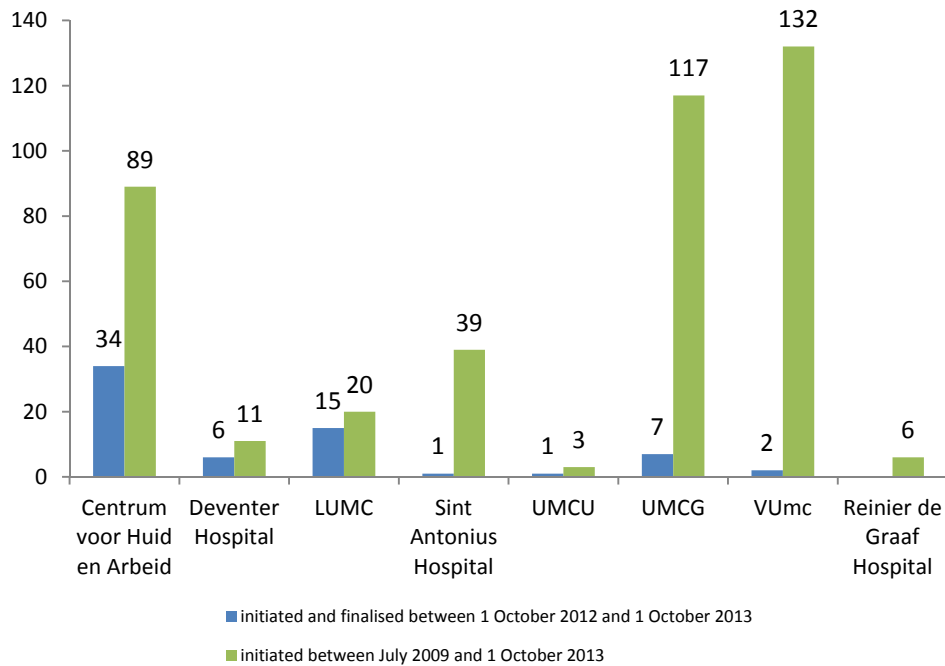


Figure 4-2 Number of usable reports per participating dermatological centre.

4.3 Description of the undesirable reaction

A comparable picture as in previous years was observed with respect to the description of the undesirable reaction. Half of the undesirable reactions reported during the period October 2012 – October 2013 were located on the hands (25%, n=31) and on the face (25%, n=30) (Appendix III, Figure III-1). In addition, relatively many undesirable reactions were observed on the arms (12%, n=15) and on or around the eyes (10%, n=12). The relatively many

reactions on the hands are for a large part related to the reports from the Centrum voor Huid en Arbeid. These reports concern mainly cases about undesirable reactions due to occupational exposure.

The reported symptoms included mainly erythema (22%, n=60), itching (21%, n=58) and scaling (17%, n=48). Furthermore, vesicles (11%, n=30), oedema and papules (both 10%, n=28) were relatively frequently reported (Appendix III, Figure III-2). Severe reactions were observed in seven cases (2%) and consisted of pain in six patients and of breathing problems in one patient.

Most patients stated that they did not know when the undesirable reaction has started, and about half of all patients still suffered from the reaction when they visited the dermatologist. For 53% (n=35) it was the first time they had an undesirable reaction to the respective cosmetic product.

4.4 Cosmetic products

For all patients involved, the dermatologists could report one or more cosmetic products to be allegedly responsible for the undesirable reaction. They reported, in total, 170 products. The most frequently reported product category was hair products (62%, n=106) followed by skin products (21%, n=35), see Figure 4-3. The top three is completed with sunscreen/tanning products, but that included only 5% (n=9) of all mentioned products.

The hair products mainly included hair styling products (56%, n=59) and hair dyes, especially permanent hair dyes and bleaching products (36%, n=38). Skin products contributing to the development of undesirable reactions were especially leave-on facial care products (40%, n=14), such as day and night creams, or body care products (34%, n=12), such as body creams.

4.5 Factors possibly related to the undesirable reaction

Of the patients that visited the dermatologist in the period October 2012 – October 2013, occupation could be related to the undesirable reaction in 26% of the cases (n=17) or was maybe related in 8% of the cases (n=5). These cases included primarily hairdressers. Twenty-eight patients (42%) suffered from an underlying skin problem, mostly atopic dermatitis, and 11 patients (17%) from an allergy, mainly to fragrances. Of these patients, three suffered from both an underlying skin problem and an allergy.

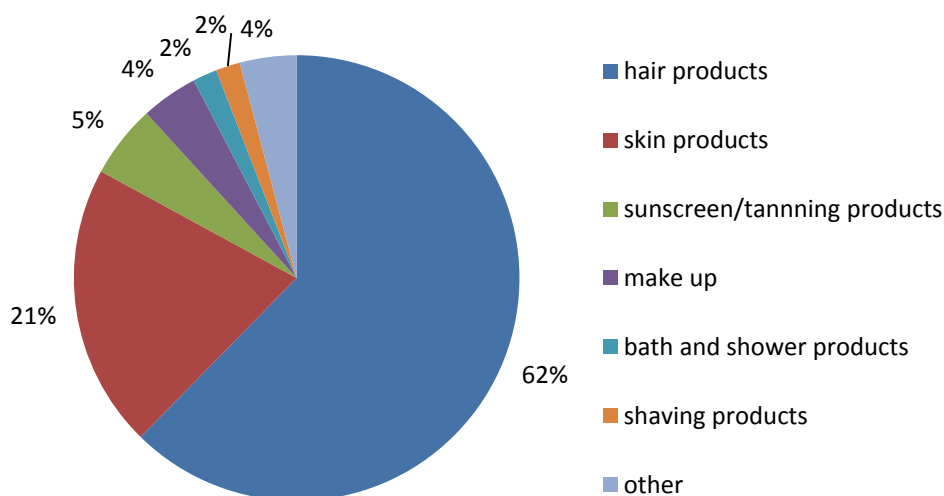


Figure 4-3 Reported product categories that probably caused undesirable reaction in % (n=170). The category other includes among others deodorants and perfumes.

4.6 Diagnosis and treatment

Based on the medical history, physical examination and the results of diagnostic patch testing, 50% of the patients (n=33) were diagnosed with allergic contact dermatitis. In addition, 21% was diagnosed with a combination of allergic contact dermatitis, atopic dermatitis and irritant contact dermatitis. Other diagnoses generally included photo-allergic contact dermatitis, a combination of allergic contact dermatitis and irritant contact dermatitis, or a combination of allergic contact dermatitis with atopic dermatitis. The final diagnosis led in 20% of the cases (n=13) to an adjustment in the prescribed treatment or the start of a new treatment. In these cases, therapy consisted of refraining from using the cosmetic product.

4.7 Patch tests

Since the start of the CESES project in 2009, 417 patients seen by dermatologists with an undesirable reaction probably attributed to cosmetic products have been patch tested with the European baseline series. For 94% of these patients (n=390) a positive response to one or more allergens was observed, mainly to methylchloroisothiazolinone (MCI)/methylisothiazolinone (MI) and/or MI (26%, n=101), fragrance mix I (25%, n=97), nickel sulphate (22%, n=87), fragrance mix II (18%, n=72) and PPD (15%, n=60) (see Table 4-1). Ammonium persulfate, a frequent contact allergen in hairdressers, was one of the responsible allergens in 11% of the patients with a positive response.

Table 4-1 Patch test results with European baseline series and additional substances in patients seen by participating dermatologists since the start of the CESES project in 2009 (top 10).

Allergen	% positive
methyl(chloro)isothiazolinone (MI and Kathon CG ® (MCI/MI)) ¹	26%
fragrance mix I ²	25%
nickel sulphate	22%
fragrance mix II ³	18%
p-phenylene diamine (PPD)	15%
cocamidopropyl betaine (CAPB)	13%
ammonium persulfate	11%
methyldibromo glutaronitrile (MDBGN)	10%
lanoline (wolvet)	9%
myroxylon pereirae	8%

For some ingredients mentioned in Table 4-1, such as MI and PPD, concentration limits are established (EC No 1223/2009). MI may be used in cosmetic products up to a maximum concentration of 0.01% and the combination MCI/MI (3:1) up to concentrations of 0.0015%. PPD can be used in cosmetics at a maximum on-head concentration of 2% (calculated as free base). Use of the fragrance ingredient hydroxyisohexyl 3-cyclohexene carboxaldehyde (HICC, Lyril ®) must be mentioned in the list of ingredients on the label of the cosmetic product when its concentration exceeds 0.001% in leave-on products and 0.01% in rinse-off products. This obligation also applies to 25 other fragrances, such as cinnamyl alcohol and eugenol, for the same concentration limits. The use of nickel sulphate and methyldibromo glutaronitrile (MDBGN) in cosmetics is prohibited, which means that these reactions are likely not the result of using cosmetics at the present time.

For completeness, the same analysis was conducted for the patients seen by dermatologists in the period 1 October 2012 – 1 October 2013. The patch test results in these groups of patients are presented in Appendix IV.

An additional patch test with the batch-specific ingredients of the cosmetic product was requested for 154 of the 417 cases (37%) reported in the period July 2009 – October 2013. This patch test resulted in positive responses to one or more of the tested ingredients in 46 patients so far. The results show that 26 patients (55%) developed a reaction to surfactants and/or emulsifying agents, 10 patients (21%) to preservatives, nine patients (19%) to fragrances and seven patients (15%) to viscosity controlling substances. Appendix V provides a more detailed overview of the outcomes of the batch-specific patch tests. In the past, special attention was given to co/cross polymers for which several patients tested positive and to the UV-filter octocrylene. In the current period, one additional patient showed a positive response to an acrylates/C10-30 alkyl acrylate crosspolymer in a sunscreen. In addition, one other case of a positive response to the UV filter octocrylene was observed.

¹ All reactions to MI and/or MCI/MI are added, hence it is possible that a patient is counted twice. Of all patients with a positive patch test result, 5% had a positive response to MI and 16% to MCI/MI, and 2% to both MI and MCI/MI.

4.8 Causality assessment

Based on the outcomes of the patch test with the European Baseline patch test series and the cosmetic product itself, the final diagnosis, and, when performed, the patch test with batch-specific ingredients of the cosmetic product, a causality assessment was performed by a senior dermatologist. Regarding the outcomes of the patch test with the European Baseline patch test series, only relevant cosmetic allergens were taken into account for causality assessment. The causality between the undesirable reaction and the reported cosmetic product was clearly demonstrated in 316 (89%) of the 355 patients for which the causality was established. For 161 patients (45%) this causality was likely and for 155 patients (44%) very likely. The causality was unlikely or questionable for 39 patients (11%).

5 Early Warnings

An important objective of CESES is the possibility to warn the NVWA in case severe undesirable reactions occur or in case a high frequency of undesirable reactions attributed to one cosmetic product are reported. In the period 1 October 2012 – 1 October 2013 no new Early Warnings have been reported. Additional cases were reported for five Early Warnings previously notified to NVWA.

Table 5-1 provides an overview of the cases where RIVM has notified NVWA in the past and shows whether additional cases have been reported in the current report.

Table 5-1 Early Warnings based on reports of undesirable reactions by consumers and dermatologists

Product	Reports till October 2012	New consumer reports till October 2013	New reports dermatologists till October 2013	Symptoms	Causality *	Follow up NVWA
Toothpaste	9	0	0	Burning sensation, erythema, vesicles, 'tongue and lips feel like being burned'	Not assessed	See first report, Salverda-Nijhof et al. 2011a.
Eye make-up remover	12	1	0	Itching, erythema, burning sensation, pain, running eyes, 'wounds'	Not assessed	See first report, Salverda-Nijhof et al. 2011a.
Udder cream	8	0	1	Erythema, itching, scaling, vesicles, oedema	Likely - very likely, product tested positive	Contact with manufacturer who indicated to reformulate the udder cream.
Sunscreen	5	0	0	Erythema	Very likely, product tested positive	-
Day and night cream / serum	17	7	0	Itching, erythema, burning sensation, burns, scaling, oedema, papules	Not assessed	Contact with manufacturer who concluded that it is probably a 'launch' effect, i.e. introduction of new product. Extra quality controls are undertaken.
Lipstick	15	1	0	Oedema, burning sensation, erythema, itching, scaling, vesicles	Not assessed	Contact with manufacturer who indicated that reactions may be experienced when use instructions are not followed correctly, i.e. not applying the top coat leading to dry lips. In addition, cases are too diverse to draw general conclusions.
Day and night cream	13	3	0	Burning sensation, running eyes, itching, erythema, oedema	Very likely, product tested positive	-
Sunscreens for children	13	0	0	Itching, papules, erythema, scaling, nausea, dizziness, burning sensation, oedema, breathing problems	Not assessed	Monitoring number of reported cases concerning sunscreens for children

NB. The Early Warnings for which no additional reports were received in the period October 2012 – October 2013 are presented in grey.

* Not assessed means no patch tests for confirmation were performed since all reports were done in the consumer route.

Same batch number as previous reports.

6 Discussion

6.1 Number of reports

For the current trend report, 244 consumer reports and 101 reports from dermatologists were received. This means that since the start of CESES in total 2197 relevant consumer reports have been received and 359 reports from dermatologists. In addition, 58 reports from dermatologists are currently in progress. Thus, the number of reports received from dermatologists is steadily increasing. In contrast, the number of consumer reports is gradually decreasing. This is probably a direct effect of reduced public communication about the existence of the website www.cosmeticaklachten.nl, as media attention directly led to an increase in the number of consumer reports. In addition, no new Early Warnings were sent to NVWA in the current period. The limited number of consumer reports makes it more difficult or even impossible to discover situations, in which NVWA should be notified. For a successful continuation of the consumer route and the Early Warning system within CESES, public communication about and promotion of the website is indispensable to strengthen consumer awareness of this monitoring system.

6.2 Trends in the period 2012 – 2013

In both routes, undesirable reactions were mainly reported by women. This trend has been observed for several years in CESES and supported by data in literature (see for a more detailed discussion Salverda et al., 2011). The undesirable reactions were generally characterised by relative mild symptoms, including erythema and itching. Severe symptoms concerned 2% and 11% of the reported symptoms, in the clinical and consumer route respectively, and included in most cases pain. In contrast to previous years, no cases of unconsciousness were reported. As in previous years, consumers reported that these symptoms were mainly located on or around the eyes and on the face, while dermatologists reported in the current reporting period that most symptoms were seen on the hands followed by the face. In addition, relatively more undesirable reactions were reported to occur on the arms in patients seen by dermatologists compared to consumers, who reported in their turn relatively more reactions on the neck and scalp. A reason for these differences is that also in the current period a large part of the reports from dermatologists (52%) concern hairdressers reported by the Centrum voor Huid en Arbeid. Occupational exposure to hair products makes hands to be the first body part reflecting an undesirable reaction to cosmetic products. Undesirable reactions after occupational exposure may hamper people in their profession, which will make that they are earlier inclined to visit a dermatologist.

The location of the undesirable reaction is in most cases directly linked to the application site of the cosmetic product that was reported to cause the undesirable reaction. In case of occupational exposure by hairdressers, it is not the application site that is relevant but the way the cosmetic product is applied. That is, the most frequently reported product categories were hair products, skin products and make-up, and included mainly products intended to use on or around the eyes or on the face or scalp. Most of these products were leave-on products. In addition, sunscreens were relatively often mentioned. This is the same picture as observed in previous years.

6.3 Cosmetic ingredients: patch tests

So far, 417 patients seen by dermatologists with an undesirable reaction probably attributed to cosmetic products have undergone a patch test with the European baseline series complemented with additional substances and/or the alleged cosmetic product. For 95% of these patients (n=312), the patch test resulted in a positive response to one or more allergens. In addition, 46 of the 119 patients (39%), for whom an additional patch test with the specific batch ingredients was requested, showed a positive response to one or more of the tested ingredients. Of these patients, 55% (n=26) developed a reaction to surfactants and/or emulsifying agents, 21% (n=10) to preservatives, 19% (n=9) to fragrances and 15% (n=7) to viscosity controlling substances. The actual number of ingredients tested positive as well as the number of patients with a positive response may be higher as most likely not all ingredients with an (possible) allergenic potential were tested, because they were either unavailable or tested at a too low concentration to observe a positive response.

6.3.1 *Isothiazolinones*

Isothiazolinones are currently a cause of concern with respect to the number of allergic responses and their widespread use in consumer products. A mandate for the SCCS to reassess the safety of isothiazolinones is now being prepared by the EU commission. CESES reports on isothiazolinones have been included in the request. In previous reports, CESES recognized the high number of patients tested positive for MI and/or MCI. In addition, literature data showed increasing trends in the prevalence of isothiazolinone-induced contact allergy (a.o. Geier et al., 2012; Uter et al., 2012). When looking at the patch test results of all patients included in CESES since the start in 2009 updated with the new reports received the past year, methyl(chloro)isothiazolinones are the most frequently positively tested patch test allergens. The current data show that in 26% of the patients methyl(chloro)isothiazolinones are the causative allergens. Of all patients with a positive patch test result, 5% had a positive response to MI and 16% to MCI/MI. Only 2% of all patients with a positive patch test result tested positive to both, showing that not all patients with a reaction to the mixture MCI/MI respond to MI and vice versa. In addition, 2% (n=7) showed a positive response to 2-n-octyl-4-isothiazolin-3-one (OIT) and 1% (n=2) to 1,2-benzisothiazolin-3-one (BIT). OIT is marketed for use in a range of industrial products, such as paints, but may not be used in cosmetic products. BIT is also currently not allowed to be used in cosmetics. The SCCS opinion on BIT concluded "until safe levels of exposure have been established, the use of benzisothiazolinone in cosmetic products as a preservative or for other functions cannot be considered safe in relation to sensitisation" (SCCS, 2012a). Allergic responses to OIT and BIT are therefore not expected to be directly related to the use of cosmetics.

Also in literature, new data and new case reports on isothiazolinones have been described. The case reports include primarily all cases of occupational and/or airborne contact dermatitis in patients of all ages, among which young children (Aerts et al., 2013; Bregnbak and Johansen, 2013; Bregnbak et al., 2013; Lundov and Menné, 2013; Lundov et al., 2013a; Vanneste et al., 2013). The symptoms after these kinds of exposure to isothiazolinones are generally more severe than the cases of contact dermatitis evoked by topical application of cosmetics, such as severe respiratory reactions and facial eczema, and may lead to chronic dermatitis and substantial impairment of normal life. For example, the case where a woman could not return to her freshly painted apartment (Lundov et al., 2013a) or a man whose condition does not allow him to return to his former employment (Bregnbak et al., 2013). These cases show that the

widespread use of isothiazolinones, especially MI nowadays, in all kind of industrial, household and cosmetic products is important to consider and that the aggregated exposure may result in serious problems. So far, only for cosmetics maximum permitted concentrations have been established (EC No 1223/2009). Once sensitised, it is difficult to avoid all products with isothiazolinones. Hence, cases where for example sensitisation to paint also lead to undesirable reactions to household wet wipes (Vanneste et al, 2013) or where sensitisation by occupational exposure to high concentrations of isothiazolinones subsequently leads to reactions to very low air concentrations released by a toilet cleaner (Lundov and Menné, 2013).

New data on trends in the prevalence of MCI/MI and MI contact allergy show an on-going increase (Bruze et al., 2013; Lundov et al., 2013b; Urwin and Wilkinson, 2013; Uter et al., 2013a). Also, the data provide indication that MI is now the primary sensitizer in most cases leading possibly to different cross-reaction patterns than when MCI is the primary sensitizer. It is therefore argued by these authors, on behalf of the European Society of Contact Dermatitis and the European Environmental and Contact Dermatitis Research Group to include MI in the European baseline patch test series (Bruze et al., 2013). Also Uter et al. (2013a) are in favour of the addition of MI to the European baseline patch test series as detailed analysis of risk factors associated with MI sensitisation show that patch testing with MI itself is necessary to diagnose MI allergy, in view of the relatively large number of patients testing positive to MI but not to MCI/MI. Furthermore, all authors mentioned above state that regulatory action is highly needed. Lowering the permitted maximum use concentration of isothiazolinones, especially MI, or a general prohibition of isothiazolinones or a restricted use in specific products, such as those intended for the intimate or axillary zone, may be considered according to these authors. Indeed, the current attention for MI has already led to the recommendation of Cosmetics Europe to discontinue the use of MI in leave-on skin products, including cosmetic wet wipes (Cosmetics Europe, 2013).

These new data together with the high number of undesirable reactions to isothiazolinones in CESES underline the need for a combined approach when reassessing the safety of isothiazolinones. Not only exposure via cosmetics should be taken into account but also via industrial and household products. The undesirable reactions are not only a matter of the allergenic potential of isothiazolinones but also a matter of the combined exposure to these preservative ingredients.

6.3.2 *Fragrances*

Fragrances remain important contact allergens responsible for a large part of the undesirable reactions attributed to the use of cosmetic products. Of all patients tested so far within the CESES project, 25% showed a positive response to fragrance mix I and 18% to fragrance mix II. In addition, several positive responses were noted to individual fragrance ingredients such as HICC. For a more detailed discussion on this fragrance ingredient, which received special attention over the last years due to the relatively large number of HICC-related cases of allergic contact dermatitis, see the previous trend report and the recent SCCS opinion on fragrances (de Wit-Bos et al., 2012; SCCS, 2012b). A publication on the risk factors associated with sensitisation to HICC has been recently published (Uter et al., 2013b).

6.3.3 *UV filters in sunscreens*

In the previous trend report, special attention was drawn to the UV filter octocrylene which is widely, and increasingly, used in sunscreens but also in for

example foundations and day-and-night creams with an SPF factor. Octocrylene appeared to be a strong allergen leading to contact dermatitis in children and mostly photoallergic contact dermatitis in adults with an often-associated history of photoallergy from ketoprofen (Avenel-Audran et al., 2010). In the current period, an additional case of a patient with a positive response to octocrylene, when testing the specific batch ingredients, was found. So far, three patients displayed a positive response to octocrylene within the CESES project. In addition, a case report was published of allergic contact dermatitis caused by octocrylene in a young child not previously exposed to ketoprofen-containing topical products (Dumon et al., 2012).

6.3.4 Ammonium persulfates

In the previous trend report, the high number of positive responses to persulfates, especially ammonium persulfate, was noteworthy. It was also identified that mainly hairdressers were affected and that very serious reactions can occur, including anaphylactic shock (Hoekstra et al., 2012). Persulfates are strong oxidising inorganic salts and used in hair bleaches and hair colouring preparations. Within the CESES project, one case of unconsciousness caused by an anaphylactic shock after exposure to ammonium persulfate was observed. In the past year, no new cases of unconsciousness were reported but one hairdresser did experience breathing problems.

Table 6-1 Patch test results with European baseline series and additional substances in hairdressers included by participating dermatological centres in the period July 2009 – October 2013 (n=71).

Allergen	% positive
ammonium persulfate	60%
p-phenylene diamine (PPD)	33%
nickel sulphate	29%
fragrance mix I	26%
fragrance mix II	24%
methyl(chloro)isothiazolinone (MI and Kathon CG ® (MCI/MI))	19%
toluene-2,5-diamine sulfate	17%
sodium persulfate	16%
rubber	13%
myroxylon pereirae	13%

When looking specifically to the occupational group hairdressers, 60% of the 71 hairdressers included in the CESES project so far tested positive to ammonium persulfate (Table 6-1). Ammonium persulfate thus remains the most important allergen within this specific group of patients. With respect to the other persulfates, 16% tested positive to sodium persulfate and 11% to potassium persulfate. PPD was the second important allergen in hairdressers with 33% of them showing a positive response to this cosmetic ingredient. Also in other studies, it was observed that the most important allergen in hairdressers was ammonium persulfate followed by p-toluenediamine (PTD) and PPD (Uter et al., 2007; Lyons et al. 2013).

The hairdressers seen by dermatologists within the CESES project are much younger than the rest of the population seen by dermatologists with an average age of 24 years compared to an average of approximately 40 years. Part is of course explained by the fact that the working population is younger than the general population, but this might also indicate that hairdressers are sensitised

very soon in their working life, which may have considerable impact on the further progress of their career (Hoekstra et al., 2012).

As such, in line with the recommendation in the previous report, attention should be paid to, besides PPD, persulfates within this profession by making hairdressers aware of the possible (severe) allergic reactions that can occur and hence promoting the use of gloves when using hair bleaching and hair colouring products containing persulfates.

6.3.5 *Co/cross polymers*

In the report of 2011, it was observed that three patients had a positive response to one or more co-/crosspolymers (Salverda et al., 2011). This was noteworthy as copolymers are not thought to cause allergic reactions as they do not penetrate the skin. However, in the same period, Kai et al. (2011) reported four cases of allergic contact dermatitis probably caused by the c30-38 olefin/isopropyl maleate/MA copolymer. In all cases, the consumers used a sunscreen from the same brand. Also one of the patients in the CESES project had used that specific sunscreen and showed a positive response to the c30-38 olefin/isopropyl maleate/MA copolymer. Furthermore, one patient had shown a positive test result to the acrylates/c10-30 alkyl acrylate crosspolymer in a cleansing gel. In the previous report describing the period between May 2011 and October 2012, no new cases of positive responses to co-/crosspolymers were observed. However, an additional case of a positive response to the acrylates/c10-30 alkyl acrylate crosspolymer in a sunscreen has been reported in the period October 2012 – October 2013.

Co-/crosspolymers are used in several cosmetic products because of their antistatic, film-forming, binding, suspending, viscosity-increasing, skin conditioning and emulsion-stabilising properties. As said, due to their large structures and high molecular weights, they were not expected to exhibit sensitizing properties (Quartier et al., 2006). However, in 2012, another publication was published describing two cases of allergic contact dermatitis probably attributed to the c30-38 olefin/isopropyl maleate/MA copolymer (Swinnen et al., 2012). Further investigations on the allergenic potential of co-/crosspolymers are recommended.

7 Conclusion and recommendations

- Isothiazolinones in cosmetic products remain one of the most important allergens in developing undesirable reactions. The monitoring of isothiazolinones should be continued. Furthermore, new data in literature together with the high number of undesirable reactions to isothiazolinones in CESES underline the need for a combined approach when reassessing the safety of isothiazolinones.
- Persulfates, especially ammonium persulfate, and PPD remain the most important allergens for hairdressers. They develop undesirable reactions at relatively young age which may hamper them in their further professional career. Awareness, avoidance and the use of protective measures may help this occupational group to prevent the development of undesirable reactions to these cosmetic ingredients.
- Continuous communication to the public about the possibility to report undesirable reactions probably attributed to cosmetics is of utmost importance for the successful continuation of the consumer route and the Early Warning system within CESES.
- Literature indicates that the prevalence of isothiazolinone-induced contact allergy is growing to epidemic proportions like was the case for MDBGN which is now prohibited in cosmetics. The EU commission is now preparing a mandate for the SCCS to reassess the safety of isothiazolinones. Data on isothiazolinone-induced contact allergy provides a basis for this. Hence, it is advisable to include MI in the European baseline patch test series to ensure adequate monitoring of isothiazolinone-induced contact allergy.
- For dissemination at the EU level, it would be of great value to present the results of the Dutch cosmetovigilance system during European meetings, such as the meeting of the Working Party and Standing Committee on Cosmetics, the DG SANCO subgroup on Skin Allergens, or initiatives like a Workshop on Cosmetovigilance which has once been held in May 2012.

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Appendix I Interview gezondheidsplein december 2012

"Melden van je cosmeticaklachten is belangrijk"

Bij rode huiduitslag door het gebruik van een bepaald potje dagcrème of mascara gooien we meestal subiet het product in de prullenbak. Maar daar blijft het vaak ook bij. Een bezoekje aan de huisarts slaan we vaak over, zeker als de klachten minimaal zijn. Sinds 2009 kunnen (huid)klachten door cosmeticagebruik gemeld worden bij het meldpunt Cosmeticaklachten van het RIVM. Wij spraken over het belang van dit meldpunt en het voorkomen van cosmeticaklachten met Joanne Salverda – Nijhof en Lianne de Wit – Bos van het RIVM.

Op de site cosmeticaklachten.nl kunnen mensen met huidklachten door cosmeticagebruik hun klacht indienen. Waarom hebben jullie dit initiatief in het leven geroepen?

Joanne: "Huidklachten door cosmeticagebruik heeft meer aandacht binnen Europa gekregen. Zij wil namelijk dat er meer aandacht wordt besteed aan het registreren én bewaken van de ongewenste effecten van cosmetica. Ook de Nederlandse Voedsel en Waren Autoriteit (NVWA) (red. bewaakt voedsel- en productveiligheid) wilde graag meer weten over huidklachten door cosmeticagebruik en heeft het RIVM gevraagd een registratiesysteem op te starten. Dit heeft uiteindelijk geleid tot het meldpunt én een samenwerking met een aantal dermatologen. Zij proberen te achterhalen welke ingrediënten in een product de huidproblemen veroorzaken en rapporteren dit vervolgens aan ons. Het uiteindelijke doel is om meer inzicht te krijgen in de oorzaak en aard van klachten. Hopelijk kunnen wij hiermee op termijn het aantal klachten terugbrengen."

Wat verstaan jullie precies onder cosmetica? Alleen mascara, blusher en andere make-upartikelen of ook andere producten?

Joanne: "Cosmetica is eigenlijk een heel breed begrip. Alle producten ter verzorging, ter hygiëne én ter decoratie vallen hieronder. Dus niet alleen mascara of oogschaduw, maar bijvoorbeeld ook douchegel, shampoo, tandpasta, babyverzorgings- en scheerproducten. Heb je bijvoorbeeld een kleurspoeling gebruikt of zonnecosmetica en geeft het klachten? Dan kun je dit ook gewoon melden door naar de site cosmeticaklachten.nl te gaan of te bellen naar de VWA-Warenklachtenlijn 0800-0488."

Veel mensen zullen bij cosmetica toch vooral aan vrouwenproducten denken. Merken jullie dat de term 'cosmetica' voor een bepaalde verwarring zorgt? Melden bijvoorbeeld voornamelijk vrouwen met hun make-upproblemen zich?

Joanne: "Sinds het begin van het meldpunt, 2009, hebben we zo'n 2100 meldingen binnengekregen. De meesten hiervan waren inderdaad afkomstig van vrouwen. Dit komt, denk ik, vooral doordat vrouwen meer cosmetica-artikelen gebruiken en een gevoeliger huid hebben. Daarbij zijn vrouwen meer met hun gezondheid én dat van het gezin bezig. Als zij (of een gezinslid) last hebben van eczeem of jeuk, dan gaan zij op internet op zoek naar de oorzaak. Ik denk dat zij op deze manier ook bij ons uitkomen."

Lianne vult aan: "Aan de producten waarover klachten binnenkomen, kun je ook goed zien dat vooral vrouwen ons meldpunt gebruiken. Oogmake-up, make-upremover, gezichtsverzorgings-producten en haarproducten staan bovenaan de lijst. Niet-make-up gerelateerde klachten komen minder voor, maar kunnen wel degelijk gemeld worden."

Welke klachten zijn tot dusverre het meest gemeld?

Joanne: "Dan moet je toch denken aan roodheid, jeuk, irritatie en schilfertjes. De ernstigere klachten als brandwonden, haaruitval, tranende ogen of benauwdheid worden nauwelijks gemeld."

Stel, ik heb rode uitslag door het gebruik van een bepaalde parfum. Wat moet ik dan doen?

Lianne: "Veel mensen reageren op geurstoffen en die zitten in meer producten dan mensen denken, niet alleen in parfum. Denk bijvoorbeeld maar aan douchegel of shampoo. Reageert je lichaam hierop, dan is het verstandig om te stoppen met het gebruik van het product. Vaak trekt de klacht na een paar dagen weg. Is dit niet het geval of heb je last van ernstige klachten? Ga dan naar de huisarts of dermatoloog en neem het product en de verpakking mee. Hij kan dan onderzoeken welk(e) ingrediënt(en) precies de allergische reactie veroorzaakt. En meld uiteraard ook de klacht op ons meldpunt, ook al heb je er geen last meer van."

Is het zo dat producten waarop staat 'dermatologisch getest', 'natuurlijk' of 'hypoallergeen' geen cosmeticaklachten kunnen veroorzaken?

Joanne: "Nee, dat is een groot misverstand. Deze producten veroorzaken misschien minder snel overgevoeligheidsreacties, maar het is geen garantie. Sommige mensen zijn erg gevoelig voor bepaalde stoffen. Ook is het mogelijk dat iemand in de loop van de tijd gevoeligheid voor een bepaalde stof opbouwt."

Als er een klacht gemeld is, wordt deze door het RIVM verwerkt en naar de NVWA gestuurd. De NVWA bepaalt vervolgens welke vervolgstappen worden ondernomen. Roept zij dan bijvoorbeeld de fabrikant op het matje?

Joanne: "Wekelijks maken wij de balans op van de klachten die binnengekomen zijn, zowel via de site als via de dermatologen. Als er een reden tot zorg is, dan nemen we contact op met de NVWA. Zij gaat dan op basis van onze informatie naar de fabrikant. Tot nu toe is dit drie keer gebeurd, bij tandpasta, mascara en oogmake-upremover. Uit nader onderzoek bleek dat met deze producten niks aan de hand was. Daarnaast maken we een jaarlijks rapport met al onze bevindingen."

Hebben jullie tips hoe mensen cosmeticaklachten kunnen voorkomen?

Lianne: "Veel mensen realiseren zich het niet, maar cosmetica kun je niet tot in de lengte van dagen bewaren. Ze hebben een beperkte houdbaarheidsdatum. Elke keer als jij met je vinger in een potje dagcrème zit, komen er namelijk bacteriën vrij. De groei van bacteriën wordt in principe tegengegaan doordat er conserveermiddelen aan zijn toegevoegd, maar op den duur neemt de werkzaamheid daarvan af. Verder moet je geen ingrediënten of producten gebruiken waar je niet tegen kunt. Wat heel handig is, is de allergiepas. De allergiepas kun je gratis aanvragen bij de Nederlandse Cosmetica Vereniging

met een antwoordkaart die je van de dermatoloog krijgt na onderzoek. Op deze pas staat voor welke ingrediënten je gevoelig bent. Heel makkelijk als je een nieuwe gel wilt kopen en je bent overgevoelig voor een ingrediënt met zo'n moeilijke chemische naam. Die kun je natuurlijk nooit onthouden."

Appendix II Figures consumer reports

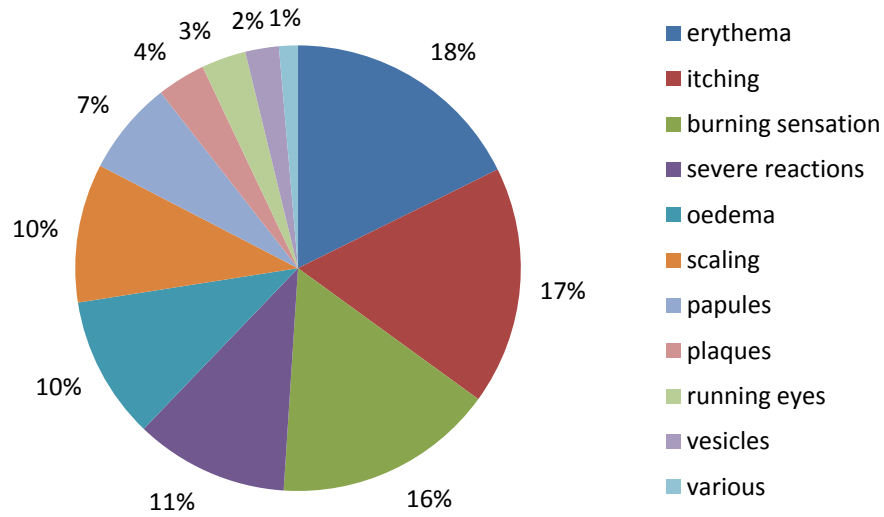


Figure II-1 Reported symptoms of undesirable reaction after cosmetics use in % (n=1023). The category various includes among others hypokeratosis. Severe reactions include blistering, nausea, pain, breathing problems, burns, dizziness and hair loss.

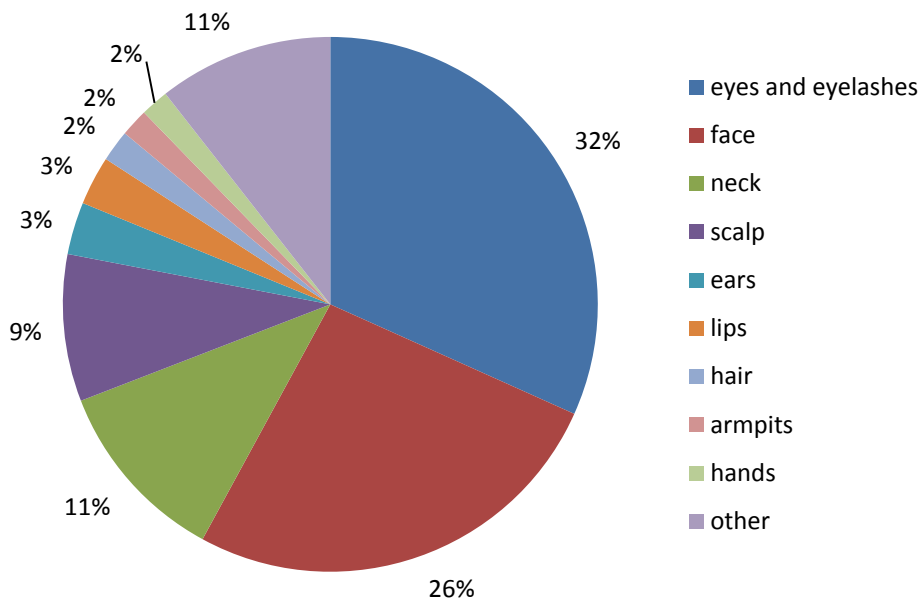


Figure II-2 Reported location of undesirable reaction after cosmetics use in % (n=342). The category other includes among others arms, whole body and oral cavity.

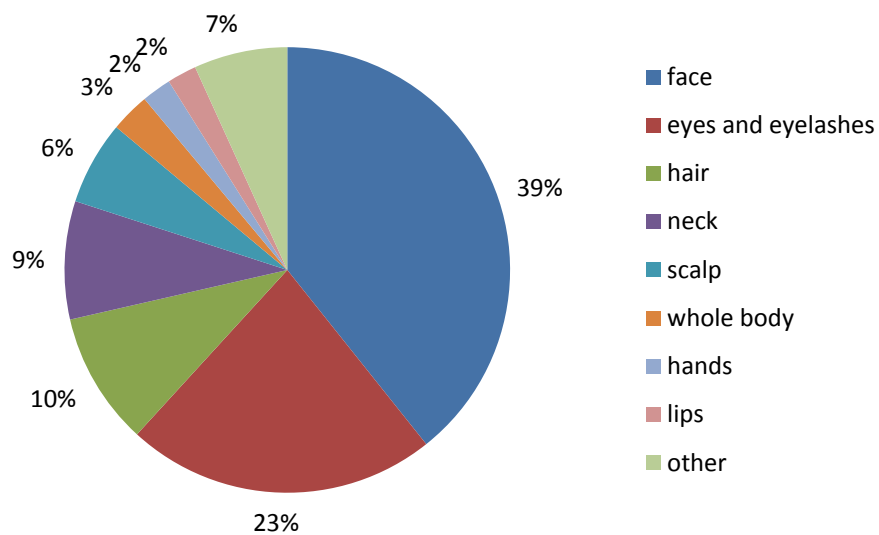


Figure II-3 Reported location of cosmetic product use in % (n=280). The category other includes among others teeth, arms and oral cavity.

Appendix III Figures reports from dermatologists

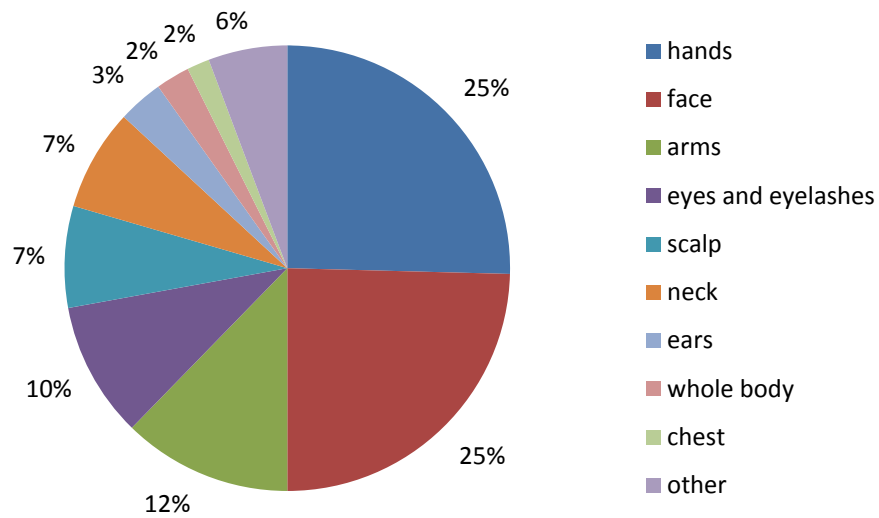


Figure III-1 Reported location of undesirable reaction after cosmetics use in % (n=122). The category other includes among others armpits, legs and feet.

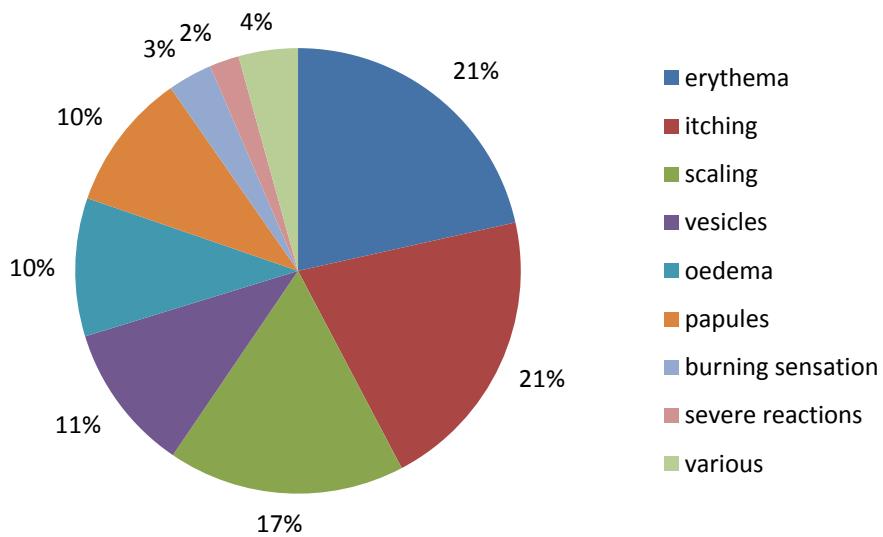


Figure III-2 Reported symptoms of undesirable reaction after cosmetics use in % (n=280). The category various includes among others bullae and plaques. Severe reactions include for these patients pain and one case of breathing problems.

Appendix IV Additional patch test results

Of the patients seen by dermatologists in the period 1 October 2012 – 1 October 2013, 62 patients (94%) showed a positive response to one or more allergens. The main allergens for which patients were tested positive included MCI/MI and/or MI to which 40% of the patients (n=25) showed a positive response, and fragrance mix I to which also 39% (n=24) showed a positive response (see Table IV-1). Nickel sulphate led in 24% of the cases (n=15) to a positive response, PPD in 23% of the cases (n=14) and fragrance mix II in 21% of the cases (n=13).

Table IV-1 Patch test results with European baseline series and additional substances in patients reported by participating dermatological centres in the period 1 October 2012 – 1 October 2013 (top 10).

Allergen	% positive
methyl(chloro)isothiazolinone (MI and Kathon CG ® (MCI/MI)) ¹	40%
fragrance mix I ²	39%
nickel sulphate	24%
p-phenylene diamine (PPD)	23%
fragrance mix II ³	21%
2,5-diaminotoluene sulphate	16%
ammonium persulfate	16%
myroxylon pereirae	15%
lanoline (wolvet)	11%
formaldehyde	10%
sodium persulfate	10%

² Fragrance mix I contains cinnamyl alcohol, cinnamaldehyde, eugenol, alpha-amyl-cinnamaldehyde, hydroxycitronellal, geraniol, isoeugenol and *Evernia prunastri* (oak moss absolute).

³ Fragrance mix II contains alpha-hexyl-cinnamaldehyde, citral, citronellol, farnesol, coumarin and hydroxyisohexyl 3-cyclohexene carboxaldehyde (Lyrall ®).

Appendix V Outcomes CESES-specific patch testing with batch ingredients performed by dermatologists

Overview of products and ingredients tested positive divided by product and patient number. – negative response, ? doubtful response, + positive response, ++ strong positive response, NT not tested. * from literature # concentration set by working group on test concentrations

Patient number	Tested product or ingredient	Substance type	Reference concentration	Test concentration	Outcome 1 st measurement	Outcome 2 nd measurement	Outcome 3 rd measurement
535	Shampoo			5% aq* (open test)	-	+	NT
	magnesium chloride	viscosity controlling	5% aq*	5% aq*	-	Irritation	NT
	piroctone olamine	preservative	1% pet	1% pet*	?	-	NT
	sodium laureth sulfate (Emal)	surfactant		0.5% aq	-	?	NT
	sodium laureth sulfate (Genapol)	surfactant		0.5% aq	-	?	NT
545	Cream				-	-	NT
	butyrospermum parkii butter	skin conditioning/emollient	30% mo	30% mo	-	+	+
545	Body milk			as is*	-	+	-
553	Cream			as is*			+
563	Lotion			pure	+	++	NT
	Peg-7 hydrogenated castor oil	emulsifier/surfactant	30% pet*	10% PET	+	+	NT
	peg-45/dodecyl glycol copolymer	emulsion stabiliser	5% pet*	2.0% PET	+	+	NT
	benzyl alcohol	preservative/solvent	5% pet*	1.0% PET	?	+	NT
	polymer/peg-2 hydrogenated castor	emulsifier	20% pet n.a.	5.00%	-	+	NT

Patient number	Tested product or ingredient	Substance type	Reference concentration	Test concentration	Outcome 1 st measurement	Outcome 2 nd measurement	Outcome 3 rd measurement
	oil/so						
565	Sunscreen			as is*	+	++	NT
	c30-38 olefin/isopropyl maleate/ma copolymer	surfactant, emulsion stabiliser		5% pet	+	+	NT
	benzophenone-3	UV filter	2% pet*	10% pet	++	++	NT
565	Tonic			as is*	-	++	NT
569	Shampoo				-	-	NT
	CI 17200	cosmetic colouring agent	1% pet*	1% pet*	-	?	NT
	sodium laureth sulfate	surfactant/ detergent/ foam layer	0.5% aq+	5% aq	+	+	NT
587	Shampoo			5% aq (open test)	-	+	NT
	sodium cocoyl glutamate	surfactant/ detergent	1% aq	1% aq	-	+	NT
	sodium coco-sulfate	surfactant/ detergent / emulsifier		1% aq	?	-	NT
596	Cleansing gel				NG	NG	NT
	acrylates/c10-30 alkyl acrylate crosspolymer	film former	1% pet	2% aq	-	+	+
	styrene/acrylates copolymer	opacifying		10% aq	-	+	+
602	Gel/cream			5% aq* (open test)	-	+	-
	coco-betaine	surfactant/ detergent/ foam layer	used conc.	6% aq	-	?	-
	sodium laureth sulfate	surfactant/	0.5% aq+	2% aq	-	?	?

Patient number	Tested product or ingredient	Substance type	Reference concentration	Test concentration	Outcome 1 st measurement	Outcome 2 nd measurement	Outcome 3 rd measurement
		detergent/ foam layer					
611	Shaving cream			5% aq (open test)*	?	+	NT
	limonene	fragrance	2% pet*	2% pet*	-	?	NT
	sodium lauryl sulfate	detergent/ foam layer	0.5% aq+	0.1% aq*	?	+	NT
	sodium cetyl sulfate/sodium lauryl sulfate/sodium myristyl sulfate/sodium stearyl sulfate/laureth-10	combination of functions, like emulsifier, surfactant, detergent, foam layer		1% aq	?	+	NT
685	Cream			as is*	?	+	NT
	methylisothiazolinone	preservative	used conc.	0.1% aq	+	++	NT
711	Sunscreen			as is*	?	+	NT
	tocopherol	antioxidant/ skin conditioner	10% pet*	10% pet*	++	+	NT
713	Cream			as is*	-	-	-
	perfume (fragrance)	fragrance	10% pet	10% pet	-	++	++
	cocamidopropyl betaine	boosting	1% aq	1% aq	-	?	+
713	Shower gel			5% aq* (open test)	-	-	-
	cocamidopropyl betaine	boosting	1% aq	1% aq	-	?	+
735	Soap			1% aq	-	-	NT
	tetrasodium edta	chelate	1% pet*	1% aq*	?	-	NT
	perfume (fragrance)	fragrance	10% pet	10% pet*	-	+	NT
	geraniol	fragrance/ tonic	5% pet*	5% pet*	-	+	NT
737	Shampoo			5% aq* (open test)	-	-	NT

Patient number	Tested product or ingredient	Substance type	Reference concentration	Test concentration	Outcome 1 st measurement	Outcome 2 nd measurement	Outcome 3 rd measurement
	polyquaternium-7	antistatic/ film former	0.1% aq*	1% aq	-	?	-
	linalool	deodorants/perfume compound	10% pet*	10% pet*	?	-	NT
737	Shower gel			5% aq* (open test)	-	-	+
	specific ingredient			5% aq* (open test)	-	?	NT
	polyquaternium-7	antistatic/ film former	0.1% aq*	0.1% aq*	?	-	NT
	perfume (fragrance)	fragrance	10% pet	10% pet*	?	-	NT
785	Styling product			5% aq* (open test)	-	-	-
	citronellol	masking	2% pet*	2% pet*	-	-	+
	limonene	fragrance	2% pet*	2% pet*	-	-	+
789	Cleansing gel (face)			5% aq* (open test)	+	+	NT
	potassium behenate	cleansing/ surfactant		1% aq	-	-	+
	potassium laurate	emulsifying/ surfactant	1% aq	1% aq	-	-	+
	potassium myristate	emulsifying/ surfactant	1% aq	1% aq	-	-	+
	potassium palmitate	emulsifying/ surfactant		1% aq	-	-	+
	sodium methyl cocoyl taurate	surfactant/ cleansing/ foaming	0.5% aq	0.5% aq	-	+	+
791	Sunscreen			as is*	+	+	NT
791	Sunscreen			as is*	+	+	NT
793	Shampoo			5% aq* (open test)	-	?	?
	cocamidopropyl betaine	boosting	1% aq	1% aq	-	?	+
793	Body milk			as is*	-	-	+

Patient number	Tested product or ingredient	Substance type	Reference concentration	Test concentration	Outcome 1 st measurement	Outcome 2 nd measurement	Outcome 3 rd measurement
797	Eye pencil				-	-	NT
	ascorbyl palmitate	antioxidant	30% pet*	30% pet*	+	+	NT
811	Body cream			as is*	-	+	+
	sucrose stearate	emulsifying/skin conditioning	20% pet+	3% aq/alc	-	+	+
	glyceryl stearate	emollient/emulsifying	20% pet*	30% pet*	-	?	+
	sorbitan tristearate	emulsifying	5% m.o.*	5% mo	-	+	+
	stearic acid	emulsifying/emulsion stabiliser/refatting?	5% pet*	5% pet*	-	-	+
899	Cream			as is*	-	+	+
	cetyl alcohol	emollient/emulsifying/opacifying/viscosity controlling	30% pet*	20% pet	-	?	+
	perfume			10% pet*	-	+	+
	peg-20 stearate	emulsifying/humectant/surfactant		30% aq/alc	-	-	+
	stearyl alcohol	emollient/emulsion stabilisers/opacifying/viscosity controlling	30% pet*	30% pet*	-	?	+
901	Shampoo			5% aq* (open test)	?	+	NT
	decyl glucoside	surfactant/	1% aq	1% aq	+	+	NT

Patient number	Tested product or ingredient	Substance type	Reference concentration	Test concentration	Outcome 1 st measurement	Outcome 2 nd measurement	Outcome 3 rd measurement
		emulsion stabilisers					
915	perfume			10% pet*	+	+	NT
915	Shampoo			5% aq*	-	?	+
	cocamidopropyl betaine	boosting	1% aq	1% aq*	-	-	+
	sodium laureth sulfate	surfactant/cleansing/foaming	0.5% aq+	2% aq*	-	?	+
915	Soap			5% aq*	-	-	+
	sodium laureth sulfate (24)	surfactant/cleansing/foaming	0.5% aq+	0.5% aq	-	?	+
	sodium laureth sulfate (25)	surfactant/cleansing/foaming	0.5% aq+	0.1% aq	-	+	+
949	Shampoo			5% aq* (open test)	-	-	+
	perfume			10% pet*	-	-	+
	sodium benzoate	preservative	5% pet*	5% aq*	-	-	?
951	Hair conditioner			5% aq	-	?	+
955	Soap-free washing gel			5% aq (open test)*	-	-	-
	alanine/biotin/glycine/leucine/lysine/magnesium asparate/niacinamide/pyridoxine hcl	combination of functions, like antistatic/conditioning		0.1% aq	-	+	+
	cocamidopropyl betaine/glycol distearate/sodium c14-16 olefin sulfonate/sorbitan laurate/potass. Sor			1% aq	-	?	+
	disodium laureth	surfactant/foaming	2% aq	2% aq	-	?	+

Patient number	Tested product or ingredient	Substance type	Reference concentration	Test concentration	Outcome 1 st measurement	Outcome 2 nd measurement	Outcome 3 rd measurement
	sulfosuccinate	/cleansing					
	laureth-2	emulsifying/surfactant/cleansing	10% aq	10% aq	-	-	+
	sodium chloride	viscosity controlling/bulking	0.9% aq*	0.9% aq*	-	-	?
	sodium laureth sulfate	surfactant/cleansing/foaming	0.5% aq+	2% aq	-	?	+
957	Cleansing product			as is	-	+	+
	citrus aurantium oil/citrus grandis oil/citrus nobilis oil/lavandula angustifolia oil/lavandula etc.	combination of functions, like astringent/ tonic/ masking		5% pet	-	+	+
	limonene	fragrance	2% pet*	2% pet*	-	?	+
959	Cream			as is*	-	+	++
	geraniol	fragrance/ tonic	5% pet*	5% pet*	-	+	+
	limonene	fragrance	2% pet*	2% pet*	-	+	+
	perfume			10% pet*	-	?	+
961	Eye contour cream			as is*	-	+	+
	methylisothiazolinone	preservative	used conc.	0.05% aq	-	+	+
963	Cream			as is*	-	-	+
	capryloyl salicylic acid	skin conditioning		1% alc	-	-	+
	paraffinum liquidum/cera microcristallina/paraffin	combination of functions, like antistatic/ emollient/ solvent/ skin?/ binding/ emulsion	pure*	pure	-	?	+

Patient number	Tested product or ingredient	Substance type	Reference concentration	Test concentration	Outcome 1 st measurement	Outcome 2 nd measurement	Outcome 3 rd measurement
		stabilisers/ opacifying/ viscosity controlling					
	sorbitan tristearate	emulsifying	5% m.o.*	5% mo*	-	-	+
	tocopherol	antioxidant/ skin conditioning	10% pet*	10% pet*	-	?	+
973	Sun allergy protection			as is*	-	-	-
	bis-ethylhexyloxyphenol methoxyphenol triazine	UV absorbers/UV filter		2% pet	-	+	++
	butyl methoxydibenzoylmetha ne	UV absorbers/UV filter	2% pet*	10% pet*	-	+	+
	octocrylene	UV absorbers/UV filter	1% pet*	10% pet*	-	-	++
973	Sun protection lotion			as is*	-	-	-
	octocrylene	UV absorbers/UV filter	1% pet*	1% pet*	-	+	+
	bis-ethylhexyloxyphenol methoxyphenol triazine	UV absorbers/UV filter		3% pet	-	+	+
	butyl methoxydibenzoylmetha ne	UV absorbers/UV filter	2% pet*	2% pet	-	+	+
	drometrizole trisiloxane	UV absorber		0.05% pet	-	-	+
	peg-30 dipolyhydroxystearate	emulsifying	30% pet+	2% pet	-	-	+
	tocopherol	antioxidant/ skin conditioning	10% pet*	10% pet*	-	-	+
995	Shampoo			5% aq* (open test)	-	?	+

Patient number	Tested product or ingredient	Substance type	Reference concentration	Test concentration	Outcome 1 st measurement	Outcome 2 nd measurement	Outcome 3 rd measurement
	potassium sorbate	preservative	5% pet*	5% pet*	-	-	?
	sodium benzoate	preservative	5% pet*	5% pet*	-	?	?
1001	Douche and shower gel			5% aq* (open test)	-	+	+
1001	Shampoo			5% aq* (open test)	-	-	+
	disodium lauroamphodiacetate/sodium chloride	combination of functions, like antistatic/surfactant/viscosity controlling	1% aq*	1% aq	+	+	NT
	piroctone olamine	preservative	1% pet	1% pet	-	+	NT
1045	Body milk			as is*	-	+	+
	citronellol	masking perfume compound/masking	2% pet*	2% pet*	-	+	+
	hydroxycitronellal	masking perfume compound/masking	2% pet*	2% pet*	-	+	+
1045	Douche gel			5% aq*(open test)	-	?	+
	linalool	deodorants/perfume compound	10% pet*	10% pet*	-	+	+
1089	Sunscreen			as is*	-	+	++
	octocrylene	UV absorbers/UV filter	1% pet*	10% pet*	-	+	+
1091	Cream			as is*	-	+	+
	diazolidinyl urea	preservative	2% pet*	2% pet*	-	+	+
	perfume			1% alc	-	+	+
1107	Shampoo			5% aq* (open test)	-	?	+
	cocamidopropyl betaine	boosting	1% aq	1% aq*	-	?	+
	cocamidopropyl betaine	boosting	1% aq	1% pet	-	-	?
	sodium benzoate	preservative	5% pet*	0.2% aq	-	-	?

Patient number	Tested product or ingredient	Substance type	Reference concentration	Test concentration	Outcome 1 st measurement	Outcome 2 nd measurement	Outcome 3 rd measurement
1109	Cream				-	-	+
	phenoxyethanol	preservative	1% pet*	1% pet	-	-	+
1117	Shampoo			5% aq* (open test)	-	-	+
	Cocamidopropyl betaine/sodium chloride	combination of functions, like surfactant/cleansing/foam boosting/viscosity controlling/bulking		2% aq	-	?	+
1121	Sunscreen			5% aq* (open test)	+	++	+
	acrylates/c10-30 alkyl acrylate crosspolymer	film formers	1% pet	1% 50/50 alc/aq	-	?	+
	octocrylene	UV absorbers/UV filter	1% pet*	1% pet	-	+	+
1199	Shampoo				-	+	NT
	butylphenyl methylpropional	masking	1% pet*	1% pet	-	-	+
	citronellol	masking	2% pet*	2% pet	-	?	?
1205	Eye shadow				-	+	NT
	butylparaben/ethylparaben/isobutylparaben/methylparaben/propylparaben/phenoxyethanol	preservative		1.5% 50/50	-	?	+
1313	Lip cream				+		
	menthoxypropanediol	refreshing/masking		5% pet	+	+	NT
1365	Sunscreen				+	+	

Patient number	Tested product or ingredient	Substance type	Reference concentration	Test concentration	Outcome 1 st measurement	Outcome 2 nd measurement	Outcome 3 rd measurement
	methylene bis-benzotriazolyl tetramethylbutylphenol/decyl glucoside/propylene glycol/xanthan gum/aq	Combination of functions, like UV absorber/UV filter/surfactant/emulsion stabilising/viscosity controlling		14% aq	+	+	NT
1365	Sunscreen			as is**	+	+	NT
1383	After sun			as is	+	+	NT
	specific ingredient			as is	++	++	NT

