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SKIN SENSITIZATION INDUCTION RISK ASSESSMENT OF INGREDIENTS

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1. INTRODUCTION

Cardno ChemRisk was asked by WEN By Chaz Dean ("WCD") to conduct a comprehensive risk and safety assessment of the cosmetic product commonly known as WEN® by Chaz Dean Cleansing Conditioner (the "WEN Products"), and, specifically, whether the product causes hair loss and/or any other adverse dermal event, which evaluation was triggered by complaints and allegations that the WEN Products caused hair loss in a very small percentage of consumers. As part of that comprehensive risk and safety assessment, we performed a quantitative risk assessment of the skin sensitizing potential of WEN's ingredients. This evaluation may inform the prioritization of chemicals of concerns and may provide guidance for potential future actions or additional safety testing.

Cardno ChemRisk used a series of inclusion and exclusion criteria to determine ingredients of potential concern for further evaluation. A quantitative risk assessment for selected ingredients was performed by comparing expected consumer levels of exposure to those levels not expected to induce a skin sensitization response. The parameters used in this assessment are widely used by cosmetic trade industry and consumer safety groups to evaluate the safety of cosmetic ingredients (Api et al. 2008b; Api et al. 2008a).

2. BACKGROUND

2.1 Background on Skin Sensitization

Skin sensitization is an immunological response caused by contact with an allergen that can result in the physical symptoms of allergic contact dermatitis (ACD). ACD develops in two stages: (1) the induction stage and (2) the elicitation stage. In the induction stage, a chemical, or skin sensitizer, reacts with skin proteins to form a conjugate. This initiates a cascade resulting in proliferation of allergen specific T-cells. In the elicitation stage, an individual is re-exposed to the same chemical triggering an immune response that leads to ACD (Gerberick et al. 2000).

Chemicals that cause skin sensitization typically react with skin proteins to induce allergenicity. Thus, there is a correlation between chemical protein reactivity and skin sensitization potential (Gerberick et al. 2000). In addition, it is known that the induction of skin sensitization is threshold-based, such that the likelihood is dependent upon the amount and frequency of dose per unit of skin area exposed (Gerberick et al. 2001). Therefore, a key component of a risk assessment for skin sensitization is use of a benchmark value known as the no expected sensitization induction level (NESIL). A NESIL value is derived based on toxicology data for a given chemical and represents a level of exposure at which no skin sensitization is expected to occur. For the purposes on quantitative risk assessment, an expected consumer exposure level to a select ingredients is compared to the NESIL to determine the risk of skin sensitization under a given exposure scenario (Api et al. 2008a).

Damage to the hair can occur when personal care or cosmetic products are used incorrectly or too frequently, which may produce changes in hair texture that correspond to morphologic changes or

even hair loss (Ahn and Lee 2002). Identified examples of such occurrences typically involve skin irritation and sensitization. For example, irritation to the skin may occur when irritants and allergens from cosmetics, such as hair dye penetrate the scalp (Ishida, Makino et al. 2011; AlGhamdi and Moussa 2012). Alghamdi and Moussa (2012) reported that hair loss was a side effect among individuals who experienced skin irritation as a result of the use of hair dyes. In addition, hair highlighting has been shown to be able to cause allergic and irritant contact dermatitis resulting in hair loss (Lund, Unwala et al. 2010). Additionally, researchers have reported cases of inflammatory alopecia and allergic contact dermatitis following topical triggers, such as fragrances, sunscreens, as well as personal care and cosmetic products (Aldoori, Dobson et al. 2016; Admani, Goldenberg et al. 2017; Liu, Zimarowski et al. 2017). Goldenburg et al. (2017) noted that the "hallmark for contact alopecia is a preceding eczematous localized inflammatory response followed by hair loss, with notable regrowth of hair occurring by 6 months after allergen avoidance…[which is] consistent with contact-associated telogen effluvium" (Goldenberg, Admani et al. 2017, p. 626). Accordingly, based on the literature, hair loss caused by a cosmetic product would not be expected to occur without symptoms of irritation or sensitization.

3. METHODOLOGY

- Inclusion and Exclusion Criteria for Ingredients of Potential Concern

Product formulation sheets for the three most commonly purchased varieties of WEN cleansing conditioner products (Sweet Almond Mint, Lavender, and Pomegranate) were reviewed to develop a comprehensive list of ingredients present in the products. A three-step inclusion criteria process was used to select ingredients for further evaluation:

1) A comprehensive literature search was conducted to identify ingredient-specific toxicological and dose-response data necessary to perform a safety assessment. Any ingredients with reported or suspected risk of skin sensitization were included for further evaluation.

2) An *in silico* analysis was conducted using the OECD toolbox (version 4.0.0.26167). Ingredient CAS numbers were used to identify canonical SMILES strings which were utilized for OECD toolbox profiling. Five profiles were run for skin sensitization: protein binding alerts for skin sensitization, protein binding by Oasis v1.4, protein binding by OECD, protein binding potency Cys (Direct Peptide Reactivity Assay [DPRA] 13%), and protein binding potency Lys (DPRA 13%). Chemicals with structural alerts for skin sensitization were included for further evaluation

3) A experienced dermatologist reviewed and classified the allergenic/sensitization potential of all listed ingredients in the analyzed WCD cleansing conditioner products. Based on literature review and 20 years of product patch testing experience, ingredients were classified according to their likelihood of causing allergic contact dermatitis: high,

moderate, low, or extremely unlikely. Ingredients identified as having a high or moderate risk of inducing an allergenic/sensitization dermal response were included for further evaluation

Certain ingredients meeting the inclusion criteria were subsequently excluded from further evaluation if they met the following criteria: 1) an ingredient was classified as safe for use in cosmetic products via safety assessment by an agency such as the Cosmetic Ingredient Review (CIR) or Research Institute for Fragrance Materials (RIFM), and 2) the ingredient-specific concentration in WEN cleansing conditioner products, per formulation sheets, was within the range of concentrations considered by CIR or RIFM during their safety assessment of the ingredient. However, these exclusion criteria did not apply to ingredient classified with a moderate to high allergen/sensitization potential per dermatologist review.

- Risk Assessment

Given the intended use of WEN cleansing conditioners as an alternative to shampoo and the alleged adverse events involving skin irritation, the risk assessment was focused exclusively on dermal exposure scenarios and resulting sensitization potential. An expected consumer exposure level (CEL) was each ingredient was calculated based upon available data for adult U.S. females (Loretz et al. 2006; Cadby et al. 2002). Specifically, based on the total surface area of the adult female scalp (800 cm^2), an estimate for the maximum amount of liquid that can adhere to the surface of the skin [10 mg/cm^2 (Tibaldi et al. 2017)], and the assumption that shampoo is applied once per day, the maximum amount of dermal exposure one can experience from the use of shampoo or conditioner was 8.0 g per day. Additionally, a retention factor, or amount of product remaining on the skin following rinsing, was applied when determining exposure to shampoo and conditioner products (Comiskey et al. 2015) (Table 1). Specifically, the ingredient-specific CEL for shampoo/conditioner use was calculated using the following formula:

$$CEL = \frac{(MDE)(RF)(C\%)}{SA}$$

Where:

MDE: maximum dermal exposure (8 g/day)
RF: retention factor (0.1%)
C%: ingredient-specific concentration (% weight/volume) in product based on formulation sheets and supplied MSDSs
SA: surface area of adult female scalp (800 cm^2)

For each ingredient, the calculated CEL was compared to the weight-of-evidence (WoE) NESIL for the ingredient if available in the peer-reviewed literature or agency documents. If a WoE NESIL was not reported, a review of the peer-reviewed literature and toxicological databases was performed in an attempt to derive one if any relevant data were available [e.g. local lymph node assay (LLNA), human repeat insult patch test (HRIPT), or human maximization test (HMT)]. If

an ingredient-specific NESIL was not available nor could be derived, the dermal sensitization threshold (DST) approach was utilized to evaluate the safety of the ingredient (Safford 2008; Safford et al. 2011; Safford et al. 2015). Briefly, this approach classifies a chemical ingredient as reactive or non-reactive based on the presence of absence of specific mechanistic domains known to be associated with skin sensitization reactions in the chemical structure (Safford et al. 2011; Safford et al. 2015; Roberts et al. 2015). If the chemical structure of an ingredient was unknown, or the ingredient contained a mixture of chemicals, the ingredient was assumed to be reactive. Based upon probabilistic assessments of available datasets, a DST of 64 µg/cm^2 was applied for reactive chemicals, while a DST of 900 µg/cm^2 was applied for non-reactive chemicals (Safford et al. 2011; Safford et al. 2015).

A margin of safety (MOS) for each ingredient was calculated by comparing the benchmark dose (NESIL or DST) to the CEL using the following equation:

$$MOS = \frac{(NESIL\ or\ DST)/(SAF)}{CEL}$$

Where:

NESIL = No Effect Sensitization Level
DST = Dermal Sensitization Threshold
SAF= Sensitization Assessment Factor
CEL = Consumer Exposure Level

A minimum sensitization adjustment factor (SAF) of 100 was used for each MOS calculation based on dermal sensitization quantitative risk assessment data for shampoo/hair conditioners (Api et al. 2008a; Safford 2008; IFRA et al. 2011). The cumulative SAF of 100 is the product of a SAF of 10 for human variability, a SAF of 3 for matrix variability, as well as a SAF of 3 for use variability (Api et al. 2008a; Safford 2008; IFRA et al. 2011). A SAF for matrix variability is due to the fact that shampoo and conditioner products consist of mixtures that could contain other ingredients which could cause irritation or enhance dermal permeability. A SAF for use variability is necessary due to the fact that the skin on the scalp is highly follicular and is considered to be more permeable than skin elsewhere on the body (Api et al. 2008a; Safford 2008; IFRA et al. 2011). In this analysis, a MOS greater than 1 indicates that exposure to the constituent in the product would not be expected to induce skin sensitization in a consumer under the examined exposure scenario.

4. RESULTS AND DISCUSSION

Thirty-three ingredients present in the analyzed the WEN Products were evaluated for inclusion in this analysis. A total of eight unique ingredients present in the WEN Products met the inclusion/exclusion criteria for further analysis in this quantitative risk assessment (Table 2). These included four botanicals, two preservatives, one conditioner, and one fragrance. It should

[redacted]

be noted that the identified fragrance was a general term referring to mixtures, and that the fragrances from the three analyzed products consisted of 39 separate chemical constituents.

- **Methylisothiazolinone and Methylchloroisothiazoline**

Methylisothiazolinone (MI) and methylchloroisothiazolinone (MCI) are active ingredients in Kathon CG, a commonly used preservative in cosmetics that is effective against fungi, yeast, and bacteria (de Groot et al. 1988). MI and MCI have been shown to be sensitizing agents at certain concentrations in multiple studies (SCCS 2015). Both in the US and Europe, the use of a mixture of MCI and MI as preservatives in cosmetic products is permitted or recommended at a ratio of 3:1 and a combined maximum concentration of 15 ppm (0.1% by weight) in rinse-off products (CIR 1992; SCCS 2009). In the most recent MI safety assessment conducted by the SCCS, a NESIL was reported of 0.83 µg/cm^2 for MCI:MI (Kathon CG) based on HRIPT data (SCCS 2015).

[redacted]

- **Stearamidopropyl Dimethylamine**

Stearamidopropyl dimethylamine is an antistatic and hair conditioning agent used in cosmetic products. The maximum concentrations of stearamidopropyl dimethylamine reported in personal care products ranges from 0.01% to 5% (Bergfeld et al. 2014). [redacted] The CIR performed a quantitative risk assessment of potential dermal sensitization for stearamidopropyl dimethylamine and derived a conservative WoE NESIL of 1,000 µg/cm^2 for hair conditioners, based on data from 11 HRIPTs, a guinea pig maximization test, and a LLNA (Bergfeld et al. 2014). The 1,000 µg/cm^2 NESIL corresponds to the highest dose tested in the HRIPTs (Bergfeld et al. 2014). The CEL for stearamidopropyl dimethylamine was 1 µg/cm^2, which corresponded to a MOS of 10, utilizing a SAF of 100 (10 for inter-individual variability, 3 for matrix variability, 3 for use variability) (Table 3).

- ***Calendula officinalis* (marigold) flower extract**

Extracts from the plant material of *Calendula officinalis*, or marigold, are commonly used in cosmetic products as skin conditioning agents. Re et al. (2009) noted that *Calendula officinalis* contains various minerals, carbohydrates, lipids, phenolic compounds, steroids, tocopherals, and other chemicals. The reported concentration of extracts derived from *Calendula officinalis* in personal cosmetic products are generally below 1 % (Andersen et al. 2010). The CIR noted that "cosmetic formulations with up to 1.0% *Calendula Officinalis* extract were not irritating in short term tests, not irritating in cumulative irritation tests, and not sensitizing in RIPT tests" (Andersen et al. 2010, p. 240S). [redacted]

[redacted] A NESIL was not reported in the literature, nor was there information available to derive a WoE NESIL. Specifically, while the CIR reported that patch testing was performed on products containing *Calendula officinalis*, these results were from unpublished reports. Therefore, the DST approach was utilized since underlying data to derive a NESIL were unavailable for review. Due to *Calendula officinalis* being a mixture of compounds, chemical structures for all the constituents were not available for this botanical. We conservatively assumed that all constituents of this botanical ingredient contained a reactive mechanistic domain, and it was assigned a DST of 64 µg/cm^2 (Safford et al. 2015; Safford et al. 2011). The CEL for *Calendula officinalis* flower extract was 0.1 µg/cm^2, which corresponded to a MOS of 6, utilizing a SAF of 100 (10 for inter-individual variability, 3 for matrix variability, 3 for use variability) (Table 3).

- ***Chamomilla recutita* (chamomile) flower/leaf extract**

A CIR report identified 11 ingredients derived from the chamomile plant (*Chamomile recutita*) used in cosmetics, including various powders, oils, and extracts (Bergfeld et al. 2016). The reported use concentrations of *Chamomila recutita* flower/leaf extract in personal cosmetic products range from 0.0002 to 0.1% (Bergfeld et al. 2016). [redacted] In a 2016 safety evaluation, the CIR noted that chamomile-derived ingredients "are safe in the present practices of use and concentration in cosmetics when formulated to be non-sensitizing" (Bergfeld et al. 2016, p. 2). A NESIL for *Chamomila recutita* flower/leaf extract was not reported in the literature. HRIPTs have been conducted on various personal care products containing *Chamomila recutita* flower/leaf extract (Bergfeld et al. 2013). However, this unpublished data to derive a WoE NESIL was unavailable for review. Therefore, we conservatively assumed that all constituents present in *Chamomila recutita* flower/leaf extract contained a reactive mechanistic domain, and it was assigned a DST of 64 µg/cm^2 (Safford et al. 2015; Safford et al. 2011). The CEL for *Chamomila recutita* flower/leaf extract was 0.1 µg/cm^2, which corresponded to a MOS of 6, utilizing a SAF of 100 (10 for inter-individual variability, 3 for matrix variability, 3 for use variability) (Table 3).

- ***Lavandula angustifolia* (lavender) oil and flower extract**

Limited information is available regarding the use of *Lavandula angustifolia* (lavender)-derived ingredients in cosmetics. It was reported that lavender oil is present in creams and lotions at concentrations of approximately 0.015%, up to 0.1% (Opdyke 1976). [redacted] A NESIL was not reported for *Lavandula angustifolia* (lavender) oil and flower extract in the literature, nor was there information available to derive a WoE NESIL. The primary constituents of lavender oil and flower extract are linalool (20-60%) and linayl acetate (25-60%) (European Medicines Agency 2011). Api et al. (2015) noted that "[b]ased on the available data, linalyl acetate does not present a concern for skin sensitization" (p. S5). It is noteworthy that RIFM and IFRA have issued evaluations regarding the sensitization

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potential of linalool, the other primary constituent of lavender oil (Api et al. 2015). Although, linalool itself is not considered a sensitizing agent, it may undergo auto-oxidation to form products capable of reacting with skin proteins (Api et al. 2015). Api et al. (2008a) reported a NESIL value of 15,000 µg/cm^2 for linalool, based on the WoE from human and animal studies. For the purposes of this analysis, we conservatively assumed that all constituents of *Lavandula angustifolia* (lavender) oil and flower extract contained reactive mechanistic domains, and were assigned DSTs of 64 µg/cm^2. We believe that this is a highly conservative assumption, as this sensitization threshold is two orders of magnitude lower than the reported NESIL for the main constituent linalool. The CELs for *Lavandula angustifolia* flower extract and *Lavandula angustifolia* (lavender) oil were 0.1 µg/cm^2 and 0.3 µg/cm^2, respectively, which corresponded to MOSs of 6 and 2, utilizing a SAF of 100 (10 for inter-individual variability, 3 for matrix variability, 3 for use variability) (Table 3).

- **Fragrances**

Levels of fragrance used in cosmetics products can range from <0.1% in lotions, creams, and shampoos up to 20% in eau de toilette and perfume extract products (Cadby et al. 2002). Any given fragrance product may contain as many as 50 to 300 different chemical ingredients that may be proprietary to the manufacturer or supplier (Bickers et al. 2003). The listed 'Fragrance (Parfum)' ingredient in WCD cleansing conditioners was identified with a moderate likelihood for allergic contact dermatitis by an experienced dermatologist. [redacted] In total, 39 unique fragrance chemicals were identified based upon MSDSs in these three fragrances. [redacted] we conservatively assumed that each chemical constituent was present at the upper bound percentage as reported by the fragrance specific MSDSs. Thirteen of the reported fragrance chemicals had reported WoE NESILs based on available data (Table 4). The available NESILs ranged from 24 to 29,500 µg/cm^2. For fragrance chemicals which 1) did not have NESILs available or 2) data was not available to derive a NESIL, the DST approach was used (Table 4). Lemon oil and lavandin grosso oil are mixtures of other chemicals, therefore, we conservatively assumed that all of the constituents contained a reactive mechanism domain, and thus applied the DST value of 64 µg/cm^2. Based on previous analyses of the dermal sensitization for fragrance ingredients in shampoo products, a SAF of 100 (10 for inter-individual, 3 for matrix, 3 for use) was used for each MOS derivation (Api et al. 2008a). The derived MOSs for fragrance chemicals ranged from 21 to 98,333 (Table 4).

5. CONCLUSIONS

Cardno ChemRisk performed a quantitative risk assessment of the skin sensitizing potential of select ingredients present in the WEN Products.

In this analysis, we analyzed the sensitization potential of ingredients in three of the WEN Products and determined that the MOSs for ingredients with allergenic potential were all greater than 1. These results indicate that exposure to the individual ingredients present in the WEN Products would not be expected to induce dermal sensitization in a consumer. The approach used in this analysis is consistent with the recommendations of regulatory and trade industry agencies and with previous risk assessment performed for individual cosmetic ingredients to determine safety of the product at issue. These findings may be complemented by additional data from *in vitro*, *in vivo*, and clinical evaluations of the WEN Products.

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Table 1. Parameters used to determine average daily exposure to shampoo

Parameter	Value	Unit	Reference
Scalp surface area (SA)	800	cm^2	Cadby et al. 2002
Maximum dermal exposure (MDE)	8	g	Cadby et al. 2002; Tibaldi et al. 2017
Retention Factor (RF)	1	%	Comiskey et al. 2015
Constituent-specific Concentration (C%)	Varies	%	Formulation Sheets and supplier MSDSs

[redacted]

Table 2. Inclusion and exclusion criteria for ingredients present in WCD cleansing conditioners

Ingredient	CAS No.	Function	INCLUSION CRITERIA			EXCLUSION CRITERIA	
			Literature Review	In Silico Evaluation	Allergen Potential[a]	CIR "Safe for Use"	RIFM
Ingredients Not Meeting Inclusion Criteria							
Water	[redacted]	Solvent			Very Unlikely		
Aloe barbadensis (aloe vera) leaf juice	[redacted]	Botanical			Very Unlikely		
Cetearyl alcohol	[redacted]	Thickener			Low		
Cucumis sativus (cucumber) fruit extract	[redacted]	Botanical			Very Unlikely		
Dicetyldimonium chloride	[redacted]	Emulsifier			Low		
Guar hydroxypropyltrimonium chloride	[redacted]	Thickener			Very Unlikely		
Hamamelis virginiana (witch hazel)	[redacted]	Astringent			Very Unlikely		
Hydrolyzed soy protein	[redacted]	Conditioner			Very Unlikely		
Hydrolyzed wheat protein	[redacted]	Conditioner			Very Unlikely		
PEG-60 almond glycerides	[redacted]	Conditioner			Very Unlikely		
Persea gratissima (avocado) oil	[redacted]	Emollient			Very Unlikely		
Prunus amygdalus dulcis (sweet almond) oil	[redacted]	Emolient			Low		
Prunus serotina (wild cherry) fruit extract	[redacted]	Botanical			Low		
Punica granatum (pomegranate) extract	[redacted]	Botanical			Low		
Rosmarinus officinalis (rosemary) leaf extract	[redacted]	Botanical			Low		

[redacted]

Tetrasodium EDTA	[redacted]	Chelator			Low		
Triticum vulgare (wheat) starch	[redacted]	Botanical			Very Unlikely		
Ingredients Meeting Inclusion Criteria, But Excluded From Quantitative Risk Assessment							
Amodimethicone[b]	[redacted]	Conditioner	X		Very Unlikely	X	
Behentrimonium methosulfate[c]	[redacted]	Conditioner	X		Low	X	
Cetyl alcohol	[redacted]	Thickener	X		Low	X	
Citric acid	[redacted]	Acidifier	X		Very Unlikely	X	
Glycerin	[redacted]	Humectant			Very Unlikely	X	
Menthol	[redacted]	Analgesic	X		Low		X
Panthenol (pro-vitamin B5)	[redacted]	Moisturizer	X	X	Very Unlikely	X	
Polysorbate-60[d]	[redacted]	Emulsifier	X		Low	X	
Ingredients Meeting Inclusion Criteria, And Selected For Quantitative Risk Assessment							
Calendula officinalis (marigold) flower extract	[redacted]	Botanical			Moderate	X	
Chamomilla recutita (chamomile) flower/leaf extract[e]	[redacted]	Botanical			Moderate		
Fragrance (parfum)[f]	[redacted]	Aroma			Moderate		
Lavandula angustifolia (lavender) extract	[redacted]	Botanical			Moderate		
Lavandula angustifolia (lavender) oil	[redacted]	Botanical			Moderate		X
Methylchloroisothiazolinone (MCI)	[redacted]	Preservative	X	X	High		
Methylisothiazolinone (MI)	[redacted]	Preservative		X	High		
Stearimidopropryl dimethylamine	[redacted]	Conditioner	X	X	High		

[a]As determined by dermatologist (E.W.) review

[redacted]

[b]The CIR determined that dimethicone crosspolymer ingredients are safe for use

[c]The CIR determined that trimoniums were safe for use when formulated to be nonirritating

[d]The CIR determined that polysorbates were safe for use when formulated to be nonirritating

[e]The CIR determined that chamomile-derived ingredients were safe for use when formulated to be non-sensitizing

[f]General fragrance term. Includes 39 unique constituents across the 3 WCD products

NR = not reported

Table 3. Estimated consumer exposure levels and margins of safety for evaluated non-fragrance ingredients

[redacted]

Ingredient	Maximum Reported Concentration (%) in WCD Cleansing Conditioners	CAS Number	Consumer Exposure Level (CEL) (µg/cm^2)	Skin Sensitization Threshold Dose (µg/cm^2)	Threshold Type	Reference	Sensitivity Assessment Factor (SAF)	Margin of Safety (MOS)
Calendula officinalis (Marigold) flower extract	[redacted]	[redacted]	[redacted]	64	DST	Assumed reactive; Safford (2011; 2015)	100	6
Chamomilla recutita (Chamomile) flower/leaf extract	[redacted]	[redacted]	[redacted]	64	DST	Assumed reactive; Safford (2011; 2015)	100	6
Lavandula angustifolia (Lavender) flower extract	[redacted]	[redacted]	[redacted]	64	DST	Assumed reactive; Safford (2011; 2015)	100	6
Lavandula angustifolia (Lavender) oil	[redacted]	[redacted]	[redacted]	64	DST	Assumed reactive; Safford (2011; 2015)	100	2
Methylchloroisothiazolinone (MCI)/ Methylisothiazolinone (MI)[a]	[redacted]	[redacted]	[redacted]	0.83	NESIL	SCCS 2015	100	2
Stearimidopropyl dimethylamine	[redacted]	[redacted]	[redacted]	1,000	NESIL	CIR 2014	100	10

[redacted]

Table 4. Estimated consumer exposure levels and margins of safety for evaluated fragrance ingredients

[redacted]

Ingredient	Maximum Reported Concentration (%)	CAS No.	Consumer Exposure Level (CEL) (µg/cm^2)	Skin Sensitization Threshold Dose (µg/cm^2)	Threshold Type	Reference	Sensitivity Assessment Factor	Margin of Safety (MOS)
[redacted]	[redacted]	[redacted]	[redacted]	900	DST	Non-reactive, Safford et al. (2015)	100	45000
[redacted]	[redacted]	[redacted]	[redacted]	64	DST	Reactive (Schiff base former), Safford et al. (2015)	100	128
[redacted]	[redacted]	[redacted]	[redacted]	900	DST	Non-reactive, Safford et al. (2015)	100	9000
[redacted]	[redacted]	[redacted]	[redacted]	10,000	NESIL	Api et al. (2008)	100	1000
[redacted]	[redacted]	[redacted]	[redacted]	10,000	NESIL	Api et al. (2008)	100	10000
[redacted]	[redacted]	[redacted]	[redacted]	11,800	NESIL	Api et al. (2008), IFRA 2009	100	23600
[redacted]	[redacted]	[redacted]	[redacted]	5,000	NESIL	Api et al. (2008), IFRA 2013	100	10000
[redacted]	[redacted]	[redacted]	[redacted]	15,000	NESIL	Api et al. (2008)	100	30000
[redacted]	[redacted]	[redacted]	[redacted]	24	NESIL	Api et al. (2008), IFRA 2009	100	2400

[redacted]

[redacted]	[redacted]	[redacted]	[redacted]	900	DST	Non-reactive, Safford et al. (2015)	100	900
[redacted]	[redacted]	[redacted]	[redacted]	900	DST	Non-reactive, Safford et al. (2015)	100	4091
[redacted]	[redacted]	[redacted]	[redacted]	23,600	NESIL	IFRA 2013	100	11800
[redacted]	[redacted]	[redacted]	[redacted]	900	DST	Non-reactive, Safford et al. (2015)	100	900
[redacted]	[redacted]	[redacted]	[redacted]	900	DST	Non-reactive, Safford et al. (2015)	100	4500
[redacted]	[redacted]	[redacted]	[redacted]	64	DST	Reactive (Schiff base former), Safford et al. (2015)	100	32
[redacted]	[redacted]	[redacted]	[redacted]	64	DST	Reactive (Schiff base former), Safford et al. (2015)	100	320
[redacted]	[redacted]	[redacted]	[redacted]	900	DST	Non-reactive, Safford et al. (2015)	100	225
[redacted]	[redacted]	[redacted]	[redacted]	900	DST	Non-reactive, Safford et al. (2015)	100	225

[redacted]

[redacted]	[redacted]	[redacted]	[redacted]	64	DST	Reactive (Schiff base former), Safford et al. (2015)	100	64
[redacted]	[redacted]	[redacted]	[redacted]	900	DST	Non-reactive, Safford et al. (2015)	100	4500
[redacted]	[redacted]	[redacted]	[redacted]	900	DST	Non-reactive, Safford et al. (2015)	100	45000
[redacted]	[redacted]	[redacted]	[redacted]	900	DST	Non-reactive, Safford et al. (2015)	100	45000
[redacted]	[redacted]	[redacted]	[redacted]	900	DST	Non-reactive, Safford et al. (2015)	100	45000
[redacted]	[redacted]	[redacted]	[redacted]	900	DST	Non-reactive, Safford et al. (2015)	100	300
[redacted]	[redacted]	[redacted]	[redacted]	64	DST	Reactive (Schiff base former), Safford et al. (2015)	100	21
[redacted]	[redacted]	[redacted]	[redacted]	4,000	NESIL	Api et al. 2008	100	1333
[redacted]	[redacted]	[redacted]	[redacted]	64	DST	Reactive (Schiff base former), Safford et al. (2015)	100	21

[redacted]

[redacted]	[redacted]	[redacted]	[redacted]	900	DST	Non-reactive, Safford et al. (2015)	100	300
[redacted]	[redacted]	[redacted]	[redacted]	64	DST	Reactive (Schiff base former), Safford et al. (2015)	100	21
[redacted]	[redacted]	[redacted]	[redacted]	900	DST	Non-reactive, Safford et al. (2015)	100	300
[redacted]	[redacted]	[redacted]	[redacted]	64	DST	Reactive (Schiff base former), Safford et al. (2015)	100	21
[redacted]	[redacted]	[redacted]	[redacted]	29,500	NESIL	Api et al. 2008, IFRA 2009	100	98333
[redacted]	[redacted]	[redacted]	[redacted]	11,800	NESIL	IFRA 2013	100	39333
[redacted]	[redacted]	[redacted]	[redacted]	1,100	NESIL	IFRA 2009	100	3667
[redacted]	[redacted]	[redacted]	[redacted]	100	NESIL	IFRA 2009	100	333
[redacted]	[redacted]	[redacted]	[redacted]	5,900	NESIL	IFRA 2013	100	19667

[redacted]

[redacted]	[redacted]	[redacted]	[redacted]	64	DST	Assumed reactive; Safford et al. (2011; 2015)	100	213
[redacted]	[redacted]	[redacted]	[redacted]	64	DST	Assumed reactive; Safford et al. (2011; 2015)	100	213
[redacted]	[redacted]	[redacted]	[redacted]	4,100	NESIL	Api et al. 2008; IFRA 2015	100	13667

[redacted]