# Isothiazolinones are still widely used in paints purchased in five European countries: a follow-up study

Andreas V. Thomsen, Jakob F. Schwensen, Rossana Bossi, Piu Banerjee, Elena Giménez-Arnau, Jean-Pierre Lepoittevin, Carola Lidén, Wolfgang Uter, Ian R. White, Jeanne D. Johansen

# Title page

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Authors: Andreas V. Thomsen[1], Jakob F. Schwensen[1], Rossana Bossi[2], Piu Banerjee[3], Elena Giménez-Arnau[4], Jean-Pierre Lepoittevin[4], Carola Lidén[5], Wolfgang Uter[6], Ian R. White[3] and Jeanne D. Johansen[1].

Affiliations:

1. National Allergy Research Centre, Department of Dermatology and Allergy, Copenhagen University Hospital Herlev and Gentofte, DK-2900 Hellerup, Denmark
2. Department of Environmental Science, Aarhus University, DK-4000 Roskilde, Denmark
3. St John's Institute of Dermatology, Guy's Hospital, London, SE1 9RT, UK
4. Laboratoire de Dermatochimie, CNRS and University of Strasbourg, 67091 Strasbourg, France
5. Institute of Environmental Medicine, Karolinska Institutet, 171 77 Stockholm, Sweden
6. Department of Medical Informatics, Biometry and Epidemiology, Friedrich-Alexander University, 91054 Erlangen, Germany

Corresponding author: Andreas V. Thomsen, National Allergy Research Centre, Department of Dermatology and Allergy, Copenhagen University Hospital Herlev-Gentofte, Kildegårdsvej 28, DK-2900 Hellerup, Denmark

Mail: Andreas.Vinther.Thomsen.01@regionh.dk

Phone: +45 38 67 39 60

Fax to National Allergy Research Centre: +45 39 77 71 18

**Conflicts of interests:**

All authors declare no conflicts of interests pertinent to the present study.

## Abstract

**Background.** An increasing incidence of contact allergy to methylisothiazolinone (MI) has been seen caused, in particular, by cosmetic products and paints. A study from 2014 showed that 93.0% of paints bought in five European countries contained MI. New regulations have been discussed for paints in EU, which may have influenced this market.

**Objectives.** To re-evaluate the use and concentrations of MI and four other isothiazolinones in water-based wall paints.

**Methods.** Water-based white wall paints (n = 60) were purchased in retail stores in five European countries: Denmark, France, Germany, Sweden and UK. The paints were analyzed for content of isothiazoliones using high-performance liquid chromatography coupled to UV detection and confirmed with high-performance liquid chromatography-tandem mass spectrometry.

**Results.** MI was identified in 55 (91.7%) of the paints, with concentrations from 1.1 to 142.7 ppm. The other isothiazolinones were identified in 20.0% (methylchloroisothiazolinone; MCI) to 88.3% (benzisothiazolinone; BIT) of the paints. BIT concentrations varied significantly between countries, whereas MI and MCI contents did not. There were no statistically significant differences between MI, MCI and BIT concentrations compared to the 2015 study.

**Conclusion.** MI and other isothiazolinones are widely used in European purchased paints. Their use does not seem to be waning.



Key words: benzisothiazolinone, dichlorooctylisothiazolinone, environmental label, methylchloroisothiazolinone, methylisothiazolinone, octylisothiazolinone, paint, safety data sheet

# Introduction

The isothiazolinones methylisothiazolinone, methylchloroisothiazolinone, the mixture methylchloroisothiazolinone/methylisothiazolinone 3:1, benzisothiazolinone, octylisothiazolinone and dichlorooctylisothiazolinone (see Table 1 for further information) are preservatives used in a wide range of industrial chemical products (as biocides) and partly (MCI, MI) in cosmetic products due to their activity against bacteria and fungi (1-5).

Although isothiazolinones have been recognized since the 1970s as contact allergens and MCI/MI (e.g. Kathon® CG) resulted in an epidemic of contact allergy in the 1980s, it is the recent and unprecedented epidemic of contact allergy to MI that has raised awareness of products containing MI (4, 6-8). The epidemic of contact allergy to MI was mainly driven by exposures to cosmetic products; however, a substantial number of the cases have been due to exposures to occupational products, for example water-based paints (9-12). A recent multi-centre prospective study of European dermatitis patients has additionally shown that 7.3% of MI-allergic patients have experienced symptoms, for example flare-up episodes of airborne allergic contact dermatitis, when being in newly-painted rooms (13). In accordance, an experimental study showed that MI may evaporate from newly painted walls for at least 42 days (14)

In 2015, a comprehensive study on the use of MI, MCI and BIT in water-based paints purchased in five European countries was published (12). 71 water-based paints were purchased from December 2013 to January 2014. It was found by HLPC-MS-MS that a total of 93.0% of the paints contained MI in concentrations of up to 180.9 ppm, whereas BIT was found in 95.8% of the paints in concentrations up to 462.5 ppm (12). Notably, a few manufacturers managed to preserve 7% (n=5) of the purchased paints without the use of MI (12).

In March 2016, the Committee for Risk Assessment (RAC) of the European Chemicals Agency (ECHA) recommended that MI should be classified (harmonised classification, legally binding) as a skin sensitiser ('Skin Sens 1A, H317') with a specific concentration limit of 0.0015% (15). The final decision on this recommendation is still awaited, and until MI has a harmonised classification as a skin sensitiser, MI adheres to the rules of self-classification: all non-harmonized skin sensitizing substances and mixtures (chemical products) (Skin Sens 1, 1A or 1B, H317) must be labelled on the

product and safety data sheet if the concentration exceeds one-tenth of the concentration limit for classification and labelling (Table 1) (16).

In this multi-centre follow-up study, we wanted to investigate the use of selected isothiazolinones in European purchased water-based paints and compare this to the results of the similar 2015 investigation in order to detect trends in the use of especially MI, but also related isothiazolinones (MCI, BIT, OIT and DCOIT).

## Materials and methods

### Paint collection and samples

A total of 60 white wall paints and wet room paints intended for consumer and/or professional use were purchased in retail stores in Denmark (Copenhagen), France (Strasbourg), Germany (Erlangen), Sweden (Stockholm) and the United Kingdom (London) from 1 June to 31 July 2016. As far as possible, the same products as in 2014 were purchased. All paints were sent by courier to the Department of Environmental Science, Aarhus University in Roskilde, Denmark, where the cans were opened for the first time and analyzed. The paints were 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 (12). A portion of 5 ml was taken with a disposable plastic syringe.

### Safety data sheets

At the time of purchase, safety data sheets were obtained as far as available at the retail outlet or subsequently from the producer's or retailer's website. The sheets were meticulously searched for any information, warnings or listings referring to isothiazolinones or for warnings concerning allergy risks. The paint cans were inspected for information on isothiazolinone content and environmental labelling. The environmental labels found consisted of 'EU Ecolabel' ('European Flower'; EU) (17), 'Svanen' (The Nordic Swan label; Denmark and Sweden) (18), 'Der Blaue Engel' (The Blue Angel; Germany) (19), 'Svalanmärkt' (Asthma and Allergy Association; Sweden) (20), 'TÜV NORD: Für Allergiker geeignet, Freiwillife Materialprüfung' (optional material testing;

Germany) and volatile organic compound (VOC) labelling (low VOC content, minimal VOC content). The TÜV NORD and VOC labels were not included in the analysis.

**Analysis of isothiazolinones in samples**

The concentration of isothiazolinones was measured in all collected paint samples. As described elsewhere (10, 12), a sample of 1 g (+/- 0.1 g) from each paint was extracted in 25 ml methanol/0.4 % formic acid (20:80 v/v) by means of ultrasound for 10 min. The suspension was filtered through a Phenex-GF/CA (fibreglass/cellulose) filter and analysed by high-performance liquid chromatography (HPLC) coupled to UV detection and confirmed by HPLC-MS-MS previous dilution of sample extracts. The analytes were separated on a Kinetex C18 (100 x 2.1 mm) HPLC column and detected at 275 nm wavelength. LC-MS-MS confirmation was performed with electrospray ionization (ESI) in positive mode. The MS was operated in multiple reaction monitoring (MRM) 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; *m/z* 214/102 and 214/71 for OIT; *m/z* 282/170 and 282/71 for DCOIT). 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 relative response of the secondary mass transition to the primary mass transition. Quantification of the analytes was done using response factors calculated from a four-point calibration curve (12, 14)

The recovery of the extraction method for paint was calculated by spiking five different paints with the analytes. The samples were spiked at three different concentrations: 0.1 µg/ml, 1.0 µg/ml or 10 µg/ml. Average recoveries obtained for MI, MCI, BIT, and OIT were 86, 83, 74, and 53%, respectively. The recovery of DCOIT was very low (5%), thus the results for this compound are probably characterised by a large uncertainty. The limit of detection and limit of quantification for all isothiazolinones were 1 ppm and 5 ppm, respectively.

**Labels**

The 'EU Ecolabel' allows for combined isothiazolinone concentrations of up to 500 ppm in indoor paints with a maximum MI concentration of 200 ppm, a maximum BIT concentration of 500 ppm, a maximum OIT concentration of 500 ppm and a maximum MCI/MI concentration of 15 ppm (17). The 'Nordic Swan label' limits the combined concentrations of isothiazolinones to 500 ppm with a maximum MI concentration of 100 ppm and a maximum MCI/MI concentration of 15 ppm (18). 'Der Blaue Engel' limits the use of MCI/MI to 15 ppm, BIT to 200 ppm and MI/BIT (1:1) to 200 ppm (19). Products labelled with 'Svalan' are recommended by the Swedish Asthma and Allergy Association. The products must be "free from allergens, perfumes and irritants in amounts so that no reported medical cases are known", except paints, for which only respiratory problems are considered. For paints, the criteria come into force 2 weeks after application (20).

**Statistics**

The data were processed with SPSS™ (SPSS™ Statistics, Chicago, IL, USA; IBM PASW Statistics) for Windows™, edition 22.0, and R statistical software (www.r-project.org), version 3.2.0.

The Mann-Whitney *U*-test was applied for (i) analysis of differences in MI, MCI and BIT concentrations found in the previously tested paints (12) and the newly found MI, MCI and BIT concentrations, (ii) analysis of differences between the MI, MCI, BIT, OIT and DCOIT concentrations in paints with environmental labels and paints with no environmental labelling and (iii) analysis of differences between the MI, MCI, BIT, OIT and DCOIT concentrations in wet room paints and white wall paints. The distribution of the measured values for MI and BIT were graphically represented by a strip chart with an overlay box plot. The Kruskal-Wallis *H*-test for global heterogeneity was applied for analysis of differences in MI, MCI, BIT, OIT and DCOIT concentrations across countries. The threshold for statistical significance was predefined as a *p*-value of $< 0.05$.

## Results

Sixty paints were analyzed for their contents of five isothiazolinones. MI was identified in 91.7% (n = 55) of the purchased paints, with concentrations ranging from 1.1 to 142.7 ppm. MCI was in 20.0% (n = 12) of the paints, ranging from 0.5 to 3.5 ppm. BIT was in 88.3% (n = 53) of the paints, ranging from 0.4 to 331.0 ppm. OIT was in 26.7% (n = 16) of the paints, ranging from 0.03 to 16.01 ppm. DCOIT was identified in 50.0% (n = 30) of the purchased paints, ranging from 0.01 to 156.2 ppm. Concomitant presence of MI, MCI and BIT is visualized in Fig. 1B. Supplemental Table S1 shows a detailed description of the sixty paints with regards to product names, analysis results, environmental labelling and safety data sheet information. As in the previous study, samples were taken from a thin layer of surface liquid when obviously present (seven paints). Concentrations of MI in this surface layer were up to 2 times larger than the concentration in the paint itself after mixing.

The distribution of MI concentrations is presented in Fig. 2A. No statistically significant heterogeneity between countries was observed for MI or MCI. However, BIT (presented in Fig. 2B), OIT and DCOIT concentrations all varied statistically significantly between countries. In paints containing DCOIT, the concentration was found to be up to 5.64 ppm with a single outlier of 156.2 ppm.

Three paints (two Danish and one German) did not contain any detectable amount of isothiazolinones. Another German paint claiming to be free of preservatives did however contain MI at a concentration of 1.05 ppm. Nine paints had an MI concentration of < 5 ppm, and seven of these paints contained no detectable MI.

MCI was found in twelve of the purchased paints, of which eight were purchased in Sweden. None of the paints purchased in France or Germany were found to contain MCI. The MI concentrations in paints containing MCI ranged from 2.85 – 96.7 ppm, and was significantly lower than the MI concentrations in paints without MCI (Mann-Whitney *U*-test, $p = 0.027$). The results suggest a higher use of MCI/MI in paints purchased bought in Sweden than in other countries. The MI

concentration was always higher than the MCI concentration, suggesting that MI is used together with MCI/MI, which now is banned in leave-on cosmetics.

Eleven of the purchased paints were wet room paints. MI and MCI contents did not differ statistically significantly between wall paints and wet room paints, but BIT, OIT and DCOIT were all found in significantly higher concentrations in wet room paints.

Thirty-one paints featured an environmental label of interest on the can (Table 2). MI, MCI and DCOIT contents did not differ statistically significantly between paint with or without environmental labels. OIT was found in lower concentrations in paints with environmental labels ($p$ = 0.034), whereas BIT concentrations were higher in paints with environmental labels ($p$ = 0.048).

The Mann-Whitney *U*-test did not show any statistically significant differences in MI, MCI or BIT concentrations between the paints purchased for the 2014 study as a whole or for any individual country.

Presence of MI, MCI and BIT according to chemical analysis, information on paint cans, and in safety data sheets was compared for each substance and between the present study and the study 2014. Agreement between the three sources of information is visualized by area-proportional Euler diagrams in Fig. 1. The agreement was generally stronger in the current study (Fig. 1D, F, H) than in the previous study (Fig. 1 C, E, G) where it was poor. In both studies, MCI was reported on cans and in safety data sheets, also when no MCI was detected by chemical analysis (Fig. 1E, F).

## Discussion

In this multi-centre follow-up study we investigated the concentrations of MI, MCI, BIT, OIT and DCOIT in water-based paint purchased in five European countries: Denmark, France, Germany, Sweden and the United Kingdom. The results show a continued extensive use of methylisothiazolinone in water-based wall paints. We found MI in 91.7% of the purchased paints in a maximum concentration of 142.7 ppm with no statistical difference between the present data and the study from 2014, where 93% of paints contained MI in up to 180.9 ppm (12). The use of MI in paint has throughout the last decade been shown to be a relevant exposure in patients with MI contact allergy, and it is well recognized that MI may evaporate from newly painted walls (14, 21-27). Additionally, a large prospective observational study showed in 2016 that approximately 7% of all patients with MI contact allergy previously had experienced allergic symptoms (dermatitis, rhinitis and/or conjunctivitis) when being in newly painted rooms (13). Currently, it is unknown to which extent consumers are primarily sensitized due to exposure to paint preserved with MI, however, a Belgium case showed that 53 ppm MI in a paint was enough to elicit airborne allergic contact dermatitis in a girl (25). Notably, 32 (53.3%) of the paints analyzed contained MI in concentrations > 50 ppm.

Although some focus throughout the past years has been on reducing the use of MI in paint, no significant change could be detected in our study. This highlights the need for sufficient legislation restricting the content of MI in particular in paint, since self-regulation has proven unsuccessful.

The concentration of OIT in paint was much lower than anticipated. A former Danish registry-based study from 2014 showed that OIT was found in relatively high concentrations in chemical products for occupational use, including varnishes and paints (3). Observational studies have additionally shown that OIT contact allergy is frequently found in painters (28, 29). The recovery of OIT in the present study was only 53%, which may have led to some under-estimation of occurrence in paints.

DCOIT is used in antifouling paints for use to impede growth of barnacles, algae and other marine organisms as the outer layer to the hull of a ship (30). However, DCOIT was found in high

concentrations, and relatively frequently, in our analyzed paints. This indicates that DCOIT may be a relevant contact allergen in especially painters with suspected contact allergy to paints.

Seven paints were found to have a thin surface layer of liquid, known as anti-skinning agent, which is added to the surface to prevent skinning during storage of the paint. The same types of isothiazolinones were found in the surface layer as in the paint itself, but in generally higher concentrations. MI concentrations in the surface layer were up to 2 times larger than the concentration found in the paint after mixing as in accordance with the previous study on analyzed paints (12). Consumers and painters using such paints may be exposed to particularly high concentrations of MI upon mixing the paints.

Labelling of paints that contain MI, regardless of concentration, is essential to avoid flare-up episodes in already sensitized individuals. There is a remarkable improvement concerning information on cans and in safety data sheets between 2014 and 2016. The explanation must be the entry into force by June 2015 of the CLP requirement to give information according to EUH208 (e.g. “Contains methylisothiazolinone. May produce an allergic reaction.”) for concentrations down to 1/10 of the concentration limit. However, our data showed that only 38.3% (n = 23) was either labelled to contain MI on the paint can, or information was given in the safety data sheet. It is, however, unlikely that the average consumer examines safety data sheets. Hence, if information is provided only in safety data sheets, secondary and tertiary prevention is not fully addressed.

Hitherto, MI needs to be labelled according to the rules self-classification. Often, self-classification applies considerably less protective classification limits than harmonized classification does, although the same criteria and guidelines shall be applied. Notwithstanding several years of delay, the Committee for Risk Assessment (RAC) concluded in its opinion that MI should be classified as ‘Skin Sens 1A, H317’, with a specific concentration limit of 0.0015% (15). This recommendation still awaits final decision, however. We suggest, for health protection, that industry applies this classification now, before required by law.

In conclusion, the proposed classification of MI as a skin sensitizer with a specific concentration limit of 15 ppm is, without doubt, an important step forward. However the continued extensive

use of MI warrants restrictions in the use of MI in paint due to the risk of contact allergy, airborne and direct contact. It is of special concern that the paints carrying an environmental label do not provide any extra safety. The current study as well as the previous one (12) showed that paints without MI, MCI or BIT do exist and thus that it is possible to preserve paint without the use of isothiazolinones.

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