Environment International 118 (2018) 235–244

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Health impact assessment of a skin sensitizer: Analysis of potential policy measures aimed at reducing geraniol concentrations in personal care products and household cleaning products

W.P. Jongeneel*, J.E. Delmaar, B.G.H. Bokkers

National Institute for Public Health and the Environment, Centre for Safety of Substances and Products, Bilthoven, The Netherlands

ARTICLE INFO

Handling Editor: Marti Nadal

Keywords:
Health impact assessment
Allergic contact dermatitis
Skin sensitization
Geraniol
Cosmetic products
Household cleaning products

ABSTRACT

A methodology to assess the health impact of skin sensitizers is introduced, which consists of the comparison of the probabilistic aggregated exposure with a probabilistic (individual) human sensitization or elicitation induction dose. The health impact of potential policy measures aimed at reducing the concentration of a fragrance allergen, geraniol, in consumer products is analysed in a simulated population derived from multiple product use surveys. Our analysis shows that current dermal exposure to geraniol from personal care and household cleaning products lead to new cases of contact allergy and induce clinical symptoms for those already sensitized. We estimate that this exposure results yearly in 34 new cases of geraniol contact allergy per million consumers in Western and Northern Europe, mainly due to exposure to household cleaning products. About twice as many consumers (60 per million) are projected to suffer from clinical symptoms due to re-exposure to geraniol. Policy measures restricting geraniol concentrations to < 0.01% will noticeably reduce new cases of sensitization and decrease the number of people with clinical symptoms as well as the frequency of occurrence of these clinical symptoms. The estimated numbers should be interpreted with caution and provide only a rough indication of the health impact.

1. Introduction

Contact allergy to fragrances has been estimated to occur in 3.7% of the general population worldwide (Thyssen et al., 2009). In Europe, prevalence estimates for contact allergy to fragrances in the general population of 1.3% in Denmark and 1.8% in Germany are reported (Schnuch et al., 2002; Thyssen et al., 2007). More recently, the European Dermato-Epidemiology Network (EDEN) consortium published the results of a large epidemiological survey of the general population in six European regions. A random sample of individuals was patch tested to Fragrance Mix I (FM I) and II (FM II). In these samples prevalence rates of 2.6% (95% CI 2.1–3.2) for FM I and 1.9% (95% CI 1.5–2.4) for FM II were found (Diepgen et al., 2015).

Like other allergic diseases, contact allergy develops in two phases. The first phase is the induction (sensitization) phase in which the immune system is primed. This is an asymptomatic event which may occur instantaneously or take place over months or years. After sensitization, re-exposure to the allergen leads to the second phase (elicitation phase) in which an inflammatory response is elicited. Clinical features of allergic contact dermatitis include eczema, oedema, rash and itching. Symptoms can range from mild to severe, and they can appear within a few hours up to 10 days after moment of contact with the allergen. The inflammatory response typically develops at the site of allergen contact. Symptoms are maximal within 2–3 days and, without further exposure to the allergen, then decline.

Contact allergy to fragrances is mostly presented with hand or facial eczema and significantly influence daily living (Lysdal and Johansen, 2009). Individuals with fragrance contact allergy usually try to avoid scented products to prevent reoccurrence of complaints. Dermal exposure to fragrances in a non-occupational setting can occur through the use of personal care products (PCPs, including cosmetics) and household cleaning products (HCPs) (Magnano et al., 2009; SCCS,

Abbreviations: AEL, Acceptable Exposure Level; EDEN, European Dermato-Epidemiology Network; EPHECT, Emission, Exposure Patterns and Health Effects of Consumer Products; FM I, Fragrance Mix I; FM II, Fragrance Mix II; GM, geometric mean; GSD, geometric standard deviation; HCP, household cleaning products; HIA, health impact assessment; HMT, Human Maximization Test; HRIPT, Human Repeat Insult Patch Test; IDEA, International Dialogue for the Evaluation of Allergens; iEID, individual elicitation induction dose; IPRA, Integrated Probabilistic Risk Assessment; iSID, individual sensitization induction dose; LLNA, local lymph node assay; NESIL, No Expected Sensitization Induction Level; PACEM, Probabilistic Aggregate Consumer Exposure Model; PCP, personal care products; QRA, Quantitative Risk Assessment; SAF, Sensitization Assessment Factors; SCCS, Scientific Committee On Consumer Safety

* Corresponding author.
E-mail address: Rob.Jongeneel@rivm.nl (W.P. Jongeneel).

https://doi.org/10.1016/j.envint.2018.04.039
Received 15 February 2018; Received in revised form 20 April 2018; Accepted 21 April 2018

2012). In 2012, the EU Scientific Committee on Consumer Safety (SCCS) assessed the existing data on the most frequently reported fragrance allergens and identified 12 established fragrance contact allergens of special concern (SCCS, 2012). Each of these substances poses a particularly high risk of sensitization to consumers and they have given rise to at least 100 reported cases of sensitization in Europe.

The aim of this paper is to present a methodology to assess the health impact of reducing the concentration of a fragrance allergen in commonly used cosmetic and consumer products. The fragrance allergen analysed is geraniol because of the availability of aggregated dermal exposure levels previously published by Nijkamp et al. (2015). Geraniol is a widely used fragrance with a rose like odour and one of the abovementioned 12 fragrance allergens of special concern. Geraniol is one of the eight substances in FM I, included in the European baseline series of allergens recommended for screening in patch tests. Consumer exposure to geraniol is common as it is widely used in cosmetics and consumer products (summarized in SCCS, 2012).

Previously, Nijkamp et al. (2015) performed a Quantitative Risk Assessment (QRA) for skin sensitization of exposure to geraniol. It was determined that aggregated exposure to geraniol from PCPs and HCPs exceeds the Acceptable Exposure Level (AEL) for skin sensitization. The QRA for skin sensitization is designed to assess the risk of induction in the general population and consists of various steps (Api et al., 2008; Api and Vey, 2008; WHO, 2012). As a novel method to assess the risk of skin sensitization, the QRA has gained more attention among regulators and academia in recent years and is still under development and discussion (Basketter and Safford, 2016; Kimber et al., 2017; Nijkamp et al., 2015; SCCS, 2012; WHO, 2012). The International Dialogue for the Evaluation of Allergens (IDEA) project has published an updated methodology for the QRA of fragrance allergens (IDEA project, 2016). Recently, the SCCS concluded that, although a lot of progress has been made, this QRA methodology still lacks some scientific rationale for certain approaches and assumptions (SCCS, 2017). In general, a QRA aims to establish AELs for fragrances that are protective for the majority of the population. AELs are informative in regulatory decisions, however the policy-making process is nowadays more and more based on a toxicological risk assessment accompanied with an explicit impact assessment (Briggs, 2008; Knol et al., 2010; SCHER; SCENIHR and SCCS, 2013; Verhoeven et al., 2012).

In the toxicological risk assessment, exposures exceeding AELs would constitute a health risk and this information would be used by risk managers and regulators to propose risk mitigation measures to eliminate the health risk. Such risk mitigation measures can be costly and policy makers need to ensure the proportionality of their decisions. In order to compare various impacts (e.g. economic) of risk mitigation measures information about the foreseen health impact is warranted. This health impact describes the outcome of the proposed risk mitigation measure in terms of clinical effects (e.g. reduction of number of cases of a specific disease) instead of a reduction of risks.

In this study, we use the input data and assumptions of the previous analysis by Nijkamp et al. (2015) to estimate the health impact: i) the yearly number of individuals newly sensitized to geraniol and ii) the number of times in a year that individuals with pre-existing contact allergy to geraniol could begin to experience clinical symptoms of contact dermatitis due to re-exposure to geraniol (so-called elicitation episodes). To estimate the health impact, we propose a methodology to further develop the risk assessment of skin sensitizers (QRA) towards a health impact assessment (HIA). First, we will adapt the QRA by introducing a probabilistic AEL to derive a newly defined individual sensitization induction dose (iSID) and individual elicitation induction dose (iEID). Subsequent exceedance of these individual sensitization and elicitation doses on a single day leads to a clinical response (either to become sensitized or experience symptoms related to allergic contact dermatitis). In a simulated population the aggregated exposure to geraniol from PCP and HCP use is determined per single day for a 14-day period for each person and combined with the iSID and iEID to determine the health impact. The HIA is performed to evaluate the health effects of different policy measures that would lower the concentration of geraniol in PCPs and/or HCPs compared to the current situation. The outcomes provide insight in the effectiveness of different policy measures in reducing the health impact from contact allergy to geraniol.

2. Methods

2.1. Scope of the health impact assessment

The geographical boundary of the HIA is limited to Western and Northern Europe[1] as the data used in the Probabilistic Aggregate Consumer Exposure Model (PACEM) to estimate the aggregated exposure is derived from countries within this region (United Kingdom, Germany, Denmark, Sweden and The Netherlands). Extrapolating to a wider geographical area might not be appropriate, as there can be differences between European regions in product use and geraniol concentrations. Indeed, Uter et al. (2009) noted differences on the aggregated level of FM I sensitization between European regions (Northeast, Southern, Western and Central Europe) based on 19,793 patients patch tested across 10 European countries in 2005/2006. The population of interest is the general adult population that can come into contact with geraniol from PCPs or HCPs in their daily routine. The time frame used in this HIA is one year.

2.2. Evaluated scenarios

The baseline scenario reflects the current situation. In this baseline scenario, the existing risk mitigating measures concerning PCPs and HCPs are that geraniol should be indicated in the list of ingredients in cosmetic products when its concentration exceeds 0.001% in leave-on products or 0.01% in rinse-off products according to EU legislation (The European Parliament and the Council, 2009). For household cleaning products, detergents[2] that contain geraniol shall indicate its presence on the list of ingredients if added at concentrations above 0.01% (The European Parliament and the Council, 2004). No trends are foreseen in the near future concerning legislation on PCPs and HCPs, voluntary agreements or changes in exposure patterns. Three policy measures, restricting the concentration of geraniol in specific product groups are evaluated. The first policy scenario is a general restriction on the use of geraniol in PCPs with a concentration limit of 0.01% as suggested by the Scientific Committee on Consumer Safety (SCCS, 2012). The second scenario is a restriction of the use of geraniol in HCPs in concentrations above 0.01%. The third scenario is a restriction of the use of geraniol in both PCPs as HCPs above 0.01%.

2.3. Hazard assessment

2.3.1. Previous QRA for geraniol

Previously, Nijkamp et al. (2015) derived an AEL of 55 μg/cm^2 in their QRA for geraniol. This AEL indicates a protective exposure level of which there is no appreciable risk of induction when the aggregated exposure in one day stays below the AEL. In short, the AEL was derived by determining an adequate No Expected Sensitization Induction Level (NESIL) from multiple local lymph node assays (LLNA) in mice and applying Sensitization Assessment Factors (SAFs) to account for differences between experimental and the real-life situation (for more detail, see Nijkamp et al. (2015)). In the same paper, a second AEL of 100 μg/cm^2 is derived based on Human Repeat Insult Patch Tests

[1] Denmark, Sweden, Finland, Germany, United Kingdom, Ireland, The Netherlands, Belgium and Luxembourg.

[2] 'Detergent' means any substance or preparation containing soaps and/or other surfactants intended for washing and cleaning processes.