

The epidemic of methylisothiazolinone: a European prospective study

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Summary

Background. The use of methylisothiazolinone (MI) in cosmetic products has caused an unprecedented epidemic of MI contact allergy. Current data concerning exposures at a European level are required.

Objectives. To describe demographics and MI exposures for European patients with MI contact allergy.

Methods. Eleven European dermatology departments from eight European countries prospectively collected data between 1 May and 31 October 2015 among consecutive patients who had positive patch test reactions to MI (2000 ppm aq.).

Results. A total of 6.0% (205/3434; range 2.6–13.0%) of patients had positive patch test reactions to MI. Dermatitis most frequently affected the hands (43.4%), face (32.7%), arms (14.6%), and eyelids (11.7%); 12.7% had widespread dermatitis. For 72.7% (149/205), MI contact allergy was currently relevant mainly because of exposure to cosmetic products (83.2%; 124/149). Of these 124 patients, 19.5% were exposed to leave-on and rinse-off cosmetic products, 24.8% only to leave-on cosmetic products and 38.9% only to rinse-off cosmetic products containing MI or methylchloroisothiazolinone/MI. The majority of these (79%) noted onset of their dermatitis between 2013 and 2015. Fifteen patients (7.3%) had previously experienced allergic reactions when they were in newly painted rooms.

Conclusion. Clinically relevant MI contact allergy remains prevalent across European countries, mainly because of exposure to rinse-off and leave-on cosmetic products.

Key words: allergic contact dermatitis; CAS no. 2682-20-4; cosmetics; exposure; methylchloroisothiazolinone; methylisothiazolinone.

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Methylisothiazolinone (MI; CAS no. 2682-20-4) was already shown to be a sensitizer in humans and guinea-pigs in the mid-1980s (1, 2). The first occupational cases of allergic contact dermatitis caused by MI were reported in 2004, and the first report on MI contact allergy related to cosmetic products was published in 2010 (3, 4). Since then, the continued use of MI as a preservative in cosmetic, household and industrial chemical products has resulted in an unprecedented increase in the prevalence of contact allergy to MI in Europe (5–13). Although MI-containing cosmetic products and household products account for most cases of contact allergy to MI, its use in products for occupational use, for example water-based paints and metalworking fluids, has also caused skin problems in workers (5, 13–18).

Scientists and national health or environmental authorities tried for several years to raise awareness of the European outbreak of contact allergy to MI (12, 19, 20). In 2013, the European Commission (EC) requested an opinion (SCCS/1521/13) from the Scientific Committee of Consumer Safety (SCCS) (21). The SCCS concluded that the European consumer was not sufficiently protected with regard to sensitization with a concentration of 100 ppm MI in cosmetic products (21): 'For leave-on cosmetic products (including "wet wipes"), no safe concentrations of MI for induction of contact allergy or elicitation have been adequately demonstrated. For rinse-off cosmetic products, a concentration of 15 ppm (0.0015%) MI is considered safe for the consumer from the view of induction of contact allergy. However, no information is available on elicitation.' Subsequent to this opinion, the European cosmetics industry submitted an additional dossier of data to support the safe use of MI at 100 ppm in rinse-off cosmetic products and leave-on hair care products (22). The SCCS, however, arrived at the same conclusion in the SCCS/1557/15 opinion as in its earlier SCCS/152/13 opinion (21, 22). In spring 2016, EU member states agreed on a ban on the use of MI in leave-on cosmetic products, which will be effective from 1 January 2017 after a 6-month transition period, during which the cosmetic industry may still produce leave-on cosmetic products containing MI.

The EC held a public consultation on the use of MI in rinse-off cosmetic products from 1 April 2016 to 1 July 2016, to seek the opinions of interested parties (23). Here, the EC proposed accepting the advice given in opinion SCCS/1557/15 to restrict the use of MI in rinse-off cosmetic products to 15 ppm MI (22, 23). Although this is an important step, the European consumer will continue to be exposed to MI at up to 100 ppm in rinse-off cosmetic products until the proposal has been implemented. It is therefore important to continuously monitor the trend of

MI contact allergy in the European population. Hitherto, no prospective European multicentre study has been performed. The purpose of this study was to investigate patients with MI contact allergy and their exposures to cosmetic products, household products and industrial chemical products containing MI during a defined period.

Materials and Methods

This prospective multicentre study was conducted at 11 centres in eight European countries (for the case record form, see Table S1; for technical details, see Table 1). During the study period from 1 May 2015 to 30 October 2015, patients with positive patch test reactions (reactions designated as +, ++, or +++) to 2000 ppm (0.2%) MI aq. were included.

Patch testing was performed according to ESCD recommendations (24). The patch tests were applied to the upper back and occluded for 2 days. In most of the centres, readings were performed on day (D) 2, D3/D4, and D7. All patients were patch tested with the European baseline series. All centres used their usual routines, and different patch test systems (Table 1) were therefore used. Demographics, patch test results and exposures to MI and methylchloroisothiazolinone (MCI)/MI were recorded for all MI patch test-positive patients in each clinic. The patients with positive MI patch test results were asked to bring all their cosmetic products, toiletries, cleaning products and products for occupational use that they used in their domestic and occupational environments. All products preserved with MI or MCI/MI were recorded with regard to product type and use (domestic versus occupational). If the substance was relevant for the present contact dermatitis, additional information, such as manufacturer and specific product name, was registered.

Descriptive analyses of the anonymized data were performed at the National Allergy Research Centre, according to pertinent guidelines (25), with SPSS™ (SPSS™ Statistics, Chicago, IL, USA; IBM PASW Statistics) for Windows™, edition 20.0.

Results

A total of 205 patients had positive patch test reactions to MI (2000 ppm aq.) among 3434 consecutively patch tested patients (6.0%, 95% confidence interval: 5.2–6.8%; range 2.6–13.0%) (Table 1). Table 2 shows that females were predominant in the group (69.8%; 143/205) of patients with MI contact allergy; 23.4% (48/205) had previous or current atopic dermatitis (not shown in Table 2), and the mean age was 47.0 years. The dermatitis was primarily localized on the hands and the facial region. One in every 10 had widespread dermatitis,

Table 1. Overview of the data of 205 European patients with methylisothiazolinone (MI) contact allergy prospectively collected in 11 dermatology departments in eight European countries

Country	Centre	Contact allergy to MI, % (n/n _{total})	Test system and producer of MI patch test material
Belgium	Leuven	7.3 (22/302)	IQ Ultra™, Chemotechnique Diagnostics
Denmark	Bispebjerg	5.0 (12/241)	Finn Chambers®, Chemotechnique Diagnostics
	Gentofte	5.2 (27/519)	Finn Chambers®, Chemotechnique Diagnostics
	Odense	5.8 (15/257)	Finn Chambers®, Chemotechnique Diagnostics
Finland	Finnish Institute of Occupational Health	13.0 (7/54)	Finn Chambers®, Chemotechnique Diagnostics
United Kingdom	Leeds	5.2 (21/404)	IQ Ultra™, Chemotechnique Diagnostics
	London	5.1 (27/526)	Finn Chambers®, Chemotechnique Diagnostics
Italy	Bari	2.6 (8/313)	Al test®, Euromedical, Calolziocorte, LC, Italy
Portugal	Coimbra	8.5 (15/177)	IQ Ultra™, Chemotechnique Diagnostics
Spain	Barcelona	6.7 (17/255)	Finn Chambers®, Chemotechnique Diagnostics
Sweden	Malmö	8.8 (34/386)	Finn Chambers®, Chemotechnique Diagnostics

Table 2. Demographics for 205 European patients with methylisothiazolinone contact allergy prospectively collected in 11 dermatology departments in eight European countries

Age (years), mean (n _{total})	47.0 (201)
1–30, % (n)	21.4 (43)
31–50, % (n)	32.2 (65)
>50, % (n)	46.3 (93)
Female sex, % (n/n _{total})	69.8 (143/205)
Previous atopic dermatitis, % (n/n _{total})	7.3 (15/205)
Current atopic dermatitis, % (n/n _{total})	18.0 (37/205)
No present contact dermatitis, % (n/n _{total})	8.3 (17/205)
Anatomical site of contact dermatitis, % (n/n _{total})	
Widespread	12.7 (26/205)
Hands	43.4 (89/205)
Face	32.7 (67/205)
Arms	14.6 (30/205)
Trunk	13.7 (28/205)
Eyelids	11.7 (24/205)
Neck	10.2 (21/205)
Legs	10.2 (21/205)
Anogenital	4.9 (10/205)
Feet	2.9 (6/205)
Scalp	1.5 (3/205)

here defined as dermatitis involvement of more than three anatomical sites (Table 2). No notable difference in the location of dermatitis was observed when MI contact allergy was stratified for current or past relevance.

Patch test results with selected allergens from the European baseline series for the 205 patients with MI contact allergy are shown in Table 3. MCI/MI elicited positive patch test reactions in 64.2% (129/201) of MI-positive patients. A total of 15% of the patients (n = 32) previously had a positive patch test reaction to either MI or MCI/MI. Polysensitization, defined as the presence of contact allergy to three or more unrelated allergens, was registered in 24.9% (n = 51) of MI-positive patients.

A total of 72.7% (149/205) MI-positive patients had current and certain relevance of their MI contact allergy resulting from exposures primarily to rinse-off and leave-on cosmetic products containing MI or MCI/MI (Table 4). A total of 83.2% (124/149) were exposed to cosmetic products containing MI or MCI/MI in their domestic and/or occupational environment: 58.4% (n = 87) were exposed to rinse-off cosmetic products, in comparison with 44.3% (n = 66) exposed to leave-on cosmetic products. Twenty-nine patients with relevant MI contact allergy were, however, exposed to rinse-off and leave-on cosmetic products containing MI or MCI/MI. Of the 149 patients with relevant MI contact allergy, 99 were exposed only to cosmetic products, 19 were exposed only to household products (primarily dishwashing detergent), 23 were exposed to cosmetic products and household products, 4 were exposed only to water-based paint and lacquer, 1 was exposed to water-based paint and cosmetic products, 1 was exposed to water-based paint, cosmetic products, and household products, and 2 were exposed only to chemical products for occupational use (glue and surface treatment for floors). Office work, healthcare work and cleaning were the most common occupations registered for the 205 patients with MI contact allergy (Table S2).

Among the 149 patients with relevant MI contact allergy who were exposed to products containing MI or MCI/MI, more than half of all patients with relevant MI contact allergy were exposed to more than one product containing MI or MCI/MI: 71 (47.7%) were exposed to one product containing MI or MCI/MI, 32 (21.5%) were exposed to two products, 20 (13.4%) were exposed to three products, 12 (8.1%) were exposed to four products, and 14 (9.4%) were exposed to more than four products. Almost 90% of patients with relevant MI contact allergy (88.6%; 132/149) were exposed to products

Table 3. Patch test results for 205 European patients with methylisothiazolinone contact allergy, and results of additional patch testing with selected allergens from the European baseline series

Allergen (% , n/n _{total})	Patch test reaction				
	Weak positive reaction (1+)	Strong positive reaction (2+)	Extreme positive reaction (3+)	Negative	Doubtful
Methylisothiazolinone	25.4 (52/205)	56.6 (116/205)	18.0 (37/205)	0.0 (0/205)	0.0 (0/205)
Methylchloroisothiazolinone/ methylisothiazolinone	29.4 (59/201)	23.9 (48/201)	10.9 (22/201)	31.3 (63/201)	4.5 (9/201)
Other selected allergens from the European baseline series					
Fragrance mix I	5.9 (11/185)	9.7 (18/185)	1.1 (2/185)	82.7 (153/185)	0.5 (1/185)
Fragrance mix II	6.6 (12/183)	4.4 (8/183)	3.8 (7/183)	84.7 (155/183)	0.5 (1/183)
<i>Myroxylon perei</i>	5.5 (10/183)	0.5 (1/183)	0.5 (1/183)	92.9 (170/183)	0.5 (1/183)
Formaldehyde	2.7 (5/184)	3.8 (7/184)	0.5 (1/184)	91.3 (168/184)	1.6 (3/184)
Quaternium-15	0.5 (1/182)	1.6 (3/182)	0.0 (0/182)	97.8 (178/182)	0.0 (0/182)
Paraben mix	0.0 (0/181)	0.6 (1/181)	0.0 (0/181)	99.4 (180/181)	0.0 (0/181)
Nickel sulfate	4.3 (8/186)	14.5 (27/186)	3.8 (7/186)	76.3 (142/186)	0.0 (0/186)
Potassium dichromate	1.6 (3/182)	1.6 (3/182)	0.0 (0/182)	95.6 (174/182)	0.5 (1/182)
Cobalt chloride	3.9 (7/181)	2.2 (4/181)	1.7 (3/181)	91.7 (166/181)	0.6 (1/181)

Table 4. Exposures to products containing methylisothiazolinone (MI) or methylchloroisothiazolinone/MI in 149 patients with clinically relevant MI contact allergy

Product category	% (n)
Both leave-on and rinse-off cosmetic products	19.5 (29)
Rinse-off cosmetic products	38.9 (58)
Leave-on cosmetic products (including wet wipes)	24.8 (37)
Household products without exposure to cosmetic products*	12.8 (19)
Paints or chemical products for occupational use	4.0 (6)
Total	100 (149)

Of the patients, 83.2% (n = 124) were exposed to cosmetic products.

*A total of 42 patients were exposed to household products: 19 only to household products, and 23 to both household products and primarily cosmetic products.

containing MI (the rest were exposed to products containing MCI/MI): 91.7% (n = 121) of these were exposed to domestic products, 18.2% (n = 24) were exposed to chemical products for occupational use or cosmetic products at their workplace, and 10.7% (n = 13) were exposed in both their domestic and occupational environments. Patients with relevant MI contact allergy had less exposure to products containing MCI/MI (36.9%; n = 55) in terms of domestic exposures (94.5%; n = 52) and occupational exposures (18.2%; n = 10). Only 12.7% (n = 7) were exposed to products containing MCI/MI in their domestic and occupational environments.

A total of 16.8% (n = 25) of patients with relevant MI contact allergy had occupational contact dermatitis resulting from occupational exposure to products containing MI or MCI/MI: cleaning agents (n = 6), water-based paint (n = 4), glue (n = 1), lacquer (n = 1),

and/or cosmetic products and household products (n = 13). Occupational contact dermatitis was seen most frequently in: nurses (n = 4), hairdressers (n = 4), cleaners (n = 3), cosmetologists (n = 2), factory workers (e.g. in glue production) (n = 2), painters (n = 2), carer (n = 1), machinist (n = 1), and others (n = 7).

The year of onset of dermatitis in the 149 patients with relevant MI contact allergy is shown in Fig. 1. Approximately 79% (100/126) developed contact dermatitis between 2013 and 2015 (until 30 October 2015).

Table 5 shows the patients' exposures to MI-containing products. Rinse-off cosmetic products containing MI were frequently registered: shampoos, baths/shower gels, and

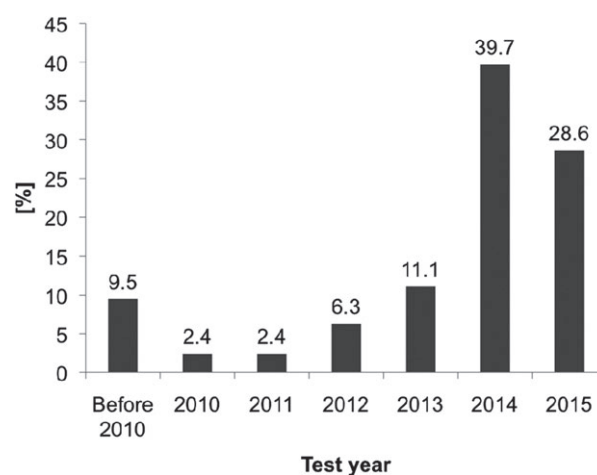
**Fig. 1.** The year of onset of contact dermatitis in 149 patients with clinically relevant contact allergy to methylisothiazolinone. n_{total} = 126 (missing data: 23).

Table 5. Exposures to domestic and occupational products containing methylisothiazolinone (MI) and methylchloroisothiazolinone (MCI)/MI in 205 European patients with MI contact allergy

Product category	MI, % (n)	MCI/MI, % (n)
Shampoo	15.7 (45)	22.5 (25)
Dishwashing liquid	12.6 (36)	8.1 (9)
Face cream/lotion	8.0 (23)	3.6 (4)
Baths/shower gel	8.0 (23)	14.4 (16)
Body cream/lotion	7.0 (20)	5.4 (6)
Liquid soap	6.6 (19)	6.3 (7)
Cleansing agent	5.9 (17)	11.7 (13)
Make-up remover	4.5 (13)	1.8 (2)
Conditioner	3.5 (10)	6.3 (7)
Wet wipes	3.1 (9)	5.4 (6)
Cream/lotion (unspecified)	2.8 (8)	0.0 (0)
Hairstyling (gel/mousse)	2.4 (7)	1.8 (2)
Paint	2.4 (7)	1.8 (2)
Household cleansing spray	1.7 (5)	1.8 (2)
Eye cream	1.4 (4)	1.8 (2)
Sunscreen/self-tanning	1.4 (4)	0.0 (0)
Hand cream/lotion	1.0 (3)	0.0 (0)
Face mask	1.0 (3)	0.0 (0)
Cream/lotion for feet	0.7 (2)	0.0 (0)
Deodorant (unspecified)	0.7 (2)	0.0 (0)
Glues	0.7 (2)	0.0 (0)
Hairstyling product (unspecified)	0.7 (2)	2.7 (3)
Deodorant (roll-on/stick)	0.3 (1)	0.0 (0)
Deodorant (spray)	0.3 (1)	0.9 (1)
Hairstyling spray	0.3 (1)	0.0 (0)
Make-up (unspecified)	0.3 (1)	0.0 (0)
Rinse-off (unspecified)	0.3 (1)	0.0 (0)
Shaving product	0.3 (1)	0.0 (0)
Others	5.6 (16)	3.6 (4)
<i>Total</i>	<i>100 (286)</i>	<i>100 (111)</i>

Of the patients, 73.1% (n = 144) and 32.8% (n = 63) were exposed to MI and MCI/MI, respectively. Patients may have been exposed to more than one product.

liquid soaps. However, leave-on cosmetic products, such as creams/lotions and body creams/lotions were also frequently registered (Table 5). Some brands of product were mentioned more frequently than others as having caused allergic contact dermatitis in 149 patients with relevant MI contact allergy: Clarins® (n = 20), Pantene™ (Procter & Gamble) (n = 16), TRESemmé® (Unilever) (n = 13), Nivea® (Beiersdorf AG) (n = 13), Fairy® (Procter & Gamble) (n = 10), Head & Shoulders® (Procter & Gamble) (n = 8), Dove® (Unilever) (n = 5), Dreft® (Procter & Gamble) (n = 4), L'Oréal (n = 4), and Revlon® (n = 4).

A total of 7.3% (15/205) MI-positive patients had previously experienced allergic reactions when they were in newly painted rooms: contact dermatitis (n = 13), rhinitis (n = 2), and/or conjunctivitis (n = 1). However, none experienced asthma. Eight patients (3.9%) experienced

allergic reactions to airborne exposures other than paint, mainly cleaning agents.

Discussion

This multicentre study of 205 patients with MI contact allergy from eight European countries showed that MI contact allergy remains frequent across all countries; however, there are national differences. Dermatitis in patients with MI contact allergy was most often localized to the hands and face, and 72.7% of the patients had current relevance of their MI contact allergy, primarily resulting from the use of rinse-off and leave-on cosmetic products containing MI or MCI/MI.

To our knowledge, this is the first prospective study to investigate the prevalence of MI contact allergy and to perform exposure analysis in a broad selection of European patients with MI contact allergy. Our results are in line with those of prior retrospective observational studies of consecutive patients with MI contact allergy (5–13, 26). The majority of patients with relevant MI contact allergy (79%; 100/126) had an onset of their contact dermatitis between 2013 and 2015. However, the number of patients with MI contact allergy in 2015 is probably underestimated, as we only included patients until October 2015.

Notably, our results show that 83.4% of patients with relevant MI contact allergy had been exposed to cosmetic products containing MI or MCI/MI. The epidemic of MI contact allergy has been driven by the use of MI in cosmetic products. The use of MI in rinse-off cosmetic products is of particular concern, as its use at the currently permitted concentration up to a maximum of 100 ppm can elicit contact dermatitis in patients with MI contact allergy, according to use tests (27). The use of MI in rinse-off cosmetic products may, purely on the basis of our exposure results, be of even more concern than the use of MI in leave-on cosmetic products, as our patients were exposed to many more rinse-off cosmetic products than leave-on cosmetic products. Exposure analyses on the use of MI in cosmetic products based on the European mandatory ingredient labelling have previously provided estimates of exposure varying between ~0.5% and 3.3% (28–30). In one analysis, it was shown that the frequency of the use of MI in leave-on and rinse-off cosmetic products was approximately equal (28). According to our data, the restriction on the use of MI in rinse-off cosmetic products to 15 ppm MI, as previously suggested by the SCCS (22), seems to be justified. Currently, a public hearing held by the EC is being conducted concerning its implementation (23).

Water-based paint is a source of clinically relevant exposure to MI (17, 31–33). It has recently been

recognized that MI is extensively used as a preservative in European water-based paints, although in varying concentrations (0.7–180.9 ppm) (17). MI evaporates from newly painted surfaces, and may result in airborne allergic contact dermatitis (15). Our data show that 16.8% of the patients with relevant MI contact allergy were exposed to products for occupational use (including water-based paints), cosmetic products and household products containing MI or MCI/MI at their workplace. This is in accordance with the findings of other European studies (5, 13). Until March 2016, MI was not officially classified as a skin sensitizer in the EU. Accordingly, industry could legally omit information regarding the content of MI in their chemical products for occupational use, as long as the rules of self-classification according to the regulation on classification, labelling and packaging of substances and mixtures (CLP Regulation) were adhered to (34). This has previously been shown to be the case for water-based paints purchased in Europe (17). However, the Committee for Risk Assessment concluded, on 11 March 2016, that MI should be classified as 'Skin Sens 1A, H317', with a specific concentration limit of 0.0015% (35). We suggest that the use of MI should be fully restricted in water-based paint in order to protect European workers and consumers, as water-based paints can be preserved without the use of MI (17).

Interestingly, we found a relatively high frequency of polysensitization and simultaneous contact allergy to fragrance mix I, fragrance II and formaldehyde in patients with MI contact allergy, which is in accordance with a recent Spanish and Swedish study (Table 3) (36, 37). It has previously been estimated that the frequencies of contact allergy to fragrance mix I, fragrance II and formaldehyde are approximately doubled in patients with MI contact allergy as compared with the frequency in patients without MI contact allergy (37, 38). However, our results on polysensitization should be interpreted with caution, as it is possible that not all positive patch test results were registered (Table S1).

Nearly 65% of all patients with MI contact allergy had positive patch test reactions to MCI/MI, which is similar to what has been found in other studies (7, 28, 38). Hitherto, immunological cross-reactivity between isothiazolinones

has mainly been discussed in observational studies (5, 39–41). A recent French experimental study of three-dimensionally reconstructed human epidermis concluded that immunological cross-reactivity between MI and MCI was unlikely, as their *in situ* chemical behaviour was different (43). However, a recent murine study based on a modified local lymph node assay concluded that immunological cross-reactivity existed between MI, octylisothiazolinone, and benzisothiazolinone (44). Our current study does not include data that may or may not verify potential immunological cross-reactivity between isothiazolinones.

In conclusion, it is of concern that clinically relevant MI contact allergy remains prevalent across European countries. MI used in rinse-off and leave-on cosmetic products continues to cause problems for the European consumer. Cosmetics producers have not managed to self-regulate the use of MI in their products on the European market, and the use of MI in a number of cosmetic brands is of particular concern, as these cosmetic brands were frequently recorded in our study.

The planned European restriction on the use of MI in cosmetic products and adherence to the CLP Regulation are important and necessary to ensure the population's health.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Pre-printed paper form for registration of demographics, patch test results and exposures to methylisothiazolinone (MI) and methylchlorisothiazolinone in combination with MI (MCI/MI) for each patient with MI contact allergy included in the prospective study conducted at 11 centres in eight European countries from 1 May 2015 to 30 October 2015.

Table S2. Occupational classification of 205 European patients with methylisothiazolinone contact allergy.

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Table S1. Pre-printed paper form to registration of demographics, patch test results and exposures to methylisothiazolinone (MI) and methylchloroisothiazolinone in combination with MI (MCI/MI) for each patient with MI contact allergy included in the prospective study conducted at 11 centres in 8 European countries from 1 May 2015 to 30 October 2015.

to use MI in stay-on cosmetics.	
Aim	To identify current exposures to MI in patients with MI allergy in incident cases of MI allergy and qualify causative exposures and reaction patterns.
Test technique	Ordinary test routines with regard to test system and reading times are used. A micropipette is used to apply 15 µl and 20 µl of each formaldehyde solution to the filter paper in a Finn Chamber and Van der Bend chamber, respectively. In patients with a positive reaction to MI 0.2% the Form A is filled in concerning clinical characteristics. One form for each patient. The patient is asked to bring all their cosmetic products, cleaning products and other types of relevant products e.g. from work place. It is recorded if MI or MCI/MI is present and the number of products containing one or more of these substances are recorded. If one or more of the products are responsible for the current dermatitis, more details about these products are given. At the end of the study Form B is filled in about total numbers tested in the period ect.
Test preparations	The Clinic use their ordinary routine.
Test period	May 1, 2015 - September 31, 2015 (6 months).
Publication	Jakob Schwensen (PhD student), Wolfgang Uter and Jeanne Daus Johansen write the article with EECDRG members of participating clinics as co-authors.

-scent				
Sunscreen				
Self-tanning				
Deodorant				
-spray				
-roll-on/stick				
Make-up				
-face masks				
-eye make-up				
-tinted bases				
-make-up remover				
Wet wipes				
Hairstyling				
-gels/mousse				
-sprays				
Nail care				
Mouths washes				
Rinse of cosmetics				
-liquid soap				
-bath/shower gel				
-shampoo				
-conditioner				
Shaving products				
Cleaning agents				
Household cleaning spray				
Dishwashing liquid				
Polish				
Glasses				
Cutting oils				
Others (write which):				

Questionnaire on MI-allergy and exposures: Patient form (A) p.1
(To be filled in for each patient with a positive reaction (at least +) to MI)

Clinic..... Patient initials..... Date.....

Sex ☐ male ☐ female Age in years..... Occupation.....

Localisation of Dermatitis

Present dermatitis ☐ Atopic dermatitis, presently ☐
Hands ☐ Atopic dermatitis, previously ☐
Arms ☐ Age of debut of AD.....
Trunk ☐
Neck ☐ Previously patch tested: yes ☐ year.....
Eyes ☐ Known positive to MI or MI/MCI ☐
Scalp ☐
Face(rost) ☐
Legs ☐
Feet ☐
Genital/ano area ☐
No present dermatitis ☐
Onset of present dermatitis: month..... year.....

Patch test results: (only record if positive at -at least one reading)

Test preparation	D2	D3/4	D5/7	Comments
Methylisothiazolinone 0.2%				
MCI/MI 0.02%				
Fragrance mix I				
Fragrance mix II/HCC				
Balsam of Peru				
Formaldehyde				
Quaternium 15				
Parabens				
Nickel				
Chromium				
Cobalt				
Others from baseline series:				

Patient form (A) p.3 Patient initials.....

Current relevance: If you judge any of the above products to have caused or contributed to the (current) dermatitis, Please give more details her:

Product type	name	producer	Comments eg. Batch no.

Airborne exposures?

Reacted in newly painted rooms? Yes ☐ No ☐
If yes:
With dermatitis ☐
With rhinitis ☐
With asthma(like) symptoms ☐
With conjunctivitis ☐

Reacted to other airborne exposure? Yes ☐ No ☐
If yes:
Type of exposure:.....

Reaction type:
With dermatitis ☐
With rhinitis ☐
With asthma(like) symptoms ☐
With conjunctivitis ☐

To be sent to:
(When the study is terminated)

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Table S2. Occupational classification of 205 European patients with methylisothiazolinone contact allergy.

Occupation	% (n)
Office worker	21.5 (44)
Retired	16.1 (33)
Healthcare worker	9.3 (19)
Cleaner	4.4 (9)
Student	4.4 (9)
Hairdresser	3.9 (8)
Housewife	2.9 (6)
Unemployed	2.9 (6)
Painter	2.4 (5)
Kitchen worker	2.4 (5)
Shop assistant	2.4 (5)
Teacher	2.0 (4)
Cosmetologist	1.5 (3)
Metal processing worker	1.5 (3)
Carer	1.5 (3)
Baker	1.0 (2)
Unknown	6.3 (13)
Others	13.7 (28)