Regulatory Toxicology and Pharmacology 72 (2015) 673–682

Contents lists available at ScienceDirect

Regulatory Toxicology and Pharmacology

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

Use of an aggregate exposure model to estimate consumer exposure to fragrance ingredients in personal care and cosmetic products

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ARTICLE INFO

Article history:
Available online 10 June 2015

Keywords:
Exposure assessment
Risk assessment
Aggregate exposure
Fragrance ingredients
Cosmetics
Personal care products

ABSTRACT

Ensuring the toxicological safety of fragrance ingredients used in personal care and cosmetic products is essential in product development and design, as well as in the regulatory compliance of the products. This requires an accurate estimation of consumer exposure which, in turn, requires an understanding of consumer habits and use of products. Where ingredients are used in multiple product types, it is important to take account of aggregate exposure in consumers using these products. This publication investigates the use of a newly developed probabilistic model, the Creme RIFM model, to estimate aggregate exposure to fragrance ingredients using the example of 2-phenylethanol (PEA). The output shown demonstrates the utility of the model in determining systemic and dermal exposure to fragrances from individual products, and aggregate exposure. The model provides valuable information not only for risk assessment, but also for risk management. It should be noted that data on the concentrations of PEA in products used in this article were obtained from limited sources and not the standard, industry wide surveys typically employed by the fragrance industry and are thus presented here to illustrate the output and utility of the newly developed model. They should not be considered an accurate representation of actual exposure to PEA.

1. Introduction

Fragrance ingredients are used in a wide variety of consumer products including both personal care and household products. Use of cosmetic and personal care products forms part of the daily routine for most people in almost every country in the world. Ensuring the toxicological safety of fragrance ingredients in such products, when used as directed, is essential and forms an integral step in product development and design, as well as in the regulatory compliance of the products (Nohynek et al., 2010; Pauwels and Rogiers, 2010). Consumer safety is assessed by conducting risk assessments for each ingredient present in the product. This requires knowledge of how much of each ingredient a consumer is exposed to which, in turn, relies on an accurate estimation of the day to day exposure to consumers of those products. Understanding consumer habits in terms of how often products are used, on which areas of the body they are used and how much of each product is used on each occasion plays a central role in estimating this exposure.

It is recognised by industry and regulators alike that some ingredients are unique to certain product categories and are unlikely to be used in multiple products, while there are other ingredients that are present in multiple consumer products, which may include personal care and cosmetic products, household care products and other sources such as foods. In conducting risk assessments for such multiple use ingredients it is important to understand the overall, or aggregate, exposure from all products that a consumer may use in their day-to-day routines. Fragrance ingredients are one such group of ingredients that may be present universally across multiple

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http://dx.doi.org/10.1016/j.yrtph.2015.05.017
0273-2300/

product types. Thus there is a need when evaluating the safety of fragrance ingredients to take into consideration the aggregate exposure for consumers from all of product types.

Typically, in the past, estimates of aggregate exposure to fragrance ingredients have been made using two methods. The first approach is to measure annual volumes of fragrance ingredients used over specific geographical areas. This gives a crude estimate of consumer exposure and is primarily used in estimates of environmental exposure (Cadby et al., 2002). The second method is to estimate consumer exposure from each product which may contain the ingredient, using a mean or maximum level of inclusion and a high percentile value (such as 90th or 95th) for the amount of product used by consumers for each application. These individual, high end, exposures are then simply summed to give an aggregate exposure. Use of this method for fragrance ingredients is discussed in detail by Cadby et al. (2002) and is also proposed by the European Scientific Committee on Consumer Safety (SCCS) for assessing exposure to preservatives used in personal care products (SCCS, 2012). Clearly such an approach provides a very conservative estimate of aggregate exposure to a fragrance ingredient since it does not take into account the fact that consumers may not use all products included in the calculation, or may not use all products on any one day. It also assumes that all products used by the consumer contain the fragrance at a given high level. With well over 2500 different fragrance ingredients in current use (European Commission Cosmetic Ingredient Database, CosIng) it is highly unlikely that the wide range of fragrance-containing products used by a consumer in any given day will all contain a particular fragrance material at significant concentrations, let alone at the maximum current use levels in every product.

More recently a publication by Cowan-Ellsberry and Robison (2009) described a method of incorporating information on non-use and co-use of products to provide a more accurate estimate of aggregate exposure. In that case they were looking at a number of parabens used in personal care and cosmetic products as preservatives. Using a limited data set on consumer habits, and incorporating deterministic (worst case) estimates of paraben concentrations in products, they were able to demonstrate the importance of incorporating non-use and co-use statistics into the calculation, estimating that actual consumer exposure based on their model was 51–92% lower than the figure obtained using simple addition methods. The over conservative nature of simple deterministic methods in estimating paraben exposure is also supported by limited biomonitoring data which shows that total systemic exposure from all sources and routes of exposure is considerably lower than previous deterministic estimates (Ye et al., 2006), emphasing the need for accurate and realistic methods to estimate consumer aggregate exposure to cosmetic ingredients.

In the last decade a considerable amount of work has been carried out to establish trends for use of personal care and cosmetic products which now begin to allow more accurate assessment of exposure to ingredients used in these products. The availability of accurate statistical distributions of the quantities and frequencies of use of some consumer products (Hall et al., 2007, 2011; Loretz et al., 2005, 2006, 2008) has made the development of probabilistic methods of estimating consumer exposure possible (McNamara et al., 2007).

Since 2010, the Research Institute for Fragrance Materials, Inc. (RIFM) has been working with Creme Global to develop a model to estimate the aggregate exposure to fragrance ingredients which are used in a range of common consumer products. Creme Global (www.cremeglobal.com) is a well-established partner in modelling exposure for cosmetics and foods, and their methodology is being applied to support exposure estimates for regulatory submissions as well as used by some regulatory bodies such as the US Department of Agriculture (USDA) and the Food Safety Authority of Ireland (FSAI) to calculate consumer exposure. The key initiative of this project in developing the model described was to provide the methodology to estimate consumer exposure to fragrance materials from dermal and oral (toothpaste, mouthwash, lipstick etc.) exposure to personal care and cosmetic ingredients in Europe and the USA. The model utilises habits and practices data from a number of sources to simulate exposure in a population. The use of probabilistic (Monte Carlo) simulation allows the full distributions of these data sets to be incorporated, providing a more realistic estimate of aggregate exposure to individuals across a population. Output from the model provides exposure in absolute terms (mg) and systemic exposure per unit body weight (mg/kg bw/day). Also, since the route of exposure for most of the products is dermal, output is provided as amount per skin surface area ($\mu g/cm^2$) for different body areas. This latter capability provides more accurate exposure estimates for risk assessment of local endpoints such as skin irritation and sensitisation. Details of the model can be found in a concurrent publication (Comiskey et al., 2015).

In this publication we describe how the model can be used to calculate consumer exposure to fragrance materials that are commonly used in consumer products. Simulations have been conducted using an example fragrance, 2-phenylethanol (PEA), based on limited data of inclusion levels of this fragrance in products. As such, the results presented represent only an illustration of the utility of using this model. Collection of data on actual use levels of fragrance ingredients in products from a wider range of fragrance houses and personal care and cosmetic product manufacturers is ongoing, and will provide more accurate estimates of exposure in the future.

2. Materials and methods

2.1. The Creme RIFM aggregate exposure model

Determination of aggregate exposure to a number of fragrance ingredients was conducted using a model developed by Creme Global in conjunction with RIFM (described here as the Creme RIFM model). Full details of the model are given in a concurrent publication (Comiskey et al., 2015).

The model uses probabilistic (Monte Carlo) simulation to allow sampling from distributions of data sets providing a more realistic estimate of aggregate exposure to individuals across a population. The Creme RIFM model is designed to be a realistic representation of the population's product usage and dermal exposure. Output from the model provides both product exposure and fragrance ingredient exposure, which can be expressed [depending on product or fragrance exposure] in absolute terms (g or mg), systemic exposure per unit body weight (mg/kg bw/day or μg/kg bw/day) and amount per skin surface area (mg/cm^2 or $\mu g/cm^2$) for different body areas. All of the sources of exposure data in the model are based on information of varying detail and completeness. Where any uncertainties exist, conservative assumptions are used in the model.

Aggregate consumer exposure is calculated based in the following data:

1. Frequency of product use (consumer habits).
2. Skin sites of application of the products.
3. Amount per use of each product.
4. Chemical concentration of fragrance ingredient in the product.
5. Retention factor.
6. Penetration factor.
7. Subject bodyweight and height.
8. Surface area of product application areas/body sites.

These data were obtained from a Kantar World Panel Survey (http://www.kantarworldpanel.com/global) and from a variety of