Prevalence of allergic contact dermatitis caused by hydroxyisohexyl 3-cyclohexene carboxaldehyde has not changed in Denmark

Maria V. Heisterberg1, Grete Laurberg2, Niels K. Veien2, Torkil Menné1, Christian Avnstorp3, Knud Kaaber4, Klaus E. Andersen5, Mette Sommerlund6, Anne Danielsen7, Bo Lasthein Andersen8, Berit Kristensen9, Ove Kristensen9, Niels Henrik Nielsen10, Jens Thormann11, Susanne Vissing12 and Jeanne D. Johansen1

1Department of Dermato-Allergology, National Allergy Research Centre, Gentofte Hospital, University of Copenhagen, 2900 Hellerup, Denmark, 2Dermatology Clinic, Vesterbro 99, 9000 Ålborg, Denmark, 3Dermatology Clinic, Roskildevej 264, 2610 Rødovre, Denmark, 4Dermatology Clinic, Bredgade 30, 7400 Henning, Denmark, 5Department of Dermatology, Odense University Hospital, 5000 Odense, Denmark, 6Department of Dermatology, Aarhus University Hospital, 8000 Århus, Denmark, 7Dermatology Clinic, Banegårdspladsen 1, 5, 1570 København V, Denmark, 8Dermatology Clinic, Det Gule Pakhus, Havnepladsen 3A, 5700 Svendborg, Denmark, 9Dermatology Clinic, Bredgade 50, 4400 Kalundborg, Denmark, 10Dermatology Clinic, Bindeledet 15, 2880 Bagsværd, Denmark, 11Dermatology Clinic, Skovgade 23C, 7100 Vejle, Denmark, and 12Dermatology Clinic, Gl. Hovedgade 14, 2970 Harsholm, Denmark

doi:10.1111/j.1600-0536.2012.02125.x

Key words: detergents; hydroxyisohexyl-3-cyclohexene carboxaldehyde; irritant contact dermatitis; cosmetics.

Hydroxyisohexyl 3-cyclohexene carboxaldehyde (HICC) is a fragrance ingredient that is often used in cosmetic products (1, 2). Because of this frequent use in cosmetic products, as well as its use in higher concentrations than the recommended safe-use concentration, HICC is one of the most frequent causes of allergic contact dermatitis (3–10). In order to reduce the prevalence of contact allergy to HICC, the International Fragrance Association (IFRA) has made several attempts to restrict its use. The first IFRA recommendation to restrict the use of HICC in cosmetic products was made in 2003 (11), when a limit of 1.5% in both leave-on and rinse-off cosmetic products was recommended. The most recent IFRA recommendation (October 2009) was to restrict the use concentration in cosmetic products to a maximum of 0.02% in lip products, deodorants, and intimate wipes. For all other cosmetic products, a maximum limit of 0.2% was recommended (12). The EU Cosmetic Directive lists HICC as one of the 26 fragrance ingredients to be specifically declared on the ingredient label of cosmetic products when present in concentrations of 0.001% in leave-on products and 0.01% in rinse-off products (13). The EU’s Scientific Committee on Consumer Products and Non-food
Products for Consumers has recommended a maximum concentration of 0.02% in cosmetic products. However, this has never been implemented in legislation (14). Despite these attempts to reduce the high level of exposure to HICC, no decrease in allergy to HICC has, thus far, been reported (15).

The aim of this study was to investigate and update the occurrence of contact allergy to HICC among eczema patients following the implementation by the fragrance industry of several restrictions on the use of HICC.

Data were retrieved from a clinical database of the Danish Contact Dermatitis Group (DCDG). Data on all eczema patients patch tested with HICC 5% pet. in the baseline series were retrieved (n = 37 860). The data covered the period from January 2003 to December 2011. Data from before 2008 have been reported previously (15). The demographic characteristics of the patch tested patients are shown in Table 1. The patch tests were performed according to international guidelines (16), with Finn Chambers® applied on the back with Scanpor® tape (Vitalfo Scandinavia, AB, Allerød, Denmark) for 2 days. Readings were performed on days 2 and 3 or 4 and 7, according to the recommendation of the International Contact Dermatitis Research Group (17). Clinical relevance was evaluated and recorded according to standardized guidelines set by the DCDG. In this study, clinical relevance includes present and/or past relevance based on (i) medical history, (ii) results of patch and/or use tests, (iii) ingredient labelling, or (iv) chemical analysis. Data administration and statistical analysis were performed with SPSS™ version 15 and Excel™ 2003.

Allergic contact dermatitis caused by HICC was observed in 2.5% (n = 928) of the 37 860 persons patch tested. A fluctuation around 2.5% was observed, with a maximum of 2.8% (2008) and a minimum of 2.1% (2003). Overall, there was no change in the prevalence of allergy over a period of 9 years (Fig. 1). Most reactions were of clinical relevance (74.1%). The majority were of present relevance (51.3%) compared to past relevance (36.6%). Figure 2 shows the present and/or past clinical relevance of positive patch test results stratified by patch test year. A slight increase in present relevance and a decrease in past relevance were observed from 2010 to 2011. However, these tendencies were very small and not of statistical significance. Overall, there was no difference in the prevalence of clinical relevance, past or present, over time.

Women were statistically significantly more likely to have a positive patch test reaction to HICC than men [odds ratio (OR) 1.6; 95% confidence interval (CI) 1.39–1.85]. Facial dermatitis (OR 1.24; 95% CI 1.07–1.45), age ≥40 years (OR 1.26; 95% CI 1.10–1.44), hand eczema (OR 1.34; 95% CI 1.17–1.53) and occupational dermatitis (OR 1.32; 95% CI 1.09–1.60) were statistically significantly associated with HICC allergy. Lower leg dermatitis was statistically significantly less common (OR 0.57; 95% CI 0.37–0.88) in subjects with a positive patch test reaction.

### Table 1. MOAHLFA index of eczema subjects consecutively patch tested with hydroxyisohexyl 3-cyclohexene carboxaldehyde (HICC)

<table>
<thead>
<tr>
<th>Index</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td>12 872</td>
<td>34.0</td>
</tr>
<tr>
<td>O</td>
<td>3977</td>
<td>10.5</td>
</tr>
<tr>
<td>A</td>
<td>6491</td>
<td>17.1</td>
</tr>
<tr>
<td>H</td>
<td>13 825</td>
<td>36.5</td>
</tr>
<tr>
<td>L</td>
<td>1527</td>
<td>4.0</td>
</tr>
<tr>
<td>F</td>
<td>7277</td>
<td>19.2</td>
</tr>
<tr>
<td>AA</td>
<td>22 201</td>
<td>58.6</td>
</tr>
<tr>
<td>Total</td>
<td>37 860</td>
<td>100</td>
</tr>
</tbody>
</table>

MOAHLFA: A, atopy; F, face affected by dermatitis; H, hand dermatitis; L, leg dermatitis; M, male; O, occupational causation of dermatitis; and AA, age ≥40 years.
test reaction to HICC. Previous studies have reported a positive association between fragrance allergy, being a woman, and having facial eczema (18–20). Hand eczema and occupational eczema have not previously been associated with fragrance allergy. However, the statistically significant differences between some of the demographic characteristics may not be of clinical significance, and may primarily be a consequence of the large number of eczema patients tested.

In conclusion, allergy to HICC continues to be very frequently observed (2.5%). No change in the prevalence of positive patch test reactions over the last 9 years was found. Furthermore, no changes in the prevalence of clinically relevant reactions were seen, and HICC is therefore still a very relevant, frequent cause of contact allergy. The many attempts to reduce exposure to HICC in cosmetic products by the IFRA do not appear to be sufficient in order to reduce allergy to HICC.

References

15 Braendstrup P, Johansen J D. Hydroxyisohexyl 3-cyclohexene carboxaldehyde (Lyral) is still a frequent allergen. Contact Dermatitis 2008: 59: 187–188.
19 Heisterberg M V, Menné T, Johansen J D. Contact allergy to the 26 specific fragrance ingredients to be declared on cosmetic products in accordance with the EU cosmetics directive. Contact Dermatitis 2011: 65: 266–275.
20 Heisterberg M V, Menné T, Andersen K E et al. Deodorants are the leading cause of allergic contact dermatitis to fragrance ingredients. Contact Dermatitis 2011: 64: 258–264.