Food and Chemical Toxicology 83 (2015) 103–110

Contents lists available at ScienceDirect

Food and Chemical Toxicology

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

Aggregate exposure modelling of zinc pyrithione in rinse-off personal cleansing products using a person-orientated approach with market share refinement

Sarah A. Tozer [a, *], Seamus Kelly [b], Cian O'Mahony [b], E.J. Daly [b, 1], J.F. Nash [c]

[a] The Procter and Gamble Company, P&G Technical Centres Ltd., Whitehall Lane, Egham, Surrey, TW20 9NW, United Kingdom
[b] Creme Global Ltd, The Tower, Trinity Enterprise Centre, Grand Canal Quay, Dublin 2, Ireland
[c] The Procter and Gamble Company, Cincinnati, OH 45202, USA

ARTICLE INFO

Article history:
Received 8 May 2015
Received in revised form
30 May 2015
Accepted 6 June 2015
Available online 16 June 2015

Keywords:
Aggregate exposure
Probabilistic modelling
Zinc pyrithione

ABSTRACT

Realistic estimates of chemical aggregate exposure are needed to ensure consumer safety. As exposure estimates are a critical part of the equation used to calculate acceptable "safe levels" and conduct quantitative risk assessments, methods are needed to produce realistic exposure estimations. To this end, a probabilistic aggregate exposure model was developed to estimate consumer exposure from several rinse off personal cleansing products containing the anti-dandruff preservative zinc pyrithione. The model incorporates large habits and practices surveys, containing data on frequency of use, amount applied, co-use along with market share, and combines these data at the level of the individual based on subject demographics to better estimate exposure. The daily-applied exposure (i.e., amount applied to the skin) was 3.79 mg/kg/day for the 95th percentile consumer. The estimated internal dose for the 95th percentile exposure ranged from 0.01–1.29 μg/kg/day after accounting for retention following rinsing and dermal penetration of ZnPt. This probabilistic aggregate exposure model can be used in the human safety assessment of ingredients in multiple rinse-off technologies (e.g., shampoo, bar soap, body wash, and liquid hand soap). In addition, this model may be used in other situations where refined exposure assessment is required to support a chemical risk assessment.

1. Introduction

Understanding human exposure to consumer products is fundamental when conducting a quantitative toxicological risk assessment of the ingredients in the products. Historically, aggregate exposure has not been evaluated routinely or has been estimated based on deterministic methods. However, more and more, estimates of aggregate exposure are becoming an expectation for some chemical risk assessments. For example, in the Scientific Committee for Consumer Safety (SCCS) Notes of Guidance for the Testing of Cosmetics and their Safety Evaluation (SCCS, 2012), it is recommend that preservatives are assessed considering aggregate exposure. Also, in the European Cosmetics Regulation (EC) 1223/2009, substances classed as carcinogenic, mutagenic or toxic to reproduction (aka CMR) class 1A/1B should be assessed for total (aggregate) exposure, considering their simultaneous presence in cosmetics, foods, medicines, and in products covered by REACh (i.e., Registration, Evaluation, Authorisation and Restriction of Chemicals) legislation. In addition, the SCCS has requested the consideration for aggregate exposure for a number of chemicals including citral, farnesol, and phenylacetaldehyde, silver (SCCS, 2008), and ethyl lauroyl arginate (SCCS, 2014). As these aggregate exposure estimates could potentially be used to calculate acceptable "safe levels" and/or conduct quantitative human risk assessments for cosmetic ingredients, there is a need to use methods that are capable of producing refined, realistic aggregate exposure estimations. To this end and to get a more accurate estimate of ingredient exposure, it is necessary to examine the patterns of use of the combinations of products by the population.

A tiered approach is recommended for aggregate exposure estimates (Delmaar JE and van Engelen JGM, 2006; Meek et al., 2011), which begins with a rough deterministic estimation of exposure

* Corresponding author.
E-mail addresses: tozer.sa@pg.com (S.A. Tozer), seamus.kelly@cremeglobal.com (S. Kelly), cian.omahony@cremeglobal.com (C. O'Mahony), dalyej@gmail.com (E.J. Daly), nash.jf@pg.com (J.F. Nash).
[1] Present address: Maiden Hall, Kilmallock, Co. Limerick, Ireland.

http://dx.doi.org/10.1016/j.fct.2015.06.005
0278-6915/

and evolves to a more complex person-orientated probabilistic approach. However, to date, there are no standard methods recognized for doing such exposure assessments. In general, aggregate exposure is estimated using a simplistic approach of adding deterministic exposures from all the individual product types in which the chemical might be present (SCCS, 2012). Such methods assume that everybody in the population uses all the products containing the chemical daily. This grossly exaggerates the aggregate exposure. An approach has been described for refining a deterministic aggregate exposure assessment to the paraben preservatives (i.e., methy-, ethyl- and isopropyl paraben) in personal care products by incorporating data on co-use and non-use patterns of product usage, and the presence probability of the ingredient (Cowan-Ellsberry and Robison, 2009). This has led to considerable refinement in exposure (51–92%). Co-use is the term describing the combination of products used by the same subject and by applying the co-use statistics, a more refined aggregate exposure model can be developed that better reflects population exposure. Since product use data are readily available for many cosmetic products (Hall et al., 2007, 2011; Loretz et al., 2005, 2006, 2008) the co-use approach offers a practical method to refine aggregate exposure assessments. Recently co-use data has been incorporated into high tier exposure estimates in the Probabilistic Aggregate Consumer Exposure Model (PACEM) tool to estimate exposure to ethyl paraben, diethyl phthalate and cyclosiloxane in a Dutch population (Delmaar et al., 2014; Dudzina et al., 2015; Gosens et al., 2013).

Another refinement to more accurately reflect aggregate exposure estimations in populations is the incorporation of presence probability data, which describe the likelihood the ingredient is present in a product, since only the consumers using products containing the ingredient will be exposed. Incorporation of presence probability data into exposure assessments is being done already in the area of food safety (Mistura et al., 2013). To give a cosmetics example, consumers using only “fragrance/perfume free” cosmetics would not, generally speaking, be exposed to perfume raw materials through the use of these products. When presence probability data is combined with reliable market share data for the products it can be used to determine the probability of exposure, which can be incorporated to refine the exposure assessment. Another cosmetics example could be users of antidandruff shampoos exposed to antifungal chemicals like zinc pyrithione (ZnPt), ketoconazole or climbazole (Schwartz et al., 2013; Liu et al., 2014). In 2013, the SCCS reviewed an application to consider whether 2% ZnPt (CAS# 13463-41-7) in rinse off hair products, such as shampoos, could be supported and concluded it to be safe for the consumer (European Commission and Directorate General for Health and Consumers, 2013). However, they noted that aggregate exposure to ZnPt from other sources, e.g., if used as a preservative or as an active ingredient in, for example, liquid hand soap (Guthery et al., 2005; Seal et al., 2005; Shintre et al., 2006), has not been considered in the dossier that was submitted. Therefore, we have developed a model to estimate the external aggregate exposure to ZnPt following the use of real, e.g., antidandruff shampoo, and hypothetical, e.g., liquid hand soap, rinse-off personal cleansing products. This approach can also be applied to the exposure assessment of other chemicals used in other personal care and cosmetic products.

When considering aggregate exposure, it is not practical to directly measure the usage habits for the entire population. Using probabilistic techniques, with a person-orientated approach, a simulated population can be generated whose product usage habits reflect that population. In the present study, average daily applied external aggregate exposure of ZnPt was estimated following use of five rinse-off products (i.e., shampoo, shower gel, bar soap, liquid hand soap and cleanser) in North American and European consumers, and was expressed in units of mg of ZnPt per unit body weight. A simulated population was created from these data for subsets of the population, including co-use and presence probability data, and inferring from these data the likely usage habits for the general population. The aggregate exposure estimates generated in this study are compared to estimates generated using a simpler methodology, such as a deterministic approach. The exposure values generated can be used for the purposes of quantitative risk (safety) assessment.

2. Materials and methods

ZnPT has several functions in cosmetics. Aside from its well known anti-dandruff properties, ZnPT is approved for use as a preservative to protect cosmetics and personal care products from spoilage. The products considered in this aggregate exposure study were a shampoo, bar soap, liquid hand soap (LHS), body wash (shower gel), and an underarm cleanser, all of which are rinse-off products. ZnPt, the ingredient of interest, was at 2% as antidandruff active in shampoo and 0.5% in all other products (see 2.1.7. ZnPt Concentration in Products).

2.1. Data sources

Consumption data were collected from several habits and practices (H&P) surveys conducted in the United States, supplemented with data from previously published studies of this kind from Europe, and U.S. national survey data, e.g., NHANES, where applicable.

2.1.1. Frequency of use and co use data

These data were obtained from two on-line surveys conducted by Procter and Gamble (P&G) where the participants represented the US population in terms of age, gender and ethnicity.

2.1.1.1. H + P CORE 2010

H + P CORE 2010 (n = 3814, age 18–65+) was a study carried out to examine consumer habits regarding the use of personal care products, and asked specific questions on the frequency of use for LHS, shower gel, and shampoo.

2.1.1.2. H + P Body Care 2010

H + P Body Care 2010 (n = 448, age 18–64) subjects are a subset of the H + P CORE 2010 study, chosen because they report using body care products. This data set contains frequency of use information for all of the products, and so provides the co-use data.

2.1.2. Subject demographic data

H + P CORE 2010 was the primary data used providing demographic information for each subject [gender, age group (18–24, 25–34, 35–44, 55–64, 65+) and ethnicity (black, Hispanic, white, other)]. There were 48 distinct combinations of gender, age group, and ethnicity. However, no information was available for the demographic group: female, 65+, Hispanic. Thus, the remaining 47 demographic groups were represented and used in the study. Each subject was placed in a category matching the subject's demographic details.

Each participant in the databases used in the study was allocated an appropriate combination of gender, age group and ethnicity from the H + P CORE 2010 study.

2.1.3. National health and nutrition examination survey (NHANES)

NHANES contains demographic information for the US population. The 2007–2008 NHANES survey [Centers for Disease Control