Methylisothiazolinone and benzisothiazolinone are widely used in paint: a multicentre study of paints from five European countries

Jakob F. Schwensen[1], Michael D. Lundov[1], Rossana Bossi[2], Piu Banerjee[3], Elena Gimenez-Arnau[4], Jean-Pierre Lepoittevin[4], Carola Lidén[5], Wolfgang Uter[6], Kerem Yazar[5], Ian R. White[3] and Jeanne D. Johansen[1]

[1]*Department of Dermato-Allergology, National Allergy Research Centre, Gentofte University Hospital, 2820, Ledrebrog Allé 40, Gentofte, Denmark,* [2]*Department of Environmental Science, Aarhus University, Roskilde 4000, Frederiksborgvej 399, Aarhus, Denmark,* [3]*St John's Institute of Dermatology, St Thomas' Hospital, London, SE1 7EH, Lambeth Palace Road, UK,* [4]*Laboratoire de Dermatochimie, CNRS and University of Strasbourg, 67091 Strasbourg, France,* [5]*Institute of Environmental Medicine, Karolinska Institutet, SE-171 77 Stockholm, Sweden, and* [6]*Department of Medical Informatics, Biometry and Epidemiology, Friedrich-Alexander University, 91054 Erlangen, Waldstr. 4–6, Erlangen, Germany*

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Summary

Background. In view of the current epidemic of contact allergy to methylisothiazolinone (MI), it is important to clarify the extent of use of MI and related isothiazolinones in paints currently available for the consumer and worker in Europe.
Objectives. To elucidate the use and concentrations of MI, methylchloroisothiazolinone (MCI) and benzisothiazolinone (BIT) in paints on the European retail market.
Methods. Wall paints (n = 71) were randomly purchased in retail outlets in five European countries. The paints were quantitatively analysed for their contents of MI, MCI and BIT by high-performance liquid chromatography coupled to tandem mass spectrometry.
Results. MI was found in 93.0% (n = 66) of the paints, with concentrations ranging from 0.7 to 180.9 ppm, MCI in 23.9% (n = 17), ranging from 0.26 to 11.4 ppm, and BIT in 95.8% (n = 68), ranging from 0.1 to 462.5 ppm. High concentrations of MI were found in paints from all five countries. Paints purchased in Denmark and Sweden contained especially high concentrations of BIT.
Conclusion. The use of MI across European countries is extensive. In view of the ongoing epidemic of MI contact allergy, an evaluation of the safety of MI in paints is needed.

Key words: benzisothiazolinone; environmental label; methylchloroisothiazolinone; methylisothiazolinone; paint; safety data sheet.

The isothiazolinones methylisothiazolinone (MI, CAS no. 2682-20-4), methylchloroisothiazolinone (MCI, CAS no. 26172-55-4) and benzisothiazolinone (BIT, CAS no 2634-33-5) are antimicrobial agents. The first two are used as preservatives in cosmetic products, and all three are used as biocides in chemical products (non-cosmetic products), for example paints (1–3). Isothiazolinones have been used for >30 years, and isothiazolinones have a well-known capacity to induce skin sensitization (4, 5).

The allergenicity of isothiazolinones is exemplified by epidemics of sensitization to isothiazolinones, for example the epidemic of contact allergy to MCI/MI (3:1 fixed combination; CAS no. 55965-84-9) in the early 1980s. Subsequently, restrictions on the use of MCI/MI in cosmetics and their classification as skin sensitizers in chemical products have led to a decreasing prevalence of contact allergy to MCI/MI in several European countries,

Correspondence: Jakob F. Schwensen, Department of Dermato-Allergology, National Allergy Research Centre, Copenhagen University Hospital Gentofte, Niels Andersens Vej 65, 2900 Hellerup, Denmark. Tel: +45 39777303. E-mail: jakob.ferloev.schwensen.03@regionh.dk

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and the prevalence of MCI/MI contact allergy had, until recently, stabilized at ~ 2% (6–9).

In 2000, MI was introduced by industry as a standalone preservative, that is, without MCI, for use in chemical products ('mixtures' according to the CLP regulation) with no upper limit on concentration. In 2005, MI was permitted for use in cosmetic products at a concentration of up to 100 ppm (10). MI was, according to the local lymph node assay, a strong sensitizer (EC3 0.4), but less potent than MCI/MI (11). However, since 2009, the prevalence of contact allergy to MI has increased at an alarming rate throughout Europe (12–19).

The Scientific Committee on Consumer Safety did not consider BIT to be safe for use as a preservative in cosmetic products (20), and so far the prevalence of BIT allergy has remained stable (19). BIT is used as a biocide in a broad range of chemical products (20). Isothiazolinones, especially MI and BIT, are widely used as biocides in paint (2, 3, 21). Moreover, working as a painter has been associated with MI sensitization (15, 22, 23), and several case reports have verified the pattern of paint (both domestic and occupational exposure) being a risk factor for contact allergy to MI.

Isothiazolinones can cause contact allergy by direct skin exposure. As MI is volatile and can therefore evaporate, it may cause airborne allergic contact dermatitis, asthmatic symptoms, and even systemic allergic dermatitis (21, 24–32).

In contrast to the more regulated market for isothiazolinones in cosmetic products, industry can omit warning labelling and information on the use of isothiazolinones in paints. This can be done if the substance is not classified as a skin sensitizer (H317) according to the CLP regulation, or R43 according to its predecessor (the Dangerous Substances Directive), either by legally binding harmonized classification or by notification by industry (also called self-classification). It is problematic for both the consumer and worker with contact allergy to isothiazolinones and for the clinician that product labels and safety data sheets often do not contain information on the isothiazolinone content in the paint, despite a relatively high concentration (33).

In view of the unprecedented epidemic of contact allergy to MI, the presence of isothiazolinones in paints is of particular interest. To our knowledge, the concentrations of isothiazolinones in paints intended for use by the consumer have, on a European basis, not been analysed. The aim of this European multicentre study was to determine the concentrations of MI, MCI and BIT in water-based wall paints purchased in retail outlets for analysis of consumer exposure. Furthermore, a systematic review of the published literature regarding cases with non-occupational and occupational contact allergy to isothiazolinones in paint was conducted.

Materials and Methods

Paint collection and samples

A total of 71 white wall paints or wet room paints were purchased in retail outlets in five European countries: Denmark (Copenhagen), France (Strasbourg), Germany (Erlangen), Sweden (Stockholm), and the United Kingdom (London). The paints were randomly chosen, and represented a broad selection of the brands in each country; all paints were purchased in the period from 1 December 2013 to 31 January 2014. All paints were intended for consumer and/or professional use. Wet room paint was defined as paint intended for use in a humid environment, for example bathrooms.

All paints were sent by post or courier to the Department of Environmental Science, Aarhus University, Denmark, where the cans were opened for the first time and analysed. An attempt was made to buy the same Danish paints as 2 years earlier, but this was not possible (21).

The paint was thoroughly mixed before sampling. If a thin layer of transparent liquid was visible on top in the paint can, a sample was taken before mixing. A portion of ~5 ml was taken with a disposable plastic syringe. Analyses were performed in duplicate for randomly chosen samples (every tenth sample).

Safety data sheet and labelling

If possible, safety data sheets were collected for all paints at the time of purchase. If the store did not provide any safety data sheets with the paint, the companies' websites were immediately searched for safety data sheets. All safety data sheets were meticulously searched for warnings and listings of isothiazolinones in the paint.

Additional labelling on the paint cans was also collected. This labelling, however, consisted mainly of environmental labels, for example the European Flower. Environmental labels often have demands regarding the use of isothiazolinones in the paints, and are therefore important for this study. The following environmental and health-related labelling was present on the paint cans: 'EU Ecolabel' ('European Flower'; EU), 'Svane' (The Nordic Swan label; Denmark and Sweden), 'Der Blaue Engel' (The Blue Angel; Germany), 'Svalanmärkt' (Asthma and Allergy Association; Sweden), TÜV NORD: Für Allergiker geeignet, Freiwillige Materialprüfung (optional material testing; recommended for people suffering from allergy) and volatile organic compound (VOC) labelling (low VOC content, minimal VOC content).

The environmental label 'EU Ecolabel' limits isothiazolinones in paints to a total sum of isothiazolinones of 500 ppm, a maximum MI concentration of 200 ppm, a maximum MCI/MI concentration of 15 ppm, and a maximum BIT concentration of 500 ppm (34, 35). The 'Nordic Swan label' (Nordic Ecolabelling) limits isothiazolinones in paints to a total sum of isothiazolinones of 500 ppm, and a maximum MCI/MI concentration of 15 ppm (36). In addition to the environmental label of 'EU Ecolabel', indoor paints can undergo testing for indoor air quality with a specific methodology and, if successful, meet Class A+ ('EU Ecolabel A+'). However 'EU Ecolabel A+' has no additional requirements regarding the use of isothiazolinones in paints (37).

'Der Blaue Engel' limits isothiazolinones in paints to maximum concentrations of 50 ppm MCI/MI, 200 ppm MI, and 200 ppm BIT (38). The 'TÜV NORD' label requires, among other criteria, an MCI/MI concentration of ≤15 ppm, and BIT or BIT and MI concentrations combined of ≤200 ppm (39). Products labelled with 'Svalan' are recommended by the Swedish Asthma and Allergy Association, saying that 'The products are free from allergens, perfumes and irritants in amounts so that no reported medical cases are known' (40). A special provision is given for paints, for which 'the recommendation is valid 2 weeks after application of the paint' (41). VOCs represent a wide variety of compounds, and are used as solvents in paints to help keep the paint stable (37), but the none of the labels with VOC ('Minimal VOC, 0–0.29%'; 'Low VOC, 0.30–7.100%'; 'Medium VOC, 8–24.100%'; High VOC, 25–50%; and 'Very High VOC, more than 50%') have specific requirements regarding the use of isothiazolinone in paints, and are therefore not included as environmental labels of relevance in this analysis (42).

Analysis of isothiazolinones in paint

The concentrations of MI, MCI and BIT were measured in all collected paint samples. As described elsewhere (21), a sample of 1 g (± 0.1 g) from each paint was extracted in 25 ml of methanol/0.4% formic acid (20/80 vol/vol) by means of ultrasound over a period of 10 min. The suspension was filtered through a Phenex-GF/CA (fibreglass/cellulose) filter, and analysed by high-performance liquid chromatography (HPLC) coupled with tandem mass spectrometry. The analytes were separated on a Kinetex C18 (100×2.1 mm^2) HLPC column, and ionized with electrospray ionization operated in positive mode. The mass spectrometer was operated in multiple reaction monitoring mode, with two mass transitions (parent ion/product ion) for each analyte (m/z 116/101 and 116/71 for MI; m/z 150/87 and 150/135 for MCI; m/z 152/109 and 152/134 for BIT). Detection of the analytes was based on retention time and the most abundant mass transition corresponding to an authentic standard. Confirmation of analyte identity was based on the response of the secondary mass transition relative to the response of the primary mass transition. Quantification of the analytes was performed with response factors calculated from a four-point calibration curve (21).

The recoveries with the extraction method for paint were calculated by spiking five different paints with MI, MCI, and BIT. The samples were spiked at three different concentrations: 0.1, 1.0 or 10 µg/ml. Average recoveries obtained for MI, MCI and BIT were 85.9%, 82.6% and 58.0%, respectively.

The precision of the analysis was calculated as the relative standard deviation of replicate analytes extracted from a total of 12 pairs. The overall precision for MI was 1.3%. The overall precision for BIT was 1.5%.

Review

Literature for a review of non-occupational and occupational cases with contact allergy to isothiazolinones in paint was systematically sought from the PubMed™ database and Google™ scholar. The literature search was carried out with the MeSH terms 'methylisothiazolinone', '2-methyl-4-isothiazolin-3-one', 'methylchloroisothiazolinone', '5-chloro-2-methyl-4-isothiazolin-3-one', 'benzisothiazolinone', '1,2-benzisothiazol-3(2H)-one', Kathon CG', 'CAS no. 26172-55-4', 'CAS no. 2682-20-4', 'CAS no. 2634-33-5', 'CAS no. 55965-84-9', 'contact allergy', 'allergic contact dermatitis', 'airborne', and 'paint'. Reference lists of the relevant articles were also studied for case reports relevant for this review. Only literature in English was included. Overall, case reports were considered for inclusion if contact allergy to isothiazolinone resulting from paint exposure was detected. The last literature search was performed on 1 July 2014.

Statistics

The data were processed with SPSS™ (SPSS™ Statistics Chicago, IL, USA; IBM PASW Statistics) for Windows™, edition 20.0, and R statistical software (version 3.1.0; www.r-project.org).

The Mann–Whitney U-test was applied for (i) analysis of differences between the MI concentrations found in the previously tested Danish paints and the newly found MI contents for Danish paints (21), (ii) analysis of differences between the MI concentrations in paints with environmental labels and paints with no environmental labelling,

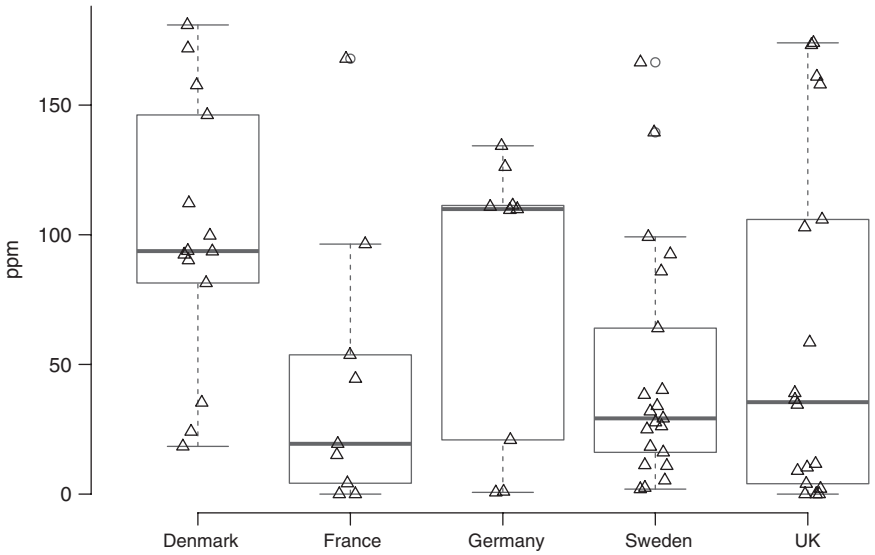

Fig. 1. The distribution of measurements of methylisothiazolinone in wall paints across five European countries, depicted as a boxplot (showing outliers beyond the 1.5-fold interquartile range as dots) with an overlay strip chart, which represents each single measurement as a triangle.

and (iii) analysis of differences between the MI and BIT concentrations in wet room paints and white wall paints. The distribution of the measured values for MI, MCI and BIT were graphically represented by a strip chart with an overlay boxplot. The Kruskal–Wallis *H*-test for global heterogeneity was applied for analysis of differences in MI and BIT concentrations across countries.

The threshold for statistical significance was predefined as a *p*-value of < 0.05.

Results

Seventy-one paints were analysed for their contents of three isothiazolinones. MI was identified in 93.0% (n = 66) of the purchased paints, and the MI concentration ranged from 0.7 to 180.9 ppm (Fig. 1). MCI was identified in 23.9% (n = 17) of the purchased paints, and the MCI concentration ranged from 0.26 to 11.4 ppm. BIT was identified in 95.8% (n = 68) of the purchased paints, and the BIT concentration ranged from 0.1 to 462.5 ppm (Fig. 2).

The distributions of MI concentration differed between countries (Fig. 1). However, no overall statistically significant heterogeneity was seen. In contrast, BIT concentrations differed statistically significantly between countries (Fig. 2).

Table S1 shows a detailed description of all 71 purchased paints regarding product name, MI, MCI and BIT concentrations, and environmental labelling. Seven paints had a low content of MI (< 5 ppm), and five paints (three British and two French) had no detectable MI content at all (Table S1). Only a paint purchased in the United Kingdom contained only MI (4.0 µg/g) with no detectable BIT or MCI. Almost all paints contained MI and BIT in combination. For example, a Danish purchased paint had 180.9 ppm MI in combination with 128.7 ppm BIT. However, many of the Swedish purchased paints contained a relatively high BIT concentration in combination with a relatively low MI concentration, for example 462.5 ppm BIT in combination with 2.47 ppm MI (Table S1).

Samples were also taken from the thin layer of transparent liquid (surface layer) visible on top of nine paints. Analysis showed that the MI concentration in this surface layer was 1.5–2.5 times higher than the MI concentration in the paint in the corresponding can. In a UK paint, an MI concentration of 421.0 ppm was found in the surface layer.

Table 1 shows the frequency of available safety data sheets for all paints in both paint stores and websites for each country. The internet web addresses for the UK purchased paints were not checked immediately after purchase, which is why the data are not included in Table 1. The frequency of environmental labelling is also shown in Table 1. A total of 49.3% (35/71) of the paints were labelled with environmental labels; a Mann–Whitney *U*-test did not reveal any statistically significant difference in MI concentration between the paints with environmental labels and the paints without environmental labels ($p = 0.881$). All of the UK paints were labelled with either 'VOC Symbol', '99% solvent free', 'Low VOC content 0.3–7.99%', or 'Minimal VOC content 0–0.29%', and, in the analysis, these were not regarded as environmental labels of relevance.

Overall, the labelling of isothiazolinone content on safety data sheets were insufficient for all European

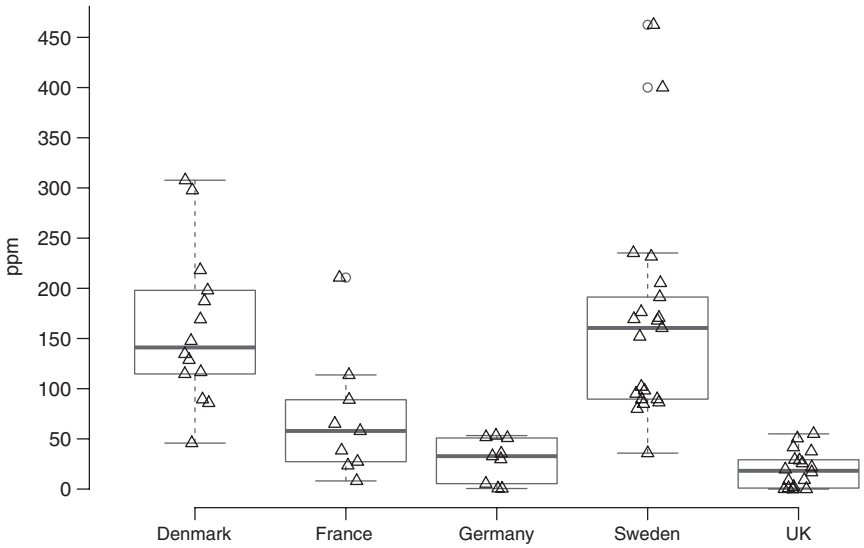

Fig. 2. The distribution of measurements of benzisothiazolinone in wall paints across five European countries, depicted as a boxplot (showing outliers beyond the 1.5-fold interquartile range as dots) with an overlay strip chart, which represents each single measurement as a triangle.

Table 1. Frequency of available safety data sheets (SDSs) for paints at stores or internet websites along with the frequency of paints having environmental labels

European country	SDS at store, % (n/total)	SDS at website, % (n/total)	Environmental labelling on paint cans, % (n/total)
Denmark	0 (0/14)	57.1 (8/14)	64.3 (9/14)
France	0 (0/9)	44.4% (4/9)*	100 (9/9)
Germany	0 (0/9)	88.9 (8/9)*	77.8 (7/9)
Sweden	0 (0/21)	100 (21/21)	42.9 (9/21)
United Kingdom	0 (0/18)	NI	0.0 (0/18)†

NI, not investigated at the time of purchase.
*SDS could be ordered by email.
†Paint cans from the United Kingdom were labelled with VOC (volatile organic compounds). These were not counted as environmental labels. See 'Results'.

countries (Table S1). The manufacturers in the German and Swedish paint markets showed that they were more proactive regarding labelling of isothiazolinone content on the paint cans than manufacturers in other European countries. Two German paints claimed to have no added preservatives on their paint cans. These two paints did indeed have MI and BIT concentrations of < 1 ppm (Table S1).

Furthermore, on a few German paint cans (n = 3), an allergy hotline telephone number was listed in case of allergic symptoms ('Allergiker-Hotline' and 'Technisches Merkblatt').

The Mann–Whitney *U*-test did not show any statistically significant differences in MI concentration between previously purchased Danish paints in a study by Lundov et al. (21) and the MI concentrations in the Danish paints purchased for the present study ($p = 0.884$).

A total of 19.7% (14/71) paints were wet room paints, and no statistically significant difference in MI concentration between wet room paints and white wall paints was observed ($p = 0.840$), but wet room paints had a statistically significantly higher BIT concentration than white wall paints ($p < 0.001$).

In the past 30 years, several case reports on contact allergy to isothiazolinones resulting from paint exposure have been published (Table 2). Older case reports have primarily presented contact hypersensitivity to MCI/MI (mixture 3:1), BIT (e.g. Proxel™) and octylisothiazolinone in paints (43–50). All of these paints probably contained MCI/MI, BIT, or other isothiazolinones, but in only a few reports were the paints analysed (48). In recent years, after the introduction of MI in 2000, several case reports on contact hypersensitivity to MI or other isothiazolinones resulting from exposure to paint have been published (24–28, 30–32, 51–55). A Danish study described, for the first time, four paint factory workers with MI sensitization and allergic contact dermatitis resulting from direct skin exposure to additives with a 10% MI solution (54). In many of the recently published case reports, allergic contact dermatitis has often developed at directly exposed skin sites, whereas some case reports have shown that emissions of MI can elicit airborne allergic contact dermatitis at indirectly exposed skin sites, for example the face or arms, or even asthmatic symptoms (21, 24–32). Some case reports have described systemic symptoms and generalized dermatitis resulting from exposure to MI and/or BIT in paints (27, 32, 55), and a few studies even reported that emergency treatment was necessary, owing to severe asthmatic symptoms (24, 26).

Table 2. Reports on non-occupational and occupational cases with contact allergy to methylisothiazolinone (MI), benzisothiazolinone (BIT) or methylcholoroisothiazolinone (MCI) related to paint exposure

Author		Year of publication	Country	Age (years)	Sex	Occupationally related dermatitis	Positive patch test reactions	Comments	Reference
Mathias		1983	Denmark	31	Male	Yes	OIT (3+)	Contact dermatitis on upper extremity	(43)
Greig		1991	New Zealand	40	Male	Yes	MCI/MI (2+), BIT (2+)	Hand dermatitis after skin exposure to paint and Proxel™ CRL solution containing BIT	(44)
Finkbeiner		1994	Germany	42	Female	No	MCI/MI (1+)	Airborne contact dermatitis (flare-ups). Previously sensitized by cosmetics	(45)
Fernandez de Corrës		1995	Spain	47	Female	Yes (flare-ups)	MCI/MI (2+)	Airborne contact dermatitis (flare-ups). Previously sensitized by cosmetics	(46)
Schubert		1997	Germany	33	Female	Yes (flare-ups)	Unknown (MCI/MI-sensitized)	Airborne contact dermatitis	(47)
Bohn	Patient 1	2000	Switzerland	46	Female	No	MCI/MI (3+)	Airborne contact dermatitis and mild dyspnoea	(48)
	Patient 2			47	Female	No	MCI/MI (3+) patch testing with the paint (3+)	Airborne contact dermatitis with later generalization	
	Patient 3			25	Female	No	MCI/MI	Airborne contact dermatitis, rhinitis, and mild dyspnoea	
	Patient 4			52	Female	No	MCI/MI (2+)	Airborne contact dermatitis, previously sensitized by cosmetics	
	Patient 5			46	Female	No	MCI/MI (2+)	Airborne contact dermatitis	
Hardcastle	Patient 1	2005	United Kingdom	–	Male	Yes	BIT (3+), MCI/MI (1+), OIT (1+?)	Hand dermatitis after skin exposure to paint (paint factory)	(49)
	Patient 2			–	Male	Yes	BIT (1+), MCI/MI (1+), OIT (1+)	Hand dermatitis after skin exposure to paint and later generalization	
Jensen		2006	Germany	13	Male	No	MCI/MI (+1)	Airborne contact dermatitis	(50)
Thyssen	Patient 1	2006	Denmark	55	Male	Yes	MI (2+), MCI/MI (1+)	Hand dermatitis after skin exposure to additives (7–10% MI) at paint factory. Contact dermatitis spread to chest, neck, and armpits	(54)
	Patient 2			40	Male	Yes	MI (1+), OIT (1+), BIT (1+?), MCI/MI (1+?)	Hand dermatitis after skin exposure to additives (7–10% MI) at paint factory	

Table 2. Continued

Author		Year of publication	Country	Age (years)	Sex	Occupationally related dermatitis	Positive patch test reactions	Comments	Reference
	Patient 3			34	Male	Yes	MI (2+), MCI/MI (1+?), OIT (1+?)	Hand dermatitis after skin exposure to additives (7–10% MI) at paint factory	
	Patient 4			53	Male	Yes	MI (2+), MCI/MI (2+), OIT (1+?)	Hand dermatitis after skin exposure to additives (7–10% MI) at paint factory. Later generalization	
Garcia-Gavin	Patient 1	2010	Spain/Belgium	55	Male	Yes	1000 ppm MI (3+)	Airborne contact dermatitis and minor dyspnoea (flare-ups). Previously sensitized by wet wipes	(51)
	Patient 2		Spain/Belgium	62	Female	No	MCI/MI (2+) and positive semi-open test result with a piece of Scotex Fresh® moist toilet paper (2+)	Airborne contact dermatitis and minor dyspnoea (flare-ups). Previously sensitized by wet wipes and Lactacyd Femina® (MCI/MI content)	
Lundov	Patient 1	2011	Denmark	36	Male	Yes	0.2% MI aqua (1+?)	Airborne contact dermatitis	(26)
	Patient 2		Denmark	57	Male	Unknown	Known MCI/MI and MI	Airborne contact dermatitis and dyspnoea (FEV1 = 39%) (flare-ups). Emergency treatment	
Kaur-Knudsen		2012	Denmark	35	Male	Yes	BIT (initially on patch testing) and MCI/MI (later flare-up symptoms)	Airborne contact dermatitis with later generalized dermatitis (flare-ups). Previously sensitized to Proxel™	(55)
Friis		2012	Denmark	64	Male	Yes	MI (2+), MCI/MI (2+)	Contact dermatitis	(52)
Kaae		2012	Denmark	23	Female	Unknown	MCI/MI (2+), MI (2+)	Airborne allergic contact dermatitis. Facial dermatitis when using Nivea® Visage cleaning product (flare-ups)	(28)
Tokunaga		2013	Japan	66	Male	Yes	MCI/MI (1+), BIT (+?)	Airborne allergic contact dermatitis	(29)
Vanneste		2013	Belgium/Sweden	39	Female	No	MI (1+)	Contact dermatitis after skin exposure to paint. Later airborne contact dermatitis caused by paint and cosmetics wet wipes (flare-ups)	(53)

Table 2. Continued

Author	Year of publication	Country	Age (years)	Sex	Occupationally related dermatitis	Positive patch test reactions	Comments	Reference
Aerts	2013	Belgium	4	Girl	No	MCI/MI (1+). No patch testing with MI	Anogenital dermatitis (wet wipes). Airborne contact dermatitis (flare-ups; paint, 53 ppm MI)	(30)
Lundov	2013	Denmark	53	Female	No	MI (1+)	Airborne contact dermatitis, dyspnoea	(31)
Bregnbak	2013	Denmark	42	Female	Yes	MI (1+)	Airborne contact dermatitis	(27)
Bregnbak	2013	Denmark	3	Boy	No	MI (2+), MCI/MI (2+)	Airborne contact dermatitis. Flare-up symptoms when re-exposed to paint, sunscreeen, wet wipes, and shampoo. The contact dermatitis mimicked atopic dermatitis	(32)
Madsen	2014	Denmark	3	Girl	No	MI (3+), MCI/MI (2+)	Airborne contact dermatitis. Previously sensitized to wet wipes	(25)
Alwan	2014	United Kingdom	52	Female	No	MI (3+)	Airborne contact dermatitis and dyspnoea. Emergency treatment	(24)

FEV1, forced expiratory volume in 1 second; OIT, octylisothiazolinone.

Discussion

In this European multicentre study, we investigated the concentrations of MI, MCI and BIT in 71 paints randomly purchased in retail outlets in five European countries: Denmark (Copenhagen), France (Strasbourg), Germany (Erlangen), Sweden (Stockholm), and the United Kingdom (London). MI was found in 93.0% (n = 66) of the paints, BIT was found in 95.8% (n = 68) of the paints, and MCI was found in 23.9% (n = 17) of the paints.

These data indicate that MI and BIT are widely used by the paint industry in relatively high concentrations across the five European countries, indicating a European problem.

In a previous study from Denmark, Lundov et al. found MI concentrations ranging from 10 to 300 ppm in 19 randomly chosen water-based paints purchased in 2012 (21). In the present experimental study, employing a current sample of European paints, the highest MI concentration was found in a Danish purchased paint, with a concentration of 180.9 ppm. In comparison with the previously mentioned study by Lundov et al., it was found that 32% (6/19) of the analysed paints had a higher MI concentration than the highest measured MI concentration of 180.9 ppm, but no statistically significant difference was found (21). However, the MI concentration varies greatly among the Danish purchased paints. Furthermore, the data indicate that the use of MI in paints is a European problem, not being limited to Denmark, and this emphasizes the need for a European evaluation of the health risk caused by MI in paints, and a regulatory limit for MI in paint.

It is likely that paint manufacturers add different isothiazolinones, and probably also other preservatives, to the paint to enhance the antimicrobial effect. By adding different preservatives to the paint, the paint manufacturers also would avoid the need for warning labelling, as the concentrations would be lower than if only a few preservatives were used in high concentrations, for example above 1000 ppm. Our data indicate that more than one isothiazolinone is often added to the paint, as only four paints contained only BIT and only one paint contained only MI. No paints contained only MCI, as expected, as MCI is employed in a fixed 3:1 combination with MI (MCI/MI 3:1). The BIT concentrations in the purchased paints varied among countries. Paints from Denmark and Sweden contained relatively high concentrations of BIT as compared with paints from France, Germany, and the United Kingdom (Fig. 2 and Table S1). Our data indicate that it is possible for the paint manufacturers to preserve paint without the use of a relatively high MI concentration, as some paints contained relatively low MI concentrations, and this was not related to the intended use of the paint, for example white wall paint versus wet room paint. However, the BIT concentration in paint may be related to the intended use of the paint, as wet room paint had a statistically significantly higher BIT concentration than white wall paint.

In a recent Danish emission test and a field experiment test, it was shown that MI is emitted from newly painted walls within hours, and that a (low) MI concentration is emitted for weeks (21). The published case reports of airborne contact allergy to MI resulting from exposure to paint (24–28, 30–32, 51, 52, 55) are now further supported, as our data indicate that MI is widely used in European paints. In the present study, the MCI concentration in paint was relatively low as compared with the MI and BIT concentrations. MI, as a separately added preservative, had obviously been used additionally to MCI (supposedly Kathon™), as the MI concentration was 2.5–101.3 times higher than the MCI concentration.

Environmental labels often also have provisions for the use of isothiazolinones in the paint; for example, the Environmental label 'EU Ecolabel' limits isothiazolinones in paints (34, 35). None of the paints with the 'EU Ecolabel' contained MI or BIT above the relatively high concentration limits (MI > 200 ppm; BIT > 500 ppm), and the environmental labelling may therefore give the consumer a false sense of security by pretending that the product is safer than the rest of the products. However, our analysis showed no difference in MI concentration between paints labelled with environmental labels and those without additional labelling.

Anti-skinning agents are used to prevent skinning during the production or storage of paints. The thin transparent liquid layer visible on top of some of the paints in the present study was most likely such an anti-skinning agent. Furthermore, the MI concentration in all surface layers was higher than that in the corresponding mixed paint. It is not known to what extent the higher concentration of preservatives in anti-skinning agents adds to the allergy risk.

The current legislation on labelling (CLP) states that chemical products (mixtures) containing a skin sensitizer above a certain concentration should be labelled with a warning to protect against sensitization (56). This is according to the rules of self-classification (notification by industry), if no legally binding (harmonized) classification has been decided. The generic concentration for classification and labelling is 10 000 ppm (1%), but lower, and specific, concentration limits should be set when appropriate. There are 1727 notifications of MI as a skin sensitizer (H317); however, only 52 give a lower specific concentration limit (1000 ppm or 0.1%) (57). The CLP also states that information should be given in safety data sheets and

on the label if the concentration of a classified sensitizer in a product is above one tenth of the concentration limit for classification (called the concentration limit for elicitation).

All analysed paints had MI concentrations well below 1000 ppm and the paint manufacturers were therefore not obliged by law to state that the paints contained MI, despite the risk of contact allergy shown in several studies (Table 2).

For the consumer and the professional decorator, it is currently almost impossible to obtain knowledge about the isothiazolinone content in the paint. Labels and safety data sheets did not generally state the presence of any of the isothiazolinones (Table S1). Safety data sheets were not available at any of the paint stores in the five European cities where the paints were purchased (Table 1). Safety data sheets could, for some of the paints, be obtained at the paint manufacturers' websites, but national differences were observed (Table 1).

The results concerning some paints from Germany and Sweden clearly show that paint manufacturers, regardless of an inadequate European regulation, are able to provide information on isothiazolinone content by labelling and in safety data sheets.

In conclusion, we emphasize an urgent need for evaluation of the regulation on the use of MI in paints for protection of the consumer, the worker, and the MI-allergic patient. It is important for sufficient product labelling of MI content to be made a legal requirement, regardless of the MI concentration. Ultimately, we must emphasize that the paint manufacturers also have a responsibility to improve the safety profile of their paints, for example by stating the use of MI on the paint container, or by limiting, or even abandoning, the use of MI in paints.

Supporting Information

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

Table S1. Detailed description of all 71 purchased paints regarding product name, product type, concentrations of isothiazolinones, labelling of the presence of isothiazolinone in the paint, and environmental labelling.

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