Data Supplement

International Nomenclature Committee
- Acryloyloxyethyl Phosphorylcholine

CIRSSC & FDA Comments
- Inhalation/Airbrush, Silicates, & Methicones

WVE Comments
- Inhalation
- MCI/MI
- Silicates

Council Use Survey & WR Grace&Co
- Zeolites

EXPERT PANEL MEETING
DECEMBER 6-7, 2021

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Bart Heldreth, PhD, Executive Director, CIR
Date: November 22, 2021
Subject: Safety Assessment of Acryloyloxyethyl Phosphorylcholine Copolymer Ingredients as Used in Cosmetics – Wave 2

The Panel previously requested structures of 2 ingredients assessed in this report; though, not enough was known about the connectivity of those 2 polymers to generate even generic structures. Recently, however, communications with polymer experts in the International Nomenclature Committee (INC) revealed that for these two graft copolymers, **Polyquaternium-10/Phosphorylcholine Glycol Acrylate Copolymer** and **Hydroxyethylcellulose/ Phosphorylcholine Glycol Acrylate Copolymer,** the cellulose derived polymers (polyquaternium-10* and hydroxyethylcellulose) lack acrylate groups that would be expected to copolymerize with the methacryoyloxyethyl phosphorylcholine (MPC). However, the use of ammonium persulfate as the initiator for the polymerization will generate free radicals from both, the cellulose derivatives and MPC. Free radical sites on polyquaternium-10 and hydroxyethylcellulose will lead to the production of graft copolymers with the MPC. The reaction mixture will also contain homopolymers of MPC; but without further information, it is difficult to say which reaction product (graft copolymers or MPC homopolymers) would be the dominant reaction product.

**(*polyquaternium-10 is a polymeric quaternary ammonium salt of hydroxyethyl cellulose reacted with 2,3-epoxypropyltrimonium chloride*)

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Jinqiu Zhu, PhD, DABT, ERT, CIR Toxicologist
Date: November 22, 2021
Subject: Comments from CIR Science and Support Committee on WVE's memo for Methicones and Silicates Safety Assessments, as well as clarifications on FDA classification of airbrush use and editorial format issues

Enclosed are the comments received from the CIR Science and Support Committee (CIR SSC) on the Women's Voices for the Earth (WVE)'s memo dated September 9, 2021, regarding the concerns relevant to inhalation exposure of particles during usage of airbrush consumer products as well as the safety assessments on Methicones and Silicates.

In the memo, the WVE provided some particle size distribution data of aerosols resulting from usage of four airbrush makeup products (data sourced from Pearce *et al.*, 2019, *Inhal Toxicol.*). The limitations of that study, as well as another paper published by the same research group, i.e., Pearce *et al.* 2020, *Toxicol. Sci.*, have been discussed, in part, in the document titled *annotated-WVEcomments_InhalationDocument_122021*. Herein, the CIR SSC further clarifies the exposure parameters under in-use conditions, and argues the further limitations of the 2 Pearce *et al*. 2019 and 2020 studies.

In addition, the CIR SSC suggests the draft Inhalation Resource Document should cover more detailed information presenting in the CIR SSC memo dated October 30, 2018, which was previously submitted to the Panel at the December 2018 meeting. For instance, the CIR SSC recommends incorporating sample calculations via a tiered approach to assess inhalation safety of cosmetic products. Accordingly, a copy of the memo provided by the CIR SSC in 2018, has also been enclosed in this Wave 2 supplement for the Panel's consideration.

Additionally enclosed, are communications between the CIR and the FDA Center for Devices and Radiological Health, as well as the Office of Cosmetics and Colors. These communications demonstrate the motivation and intended efforts to clarify current regulations relating to the categorization of airbrush use with cosmetics.

Please accept our apologies for the inconvenience and potential confusion we may have caused; the document *WVEcomments-annotated_ InhalationDocument_ 122021* included in 3 report packages was inconsistently annotated. Specifically, these annotated documents were included in three Report packages that were included in the initial December 2021 Panel meeting materials for the Inhalation Resource Document, the Methicone report, and the Silicates report. The following editorial issues have been identified, and warrant specific clarifications.

1. The following 2 sentences included in the original WVE's memo are missing in the *annotated WVEcomments*, as shown below.

"Note that the scale here is in nanometers (nm), where 10,000 nanometers = 10 microns. In this case, all of the particle sizes measured from the cosmetic airbrush are smaller than 10,000 nanometers(10 microns)."

These sentences should appear on pdf page 11 of the draft Inhalation Resource Document at https://www.cir-safety.org/sites/default/files/Inhalation.pdf, right below the Figure 2. Similarly, they should appear in the same place on pdf page 17 of the Methicone report at https://www.cir-safety.org/sites/default/files/Methicones_4.pdf, as well as on pdf page 15 of the Silicates report at https://www.cir-safety.org/sites/default/files/Silicates_6.pdf.

2. The following paragraph presented on page 12 of the draft Inhalation Resource Document at https://www.cir-safety.org/sites/default/files/Inhalation.pdf, should also appear in the same place on pdf page 18 of the Methicone report at https://www.cir-safety.org/sites/default/files/Methicones_4.pdf, as well as on pdf page 16 of the Silicates report at https://www.cir-safety.org/sites/default/files/Silicates_6.pdf.

> In addition, it is necessary to point out that, in both the Pearce 2019 and 2020 papers, aerosols were monitored using both a scanning mobility particle sizer (SMPS), that measured particle size distributions between ~ **10 – 435 nm**, and an optical particle sizer (OPS), that measured size distributions between **0.3 – 10 µm**. In comparison, Dr. Rothe indicated in her 2011 presentation (second slide from her presentation as shown above) that *"the scale on the X-axis is going **only** to **20 microns**, so **it's not really the whole distribution pattern**. So, when you remember what I showed you at the beginning, **the distribution pattern which was going up to 150 microns.**"* That is, the whole distribution pattern of aerosols resulting from application of airbrush makeup products have not been examined by the 2 Pearce studies, while the potential particle deposition fraction and deposited mass flux in human lungs during airbrush makeup use were estimated by MPPD computational model in the Pearce 2020 paper. The results showed that, for nano-sized particles, the entire exposure duration of 20 min could cause lung surface loading of 60 µg/m^2 based on the peak deposition mass flux of 3 µg/min/m^2, and for micro-sized particles, an inhaled dose within 20 min exposure was estimated to be 1.1 mg/m^2, based on the peak deposition mass flux of 55 µg/min/m^2.

3. The following sentence presented on page 13 of the draft Inhalation Resource Document at https://www.cir-safety.org/sites/default/files/Inhalation.pdf, should appear at the bottom of pdf page 18 of the Methicone report at https://www.cir-safety.org/sites/default/files/Methicones_4.pdf, as well as at the bottom of pdf page 16 of the Silicates report at https://www.cir-safety.org/sites/default/files/Silicates_6.pdf, to replace the relevant sentences, i.e.,

"However, on the basis of the currently available data, it is not clear whether the nanoparticles released during the product use include additional nanosized ingredients other than the engineered nanoparticles that were incorporated into the product, e.g., whether the released nanoparticles include derivatives from natural product ingredients, or particles from product carrier liquid."

Personal Care Products Council
Committed to Safety, Quality & Innovation

TO: Bart Heldreth Ph.D.
Executive Director – Cosmetic Ingredient Review

FROM: CIR Science and Support Committee of the Personal Care Products Council

DATE: November 15, 2021

SIBJECT: Comments from Women's Voices for the Earth on Methicones and Silicates CIR Safety Assessments

The CIR Science and Support Committee (CIR SSC) appreciates the opportunity to comment on the concerns of the Women's Voices for the Earth regarding the safety assessments on Methicones and Silicates.

We agree with the Expert Panel for Cosmetic Ingredient Safety conclusion that data are 'insufficient' to assess inhalation safety for products containing methicones and silicates that are applied by airbrush technology. The Pearce et al. 2019 manuscript that describes an airbrush "aerosol generation and exposure system" does raise a potential concern for inhalation, which the Expert Panel noted. While the study used a marketed airbrush delivery system and marketed cosmetic products, it is uncertain whether these data are representative of the entire category. Although the data generated on particle size are intriguing, actual exposure to the different parts of the respiratory tree are not demonstrated. Further, the authors note the limitations of using a glove box chamber versus a cleanroom to test exposures to particles, such as the ability to simulate exposure in a similar room size as the products that are used by consumers, more control of airflow and air ventilation systems, and control of other parameters, such as particle movement and deposition.

Another publication of interest is Pearce et al., 2020 [Pearce, K.M., Okon, I., Watson-Wright, C. 2020. Induction of oxidative DNA damage and epithelial mesenchymal transitions in small airway epithelial cells exposed to cosmetic aerosols. *Toxicol. Sci*. 177(1): 248-262.]. These authors utilized the marketed airbrush delivery system and currently marketed cosmetics. Interestingly, Figure 2 of that manuscript demonstrates very low exposure to the distal alveolar region for both the fine and ultrafine particles. This reinforces the point that the particle size is not the only factor when it comes to actual exposure to various parts of the respiratory tree. While the second manuscript raises potential concerns regarding effects of reactive oxygen species on the lungs, the authors also note the limitations of the study including the inability of the assay to demonstrate repair ability in the whole animal (i.e., did not address whether the oxidative stress could be reversed with N-acetyl cysteine).

We continue to support the use of a tiered approach to assess inhalation safety of cosmetic products as outlined in the memo provided on October 30, 2018. Although considered by the Expert Panel, the product particle size information associated with this memo is not specifically mentioned in the CIR inhalation resource document. "The data collected using current laser diffraction methodology is

generally consistent with the earlier, limited particle size data available in the literature and included in the draft Precedents document. Particle size is variable across individual products. Hairsprays have consistently larger median particle size than deodorant/antiperspirant." We suggest that additional details from this memo (reference 36 in the CIR document) be added to the Respiratory Exposure Resource Document. While particle size impacts exposure, other exposure factors are key in assessing inhalation safety. The sample calculations in the memo show the impact of other factors and should be put back into the resource document.

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review (CIR)

FROM: CIR Science and Support Committee of the Personal Care Products Council

DATE: October 30, 2018

SUBJECT: Comments on Draft Revised CIR Precedents – Aerosols Document/Submission of Aerosol Particle Size Data

The CIR Science and Support Committee is pleased to submit comments on the above referenced draft document for consideration by the CIR Expert Panel. While there is general agreement with the content of the current document, the Committee recommends that the delineation of a tiered approach to the evaluation of inhalation safety would add clarity and provide a needed framework.

During the last discussion of the Precedents document, the CIR Expert Panel requested additional information on spray product particle size for hair spray and deodorants. Data have been compiled in response to this request, and are included in this submission. The data are generally consistent with the older data previously reviewed by the Panel. The Committee notes, however, that particle size data are only infrequently needed when conducting inhalation risk assessment for cosmetic spray products due to the tiered approach to risk assessment providing an adequate margin of safety at the screening and modeling tiers. This is consistent with the very low product and ingredient exposures based on short exposure durations, ingredient content of product and total amount of product used.

General Considerations in Assessment of Inhalation Safety

While there may be some unique considerations in the evaluation of safety following exposure by the inhalation route, the basic framework for risk assessment - consisting of hazard assessment, exposure assessment, and risk characterization - is fully applicable. Both local (lung) effects and systemic effects are considered in the process. Data useful for the assessment, in addition to animal inhalation toxicity data (if available), include safety data generated using routes of exposure other than inhalation, physical/chemical properties, and data on mucosal

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membrane, skin, and eye irritation. The latter are relevant to the potential for causing local irritation to the respiratory tract. Mathematical models which take into consideration known data on lung irritants may also be useful. *In vitro* methodologies are under development and offer promising approaches for inhalation safety assessment as well.[1]

A preferred approach for the evaluation of inhalation safety is described in the 2014 publication by Steiling et al.[2] This publication stresses the critical importance of exposure assessment and describes a tiered approach to the exposure assessment of spray products. The three tiers are briefly described below:

- **Tier I** is a screening approach that employs worst case default assumptions, assuming all product leaving the container is potentially inhalable and likely to become systemically available. This approach uses existing habits and practices data (for example, see Table 2 in Steiling et al.) and assumes the total amount of sprayed product immediately enters the breathing zone (about 1 to 2 m^3 for cosmetics sprayed towards the body). This simple exposure assessment value is then compared to a systemic threshold and if the outcome is acceptable, no additional work is needed.

- **Tier II** refines the above estimate to arrive at a more realistic, though still conservative, exposure assessment. Additional refinements take into account factors such as room volume, room ventilation rate, discharge rates, spray times and particle/droplet size. Computational models of varying complexity have been developed, for example, one-box and two-box models, which vary in the number of assumed zones in which the emitted material is homogeneously dispersed. More sophisticated models may incorporate factors to determine how much of a spray/chemical is actually inhaled, exhaled, is reaching the deeper lung or is deposited.

- **Tier III** requires actual measurements of exposure under simulated use conditions, and is used for applications where computational modeling might not give a sufficient level of confidence for risk characterization.

In practice, exposure to cosmetic spray products is very low, due to low use quantities and very short exposure times. As a result, Tier I assessments may be all that is needed, and there is rarely a need to go beyond a Tier II evaluation.

[1] Behrsing, H et al. (2017) In vitro exposure systems and dosimetry assessment tools for inhaled tobacco products: Workshop proceedings, conclusions and paths forward for in vitro model use. Altern Lab Anim. 45(3):117-158.
[2] Steiling W et al. (2014) Principle considerations for the risk assessment of sprayed consumer products. Toxicol Lett. 227(1):41-9.

Sample Exposure Calculations

Sample exposure calculations using the approach described above are included here for an aerosol hair spray product.

Screening approach: (assumes all ingredient in the product is available for systemic exposure):

Aerosol Hairspray Assumptions:

Amount used per day: 9.89 g (95th percentile from Loretz et al., 2006[3])
Ingredient makes up 2% of product
Body weight: 60 kg

Exposure estimate:
9.89 g x 0.02 (ingredient) = 0.198 g (198 mg)
198 mg ÷ 60 kg = **3.3 mg/kg**

Refined exposure estimate

There are multiple factors that can be used to refine an exposure estimate. In this example, the following refinements are added:

- 2 box model (Rothe et al., 2011), in which the ingredient distributes in 1,000 L in the first 2 minutes, and distributes in 10,000 L in the next 18 minutes
- Breathing rate 10 L/minute[4]
- 25% exhaled

Exposure estimate:
First 2 minutes: 198 mg/1000 L x 10 L/minute x 2 minutes = 3.96 mg
Next 18 minutes: 198 mg/10,000 L x 10 L/minute x 18 minutes = 3.56 mg
Total exposure 3.96 mg + 3.56 mg = 7.52 mg
25% exhaled (0.75 exchange factor)
7.52 x 0.75 = 5.64 mg
5.64 mg ÷ 60 kg = **0.094 mg/kg**

Other Refinements:
The simple refined exposure calculation above provides a conservative estimate of inhalation exposure to an ingredient for all regions of the respiratory tract. Other factors can be incorporated to refine the assessment further.

For example, exposure can be further refined to adjust for the amount of material that ends up on skin/hair and is therefore not available for inhalation (see Steiling et al., 2012[5]).

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[3] Loretz L et al. (2006) Exposure data for personal care products: hairspray, spray perfume, liquid foundation, shampoo, body wash, and solid antiperspirant. Food Chem Toxicol. 44(12):2008-18.
[4] Representative inhalation rate from 2011 EPA Exposure Factors Handbook. Chapter 6 - Inhalation Rates. Accessed at https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=236252

Addition of a factor to adjust for respirable fraction (inhaled particles/droplets <10 μm) refines the amount that may reach the deep lung. If, for example, 5% of the distribution is less than 10 μm, the following calculation would apply:

0.094 mg/kg/day x 0.05 = **0.0047 mg/kg/day**

Calculations for deodorant would be conducted similarly. Spray deodorant habits and practices data are available[6].

Use of Advanced Methodology

An example of exposure assessment for antiperspirant spray products, mimicking in-use conditions and incorporating particle/droplet size data, is available in a publication by Schwarz et al. (2018).[7] Exposure to aluminum from four antiperspirant sprays containing up to 1.5% aluminum is assessed using a simple 2-box model. Exposure of the upper respiratory tract and deep lung deposition were calculated using the Multiple Path Particle Deposition Model. The total systemic exposure via inhalation was found to be less than 0.5 μg per application (less than **0.0084 μg/kg/application** for a 60 kg person). These authors also compared inhalation exposure estimates when the product was sprayed against a skin surrogate compared to spraying in the air ("free spraying"). Free spraying overestimated uptake by more than a factor of two. This study suggests that exposure estimates incorporating spray product use levels and ingredient concentrations and adjusted for distribution in 2 boxes result in highly conservative estimates of lung exposure.

Spray Product Particle Size

The CIR Expert Panel has requested that industry provide particle/droplet size data for hairspray and deodorant. In response to that request, a survey was undertaken to collect particle/droplet size information developed by companies marketing these product types. Six companies provided data on aerosol hairspray particle/droplet size, and three companies provided data on deodorant/antiperspirant[8] particle size. While no pump hairspray data were received, the

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[5] Steiling W et al. (2012) Skin exposure to deodorants/antiperspirants in aerosol form. Food Chem Tox 50: 2206-2215.

[6] Scientific Committee on Consumer Safety (2016) The SCCS Notes of Guidance for the Testing of Cosmetic Ingredients and their Safety Evaluation. 9th Revision. 25 April 2016. http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_s_004.pdf

[7] Schwarz K, et al. (2018) A methodology for the assessment of inhalation exposure to aluminum from antiperspirant sprays. Archives of Toxicology 92: 1383-1392.

[8] While the original request had been for deodorant data because antiperspirants are OTC products, both deodorant and Ap/Deo data are included in order to have a more robust data set.

particle/droplet size of pump sprays is generally larger than aerosols.[9] Laser diffraction was the method used to collect data in all cases.

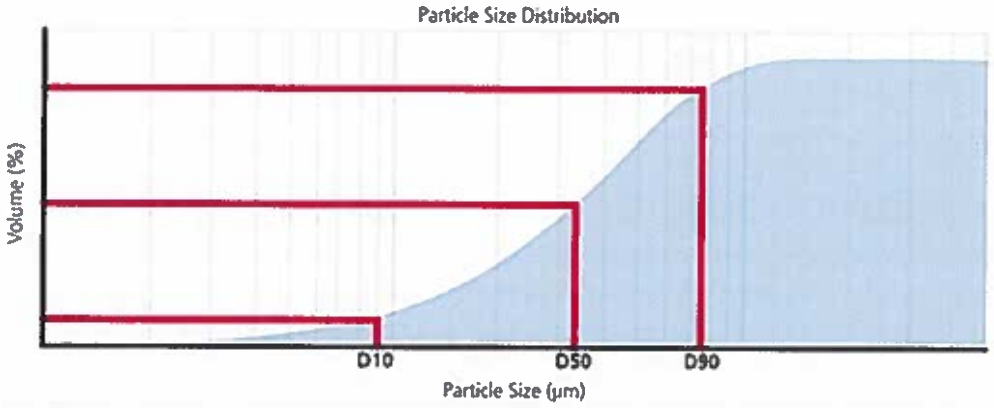
It is important to note that particle/droplet size data under simulated consumer use scenarios are only rarely needed for risk assessment. Particle/droplet size data using laser diffraction measurements of a free spray may be generated for other purposes, such as qualifying packaging, or determining consumer product acceptability. These types of particle/droplet size data, while not equivalent to consumer exposure, can be leveraged in refined exposure assessments with a full understanding of the conservative nature of the exposure estimate. While particle/droplet size is an important parameter, other exposure factors are key in assessing inhalation safety, as shown in the preceding exposure calculations. It should also be noted that particle/droplet size data generated under experimental conditions may be different from particle/droplet size in actual consumer exposures. Factors affecting the results include temperature, humidity, spray distance, spray time, container fullness, and the amount of pressure on the actuator.

Detailed information on measuring particle/droplet size from aerosol products is available in a Guidance document published by the European Aerosol Federation[10]. In the event that particle/droplet size data are required for risk assessment, there are other methodologies that can be used to further characterize the measurements, such as use of a cascade impactor, particularly for smaller solid particles.[11]

Results

Tables 1 and 2 (attached) provide a compilation of particle size data for aerosol hair spray and aerosol deodorant/antiperspirant, respectively. The data were generated using laser diffraction. Values are presented for DV10, DV50, and DV90, representing the maximum particle/droplet diameter below which 10%, 50%, or 90% of the sample volume exists, respectively. Thus, the DV50 value is the median particle/droplet size by volume, as described in the figure below[12]. Also included in the table is the percentage of particles/droplets <10 μm.

[9] Rothe H et al. (2011) Special aspects of cosmetic spray safety evaluations: Principles on inhalation risk assessment. Toxicol Lett. 205:97-104.
[10] European Aerosol Federation. (2009) Guide on Particle Size Measurement from Aerosol Products.
[11] Steiling et al. (2014) op. cit.
[12] A basic guide to particle characterization. (2015) Malvern Instruments Worldwide.



The data collected using current laser diffraction methodology is generally consistent with the earlier, limited particle/droplet size data available in the literature and included in the draft Precedents document. Particle/droplet size is variable across individual products. Hairsprays have consistently larger median particle/droplet size than deodorant/antiperspirant.

Overall Recommendations/Key Points

The CIR Science and Support Committee respectfully provides the following recommendations:

- Revise the CIR Inhalation Precedents document to clearly outline a tiered approach to assess inhalation exposure and risk assessment.
- Reference the updated particle/droplet size data in the Precedents document. These data are generally consistent with earlier data. Importantly, particle/droplet size data are generally not needed when assessing the inhalation safety of an ingredient in a spray cosmetic product.
- Revise the boilerplate language to reflect less reliance on particle size and more emphasis on exposure levels from spray cosmetic products by the inhalation route. These exposure levels are generally *de minimus*.

Conclusion

The CIR Science and Support Committee appreciates the opportunity to submit comments on the draft revised CIR Precedents – Aerosols Document. The Committee would be pleased to review and provide input on future updated versions.

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Table 1 - Aerosol Hair Spray

Company	Product Type	Dv10	Dv50	Dv90	% < 10 µM
Company A	Hairspray - Aerosol	78.68	89.07	160.6	1.0038
Company A	Hairspray - Aerosol	87.04	96.267	168.1	0.8137
Company A	Hairspray - Aerosol	85.73	95.097	166	0.8567
Company A	Hairspray - Aerosol	45.27	55.01	102.4	1.818
Company A	Hairspray - Aerosol	74.86	85.973	158.6	0.8271
Company A	Hairspray - Aerosol	44.45	53.62	97.44	1.8913
Company A	Hairspray - Aerosol	22.07	48.130	103.500	1.811
Company A	Hairspray - Aerosol	34.17	79.36	162.8	0.8167
Company A	Hairspray - Aerosol	16.53	33.63	64.06	2.231
Company A	Hairspray - Aerosol	29.07	69.657	149.4	1.509
Company A	Hairspray - Aerosol	17.31	40.617	99.4	3.094
Company A	Hairspray - Aerosol	25.99	46.43	90.63	1.929
Company A	Hairspray - Aerosol	32.54	75.387	158.1	1.0194
Company A	Hairspray - Aerosol	40.81	86.04	168.6	0.6928
Company A	Hairspray - Aerosol	25.99	46.43	90.63	1.929
Company A	Hairspray - Aerosol	40.81	86.04	168.6	0.6928
Company A	Hairspray - Aerosol	17.31	40.617	99.4	3.094
Company A	Hairspray - Aerosol	56.41	68.837	140.9	1.22
Company A	Hairspray - Aerosol	40.91	86.74	170.5	0.7047
Company A	Hairspray - Aerosol	37.48	81.35	162.7	0.822
Company A	Hairspray - Aerosol	22.26	53.31	131.7	1.885
Company A	Hairspray - Aerosol	23.12	50.65	95.66	1.58
Company A	Hairspray - Aerosol	22.84	55.853	108	1.732
Company A	Hairspray - Aerosol	24.41	61.65	144.5	1.424
Company A	Hairspray - Aerosol	16.53	33.63	64.06	2.231
Company A	Hairspray - Aerosol	12.76	30.11	61.68	5.8917
Company A	Hairspray - Aerosol	56.41	68.837	140.9	1.22
Company A	Hairspray - Aerosol	17.41	49	112.4	4.1
Company A	Hairspray - Aerosol	32.54	75.387	158.1	1.0194
Company A	Hairspray - Aerosol	71.21	181.83	431	0.262
Company A	Hairspray - Aerosol	43.26	91.08	172.6	0.7154
Company B	Hairspray - Aerosol	18.03	37.12	18.03	2.12
Company B	Hairspray - Aerosol	26.95	49.71	26.95	1.4
Company B	Hairspray - Aerosol	17.26	34.22	17.26	2.32
Company B	Hairspray - Aerosol	15.62	30.66	15.62	2.7
Company B	Hairspray - Aerosol	10.54	23.67	10.54	8.56
Company B	Hairspray - Aerosol	15.05	29.13	15.05	2.86
Company B	Hairspray - Aerosol	11.08	22.54	11.08	7.46
Company B	Hairspray - Aerosol	16	30.42	16	2.5
Company B	Hairspray - Aerosol	16.68	31.46	16.68	2.06
Company B	Hairspray - Aerosol	10.13	19.08	32.98	9.6

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Company	Product Type	Dv10	Dv50	Dv90	% < 10 µM
Company C	Hairspray - Aerosol		59.08		3.5
Company C	Hairspray - Aerosol		33.45		6.8
Company C	Hairspray - Aerosol		45.01		3.32
Company C	Hairspray - Aerosol		29.09		6.38
Company C	Hairspray - Aerosol		72.85		2.13
Company D	Hairspray - Aerosol	40.91	86.74	170.5	0.7047
Company D	Hairspray - Aerosol	43.26	91.08	172.6	0.7154
Company D	Hairspray - Aerosol	8.494	16.46	29.563	16.34
Company D	Hairspray - Aerosol	6.955	13.227	23.493	28.477
Company E	Hairspray - Aerosol	30.35	81.92	187.1	
Company E	Hairspray - Aerosol	25.13	50.47	92.73	
Company E	Hairspray - Aerosol	33.59	83.03	175.6	
Company E	Hairspray - Aerosol	20.97	45.65	89.68	
Company E	Hairspray - Aerosol	20.08	44.23	86.84	
Company E	Hairspray - Aerosol	57.61	144.9	359.4	
Company E	Hairspray - Aerosol	35.18	117.1	318.2	
Company E	Hairspray - Aerosol	27.13	89.4	229.8	
Company E	Hairspray - Aerosol	27.29	83.63	215.2	
Company E	Hairspray - Aerosol	26.43	86.22	228.8	
Company E	Hairspray - Aerosol	32.74	110.2	287.9	
Company E	Hairspray - Aerosol	32.63	103.7	270.4	
Company E	Hairspray - Aerosol	30.49	114.4	300.7	
Company E	Hairspray - Aerosol	46.71	163.5	351.2	
Company E	Hairspray - Aerosol	33.39	120.9	307.4	
Company E	Hairspray - Aerosol	30.41	102	274.5	
Company E	Hairspray - Aerosol	32.14	108.2	287.5	
Company E	Hairspray - Aerosol	34.45	112.2	297.2	
Company E	Hairspray - Aerosol	64.73	166.4	409	
Company E	Hairspray - Aerosol	52.04	133.3	341.2	
Company F	Hairspray - Aerosol	25.8	73.1	179.2	4.87
Company F	Hairspray - Aerosol	27.5	72.8	176.7	3.17
Company F	Hairspray - Aerosol	30.1	77.7	184.9	3.01
Company F	Hairspray - Aerosol	25.56	64.17	149.6	3.28

Mean ± Standard Deviation:

Dv10: (n=68) 32.69 ± 18.17; **Dv50**: (n=73) 70.54 ± 36.32; **Dv90**: (n=68) 154.78 ± 102.95; **% < 10 µM**: (n=53) 3.24 ± 4.48

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Table 2 - Aerosol Deodorant/Antiperspirant Particle Size Data

Company	Product Type	Dv10	Dv50	Dv90	% < 10 µM
Company A	AP/Deo-Aerosol		19.51		16.98
Company A	AP/Deo-Aerosol		183.63		0.36
Company A	AP/Deo-Aerosol		34.34		4.04
Company A	AP/Deo-Aerosol		24.26		11.34
Company A	AP/Deo-Aerosol		16.98		19.33
Company B	AP/Deo-Aerosol	9.2	25.4	52.2	11.25
Company B	AP/Deo-Aerosol	1.6	13	32.5	37.22
Company B	AP/Deo-Aerosol	3.5	13	37.1	36.18
Company B	AP/Deo-Aerosol	3.1	13.7	51.9	37.13
Company B	AP/Deo-Aerosol	1.4	13.2	27.9	35.41
Company B	AP/Deo-Aerosol	3.1	12.8	29.8	35.81
Company B	AP/Deo-Aerosol	1.2	12.4	30.3	38.97
Company B	AP/Deo-Aerosol	3.7	13.1	33.9	33.81
Company B	AP/Deo-Aerosol	3	17.4	42.5	28.06
Company B	AP/Deo-Aerosol	1.9	15.6	33.5	26.63
Company B	AP/Deo-Aerosol	0.7	8.4	20	60.79
Company B	AP/Deo-Aerosol	4.5	15.8	33.7	24.50
Company B	AP/Deo-Aerosol	4	17.1	43.1	27.55
Company B	AP/Deo-Aerosol	2.3	15.8	39.1	31.18
Company B	AP/Deo-Aerosol	0.8	9.9	27.4	50.34
Company C	AP/Deo-Aerosol	6.74	16.38	32.43	22.13
Company C	AP/Deo-Aerosol	8.10	18.44	37.25	16.73
Company C	AP/Deo-Aerosol	7.06	16.84	34.02	18.74
Company C	AP/Deo-Aerosol	6.46	15.40	31.0	25.06
Company C	AP/Deo-Aerosol	7.87	17.28	33.59	18.13
Company C	AP/Deo-Aerosol	6.22	17.31	37.84	24.61

Mean ± Standard Deviation:

Dv10: (n= 21) 4.12 ± 2.63

Dv50: (n=26) 22.96 ± 33.18

Dv90: (n=21) 35.29 ± 7.60

%<10 µM: (n= 26) 26.63 ± 13.43

From: Katz, Linda
To: Bart Heldreth
Cc: Alexandra Kowcz; Maisel, William; Manga, Prashiela; Shuren, Jeff
Subject: RE: [EXTERNAL] Airbrush Use with Cosmetics
Date: Tuesday, November 9, 2021 4:15:04 PM
Attachments: image003.png

Bart,

See below for my responses to your remaining 2 questions:

Secondly, are you aware of publicly available consumer uses and practices data related to the use of airbrush devices to apply cosmetics? Such use and practice data have previously been of great benefit to the Panel in assessing the risks associated with pump and propellant sprays. For airbrush device use, however, we have found no such data. Any additional data (e.g., particle sizes and volumes) or sources of such, related to respirable risks and safeties for airbrush device use, could also be of immeasurable assistance.

As you are aware, regulation of cosmetics and ingredients, with the exception of color additives, are post-market. As a result, manufacturers are not obligated to provide information to us in order to market their products. The information that we have on these products is what is available to the general public. If you have any data, including adverse event reports or other safety data, I would encourage you to share this information with us.

Thirdly, CIR commonly obtains frequency of use and product type/route of exposure data, specific to things like sprays and powders, to assess the potential for incidental respiratory exposure. The best source for such information has historically been the FDA Voluntary Cosmetic Registration Program (VCRP). Is such data/information available from the VCRP, or elsewhere, pertaining specifically to airbrush use?

Normally this type of inquiry would necessitate an FOIA request. However, because we do not have any information in the VCRP, an FOIA request is not necessary unless there is some other information that you need.

If I could be of any further assistance please let me know.

Linda

Linda M. Katz, M.D., M.P.H.
Director, Office of Cosmetics and Colors

Center for Food Safety and Applied Nutrition
Office of Cosmetics and Colors
U.S. Food and Drug Administration

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301-436-2976 (fax)
linda.katz@fda.hhs.gov

From: Bart Heldreth <heldrethb@cir-safety.org>
Sent: Friday, November 5, 2021 5:30 PM
To: Shuren, Jeff <Jeff.Shuren@fda.hhs.gov>; Katz, Linda <Linda.Katz@fda.hhs.gov>
Cc: Alexandra Kowcz <KowczA@personalcarecouncil.org>; Maisel, William <William.Maisel@fda.hhs.gov>; Sadrieh, Nakissa <Nakissa.Sadrieh@fda.hhs.gov>; Wyatt, Michael (Keith) <Michael.Wyatt@fda.hhs.gov>
Subject: Re: [EXTERNAL] Airbrush Use with Cosmetics

Thanks, Jeff! Have a great weekend.

Truly,
Bart

Dr. Bart Heldreth
Executive Director
Cosmetic Ingredient Review

From: Shuren, Jeff <Jeff.Shuren@fda.hhs.gov>
Sent: Friday, November 5, 2021 5:27:37 PM
To: Bart Heldreth <heldrethb@cir-safety.org>; Katz, Linda <Linda.Katz@fda.hhs.gov>
Cc: Alexandra Kowcz <KowczA@personalcarecouncil.org>; Maisel, William <William.Maisel@fda.hhs.gov>; Sadrieh, Nakissa <Nakissa.Sadrieh@fda.hhs.gov>; Wyatt, Michael (Keith) <Michael.Wyatt@fda.hhs.gov>
Subject: RE: [EXTERNAL] Airbrush Use with Cosmetics

Bart,

Thank you for reaching out to us. If the airbrush is being used to apply cosmetics to the epidermis, it would not be a medical device. Therefore, it would not be under CDRH's jurisdiction.

Linda will follow up on questions 2 and 3 next week.

I hope this is helpful.

Best regards,

Jeff

From: Bart Heldreth <heldrethb@cir-safety.org>

Sent: Thursday, November 4, 2021 1:09 PM
To: Shuren, Jeff <Jeff.Shuren@fda.hhs.gov>; Katz, Linda <Linda.Katz@fda.hhs.gov>
Cc: Alexandra Kowcz <KowczA@personalcarecouncil.org>; Maisel, William <William.Maisel@fda.hhs.gov>; Sadrieh, Nakissa <Nakissa.Sadrieh@fda.hhs.gov>; Wyatt, Michael (Keith) <Michael.Wyatt@fda.hhs.gov>
Subject: [EXTERNAL] Airbrush Use with Cosmetics

Memorandum

To: Jeffrey Shuren, Director
Center for Devices and Radiological Health

Linda Katz, Director
Office of Cosmetics and Colors

From: Bart Heldreth, Executive Director
Cosmetic Ingredient Review

Date: November 4, 2021
Subject: Airbrush Use with Cosmetics

The Cosmetic Ingredient Review (CIR) was established in 1976 by the industry trade association (then the Cosmetic, Toiletry, and Fragrance Association; now the Personal Care Products Council (Council)), with the support of the US Food and Drug Administration and the Consumer Federation of America. The solitary purpose of CIR is to assess the safety of individual ingredients as used in cosmetics. Although funded by the Council, CIR, the Expert Panel for Cosmetic Ingredient Safety (Panel), and the review process are independent from the Council and the cosmetics industry (much like members of an FDA special advisory committee). CIR and the Panel operate under a set of procedures. If interested, you may learn more about the Expert Panel for Cosmetic Ingredient Safety here.

Recent deliberations of the Panel have obviated the need to better understand the use of airbrush devices. Traditionally, CIR and the Panel have closely examined the use of pump and propellant sprays with regard to cosmetic product delivery. However, the use of airbrush devices to apply cosmetics has not been fully explored. As we try to construct a picture towards an actionable understanding of airbrushes devices, a number of puzzling pieces are missing from that picture, and we are hoping you would be willing to help.

Firstly, would you be willing to explain the US regulatory environment as it applies for the use of airbrush devices to apply cosmetics? Further to that end, are such devices, and their use, exclusively under the regulatory authority of CDRH?

Secondly, are you aware of publicly available consumer uses and practices data related to the use of airbrush devices to apply cosmetics? Such use and practice data have previously been of great benefit to the Panel in assessing the risks associated with pump and propellant sprays. For airbrush device use, however, we have found no such data. Any additional data (e.g., particle sizes and volumes) or sources of such, related to respirable risks and safeties for airbrush device use, could also be of immeasurable assistance.

Thirdly, CIR commonly obtains frequency of use and product type/route of exposure data, specific to things like sprays and powders, to assess the potential for incidental respiratory exposure. The best source for such information has historically been the FDA Voluntary Cosmetic Registration Program (VCRP). Is such data/information available from the VCRP, or elsewhere, pertaining specifically to airbrush use?

Thank you for taking the time to read this. If you have any questions, please do not hesitate to contact me.

Truly,
Bart

Dr. Bart Heldreth
Executive Director
Cosmetic Ingredient Review
1620 L Street, NW, Suite 1200
Washington, DC 20036-4702
heldrethb@cir-safety.org

Commitment & Credibility since 1976

Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Jinqiu Zhu, PhD, DABT, ERT, CIR Toxicologist
Date: November 22, 2021
Subject: Annotated WVE's comments on the draft Inhalation Resource Document as well as inhalation boilerplate language

Enclosed are 2 sets comments received from Women's Voices (WVE) dated November 15-16, 2021, on the updated draft of the CIR Resource – Respiratory Exposure to Cosmetic Ingredients Document, as well as on inhalation boilerplate language in the current safety assessment reports that are under review.

With regard to, November 15th WVE memo, the draft CIR Resource Document – Respiratory Exposure to Cosmetic Ingredients is about to be reviewed by the Panel at the upcoming December 2021 meeting. New data on characterization of deposited dose of inhalable aerosols released from diverse cosmetic sprays will be considered in addition to the previous sets of data as well as inputs from domain expertise. Once Panel reaches the consensus, the relevant language regarding the inhalation safety assessment should be revised accordingly. However, annotations, highlighted in yellow, have been added to the WVE memo, dated November 16th, to clarify potential misunderstandings and/or misinterpretations.

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WOMEN'S VOICES FOR THE EARTH

November 15, 2021

Re: Outdated inhalation boilerplate language in current safety assessments under review

To the CIR:

I greatly appreciate the work that has been put into updating the CIR inhalation resource document with additional data and more accurate language. I especially noted that certain language that was found to over-generalize the particle size distributions from cosmetic sprays, and the potential impacts from cosmetic powder exposures has been removed.

However, most of the safety assessments up for discussion at this meeting still contain the inhalation boilerplate language that is now outdated and no longer found in the most recent draft of the inhalation resource document. This language in the current safety assessments should be removed and these sections reworded for accuracy.

I have listed below the page numbers and specific language from the final and tentative safety assessments that need changes. All six of the new draft safety assessments (Acrylamide/Acrylate copolymers, Fatty Esters, Fatty Ethers, Glucosamine, Radish Root and Ginger) also contain similar outdated boilerplate language on inhalation as well, but for simplicity I have not quoted them below, as there is plenty of time to make the needed changes in their review processes.

Thanks very much

Alexandra Scranton

Director of Science and Research

Women's Voices for the Earth

Specifically:

https://www.cir-safety.org/sites/default/files/Barley_1.pdf

P.37 of safety assessment of Barley contains outdated inhalation boilerplate language:

“In practice, 95% to 99% of the droplets/particles released from cosmetic

sprays have aerodynamic equivalent diameters > 10 µm, with propellant sprays yielding a greater fraction of droplets/particles < 10 µm compared with pump sprays.48,49 Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and thoracic regions of the respiratory tract and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.50 Conservative estimates of inhalation exposures to respirable particles during the use of loose powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace.52-54”

https://www.cir-safety.org/sites/default/files/Equisetum%20arvense_1.pdf

P. 41 of the safety assessment of Equisetum arvense-Derived Ingredients still contains outdated inhalation boilerplate language:

“The Panel discussed the issue of incidental inhalation exposure resulting from an Equisetum arvense-derived ingredient (e.g. Equisetum Arvense Extract in cologne and toilet waters, and in other fragrance preparations (concentrations unknown)). Inhalation toxicity data were not available. However, the Panel noted that, in aerosol products, 95% - 99% of droplets/particles

would not be respirable to any appreciable amount. Furthermore, droplets/particles deposited in the nasopharyngeal or bronchial regions of the respiratory tract present no toxicological concerns based on the chemical and biological properties of these ingredients. Coupled with the small actual exposure in the breathing zone and the concentrations at which the ingredients are used, the available information indicates that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic effects. A detailed discussion and summary of the Panel’s approach to evaluating incidental inhalation

exposures to ingredients in cosmetic products is available at https://www.cir-safety.org/cir-findings.”

Question: In the absence of any inhalational toxicity data, how does the CIR panel assure the safety of products that may emit respirable particles that may be incidentally inhaled deeply into the lungs?

https://www.cir-safety.org/sites/default/files/Sugarcane_0.pdf

On both p.19 and on p.24, the safety assessment of Saccharum officinarum (Sugarcane)-Derived Ingredients still contains outdated inhalation boilerplate language:

p.19 “In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters > 10 µm, with propellant sprays yielding a greater fraction of droplets/particles < 10 µm compared with pump sprays.19,20 Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and thoracic regions of the respiratory tract and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.

Conservative estimates of inhalation exposures to respirable particles during the use of loose powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace."

And

p.24 "However, the Panel noted that in aerosol products, 95% – 99% of droplets/particles would not be respirable to any appreciable amount. Furthermore, droplets/particles deposited in the

nasopharyngeal or bronchial regions of the respiratory tract present no toxicological concerns based on the chemical and biological properties of these ingredients. Coupled with the small actual exposure in the breathing zone and the concentrations at which the ingredients are used, the available information indicates that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic effects."

https://www.cir-safety.org/sites/default/files/Portulaca%20oleracea_0.pdf

p.22 of the safety assessment

"According to VCRP data, Portulaca Oleracea Extract is reportedly used in 2 face powder formulations, and could possibly be inhaled; concentration of use data were not reported for this use. Conservative estimates of inhalation exposures to respirable particles during the use of loose powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace."

https://www.cir-safety.org/sites/default/files/Acryloyloxyethyl%20Phosphorylcholine.pdf

p.24

"Polyquaternium-61 is reported to be used in aerosol hair sprays at maximum use concentrations up to 0.000006%.9 In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters > 10 µm, with propellant sprays yielding a greater fraction of droplets/particles below 10 µm, compared with pump sprays.10-13 Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and bronchial regions and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.10,11 Polyquaternium-61 is reported to be used in face powders at maximum use concentrations up to 0.0069%. Conservative estimates of inhalation exposures to respirable particles during the use of loose powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace."

https://www.cir-safety.org/sites/default/files/Sage_0.pdf

p.30

“Furthermore, some of the Salvia officinalis (sage)-derived ingredients are used in cosmetic spray formulations, and could possibly be inhaled. For example, Salvia Officinalis (Sage) Leaf Extract is reported to be used in pump and aerosol hair sprays at up to 0.0001% and 0.002%, respectively, Salvia Officinalis (Sage) Extract is reported to be used in underarm deodorant spray at up to 0.0011%, and Salvia Officinalis (Sage) Leaf Oil is reported to be used in pump spray suntan formulations at up to 0.012%. In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters > 10 µm, with propellant sprays yielding a greater fraction of droplets/particles < 10 µm compared with pump sprays.30,31 Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and thoracic regions of the respiratory tract and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.32 33 There is some evidence indicating that deodorant spray products can release substantially larger fractions of particulates having aerodynamic equivalent diameters in the range considered to be respirable.32 However, the information is not sufficient to determine whether significantly greater lung exposures result from the use of deodorant sprays, compared to other cosmetic sprays.”

https://www.cir-safety.org/sites/default/files/Zeolites.pdf

p.91

“Moreover, Zeolite is used in cosmetic sprays and could possibly be inhaled; for example, it is reported to be used at 1% in hair spray.7 In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters > 10 µm, with propellant sprays yielding a greater fraction of droplets/particles < 10 µm compared with pump

sprays.9,10 Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and thoracic regions of the respiratory tract and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.11,12 Zeolite was reportedly used in face powders at concentrations up to 1.1% and could possibly

be inhaled.7 Conservative estimates of inhalation exposures to respirable particles during the use of loose powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace.”

WOMEN'S VOICES FOR THE EARTH

November 16, 2021

Re: Comments on the Respiratory Exposure to Cosmetic Ingredients Resource Document

To the CIR:

I greatly appreciate that the CIR expert panel and staff are continuing to work on the Respiratory Exposure resource document to incorporate new information on cosmetic aerosols and powders. I have been concerned for a number of years that the boilerplate language frequently used in CIR safety assessments has under-estimated the potential hazards of inhaling cosmetic products. Part of this concern comes from generalizations made about the potential for inhalation of cosmetics based on data from just a few types of products. I think the new draft has made some definite improvements, but still has more to be done.

While some new data has been added, it is clear that there is still a relatively small body of particle size distribution data available from a limited assortment of types of cosmetic sprays - namely pump hair sprays, aerosol hair sprays, aerosol deodorant sprays and airbrush cosmetics. This data seems to be telling us is that there can be significant variation in the particle size distributions that can be emitted from these different kinds of spray products. I think the resource document needs to be more transparent that more data is still needed to understand the potential hazards of the large variety of different types of inhalation exposures created by diverse cosmetic use.

Specifically, the inhalation resource document currently includes a number of assumptions that need to be challenged.

Assumption 1:

The particles emitted from most cosmetic sprays will be similar to those emitted from hair sprays (i.e, large and not respirable) with two exceptions 1) that deodorant sprays will emit a greater proportion of respirable particles, and 2) that the data is insufficient to characterize particle sizes from airbrush products.

Specifically p. 88 of the .pdf states this assumption by only pointing to deodorant sprays and airbrush products as cases that need further evaluation:

> *"Identifying the use of ingredients in deodorant spray and airbrush products may be especially important, because they potentially release the largest quantity of respirable droplets/ particulates among the products evaluated."*

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Challenge: While some additional data has been added to the most recent draft of the inhalation resource document, it still stands that the available data on particle size distribution from cosmetic sprays is quite limited. There are few studies available, and those that are available only have data on hair sprays, deodorant sprays and airbrush cosmetics. But there is a wide variety of cosmetic sprays on the market (that are neither deodorants, hair sprays or airbrush cosmetics). We have no data to tell us whether these other kinds of cosmetic sprays more commonly emit larger particles like hair sprays or finer respirable particles like deodorants, and shouldn't assume either of these categories to be representative of all other cosmetic sprays.

Assumption 2:

All cosmetic products in pump spray format will emit predominantly large particles that are not respirable.

Specifically p. 82 of the inhalation document states:

"*Typically, < 1% of the airborne droplets/particles released from pump sprays are in the range considered to be respirable (i.e., dae < 10 µm).*"

Challenge: The initial data on pump sprays (which has measured pump hair sprays only) indicate that the particles emitted are generally large and not respirable. However, there is data on a single cosmetic facial spray (in a pump spray format) that indicates otherwise. In the Laycock et.al. (2020) paper (citation #39 in the newest version of the respiratory resource document) there is data on particle size distributions of a cosmetic facial spray called M2Beaute. This facial spray is manufactured in a pump spray bottle. The researchers found for the M2 Beaute facial spray that "The largest aerosol particles produced were up to 4 µm in size." This means that, unlike the pump hair spray data, virtually all the particles measured from this cosmetic facial pump spray were smaller than 10 microns and therefore respirable.

Here is a picture of the M2 Beaute product that was tested:

According to the M2 Beaute website the instructions for application are:

> "*Spray the ULTRA PURE SOLUTIONS PEARL & GOLD FACIAL NANO SPRAY onto clean skin 3–5 times, morning and evening, at a distance of 15–20 cm. Once it has been allowed to absorb, additional skincare products can be applied as desired.*
>
> *Tip: Thanks to its extremely fine spray mist, the active ingredient serum can be used over make-up over the course of the day for an extra bit of care*."

https://www.m2beaute.com/en/facial-care/ultra-pure-solutions-pearl-gold-facial-nano-spray

While this was the only example, I could find in the literature of particle size data on a cosmetic pump spray that was not a hair spray, there is another paper on cleaning sprays that may also be illustrative. In this paper (Loven, et.al. 2021) seven different ready-to-use trigger cleaning sprays were tested. (These products had manual trigger sprays, none of them were aerosols with propellants.) The median particle sizes emitted by these sprays ranged from 1.9 – 3.7 microns. Here is the data for three of these products:

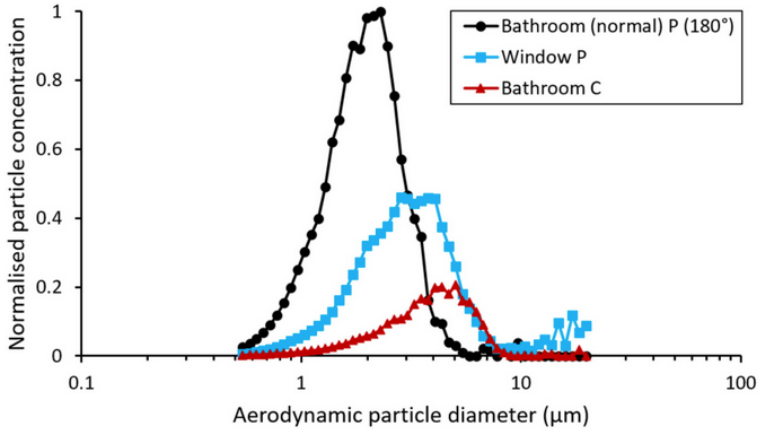

Figure 3. Particle mass size distributions for three of the seven cleaning sprays tested. The size distributions are based on APS measurements (0.5–20 μm). The particle mass concentration was normalized by the maximum concentration value.

While this study did not find any nano-sized particles emitted from the trigger sprays, it was clear that these products did emit the majority of particles smaller than 10 microns.

Source: Karin Lovén, Christina Isaxon, Aneta Wierzbicka & Anders Gudmundsson (2019) Characterization of airborne particles from cleaning sprays and their corresponding respiratory deposition fractions, Journal of Occupational and Environmental Hygiene, 16:9, 656-667, DOI: 10.1080/15459624.2019.1643466. Available at: https://www.tandfonline.com/doi/epub/10.1080/15459624.2019.1643466?needAccess=true

And there are numerous cosmetic products, particularly hair products like conditioners, that are marketed in trigger spray bottles.

It appears that the desired particle size distribution from a cosmetic spray can be specified by the manufacturer and engineered fairly precisely by their aerosol/pump/trigger spray packaging supplier. Different particle size distributions may have different functionality depending on the product. The CIR might consider adding language to the resource document on safer recommended particle size specifications for manufacturers to adhere to, to account for the diversity of products available.

Assumption 3:

Exposure to cosmetic sprays and powders are generally of short duration, involves only a very small amount of a cosmetic product, and/or are not directly applied within the breathing zone – leading to negligible exposure from incidental inhalation.

Specifically, p.87 &88 of the inhalation document .pdf include this assumption:

> "*The Panel noted that particle/droplet size data under simulated consumer use scenarios are generally not needed when conducting inhalation risk assessment due to the tiered approach to risk assessment, which provides an adequate margin of safety at the screening and modeling tiers. This is consistent with the very low product and ingredient exposures based on short exposure durations, ingredient content of product and total amount of product used.*[31]"
>
> "*In practice, exposure to aerosolized cosmetic ingredients is very low, due to low use quantities and very short exposure times*."

Challenge: Clearly the example of airbrush cosmetics challenges all of these assumptions in that it can take 20 minutes or more to apply these sprays directly to the user's face. Similarly, there are other types of cosmetic sprays that the CIR Expert panel should also consider that challenge these assumptions including:

a) Temporary hair color sprays which can involve spraying the hair with the entire contents of more than one can per application.
b) Dry shampoo spray which involves repeated spraying multiple sections of your hair.
c) Dry shampoo powder which involves considerably more loose powder application than a loose facial powder, and involves multiple applications of the powder on each section of hair. (This powder can also get resuspended as it is brushed out after application.)
d) Self tanning sprays –which can involve spraying the entire body, including the face, spraying for 10 minutes or more.
e) Makeup setting sprays which involve spraying the face at least daily, sometimes multiple times throughout the day.

Temporary hair color spray application video example:

https://www.youtube.com/watch?v=zsiKMGR5bDA

Note: L'oreal Paris website has an article on "How to use a temporary hair color spray" which makes no recommendations on reducing inhalation of the product. It also confirms that the amount of product used per application can be considerable: "…*if you're looking for all-over color, you may need to use more than one can, depending on the length and thickness of your mane*."

https://www.lorealparisusa.com/beauty-magazine/hair-color/hair-color-trends/temporary-hair-color-spray

Dry shampoo spray application video example:

https://www.youtube.com/watch?v=y6Tab2ywdK0

Dry shampoo powder application video example:

https://www.youtube.com/watch?v=HOwk3RiTfPM

Makeup setting spray examples:

https://www.urbandecay.com/all-nighter-setting-spray-by-urban-decay/ud803.html

Urban Decay All Nighter Setting Spray

"Shake bottle well to activate the formula. Spray in an "X" and "T" formation repeatedly (about 3-5 times) until face is fully saturated."

https://www.onesizebeauty.com/products/on-til-dawn-setting-spray?variant=40781518438599

ON 'TIL DAWN MATTIFYING WATERPROOF SETTING SPRAY

"Shake well before each use, and keep eyes closed during application. Hold 10-12 inches away from face, and spray in a circular motion for even distribution on skin."

(This product is an aerosol spray.)

https://www.sephora.com/product/milk-makeup-hydro-grip-set-refresh-spray-P463071?

MILK MAKEUP - Hydro Grip Setting + Refreshing Spray

-Press the hydro-fine mist pump for an all-over, even halo distribution onto skin.

-Hold bottle eight to 10 inches away from face and mist evenly onto skin two times. Close mouth and eyes while spraying.

-Use before makeup application to seal in skincare, prep, hydrate, and provide a natural-looking glow.

Use as a setting spray to lock in your look for up to 12 hours after makeup application. Allow formula one minute to set makeup.

-Reapply throughout the day as desired to refresh skin and revitalize makeup.

Self tanning spray application video example:

https://www.youtube.com/watch?v=T68IXR42gyY

Potential hazards from the inhalation of cosmetics are much more complex than the CIR has previously taken into account. Cosmetic products can be inhaled, and the cosmetic ingredients in them can lead to potential harm. Epidemiological studies of cosmetologists, hair and nail salon workers support this assertion, as they commonly show that people in these occupations have significantly higher risks of

asthma[1,2,3] idiopathic pulmonary fibrosis[4], chronic bronchitis[5], work-related cough[6] and decreased lung function[7]. Strong recommendations from the CIR expert panel can help reduce these inhalation exposures and prevent possible disease is cosmetics users and salon workers alike.

Thank you for your careful consideration of these comments.

Alexandra Scranton
Director of Science and Research
Women's Voices for the Earth

[1] Kwok C., Money A., Carder M., Turner S., Agius R., Orton D. and Wilkinson M. (2014) Cases of occupational dermatitis and asthma in beauticians that were reported to The Health and Occupation Research (THOR) network from 1996 to 2011. Clinical and Experimental Dermatology. Vol. 39, pp:590- 595. 2014.
[2] Kreiss K., Esfahani RS., Antao VC., Odencrantz J., Lezotte DC. and Hoffman RE. (2006) Risk factors for asthma among cosmetology professionals in Colorado. Journal of Occupational and Environmental Medicine. Vol. 48, No. 10, pp: 1062-1069. October 2006.
[3] Leino, T., Tammilehto, L., Hytonen, M., Sala, E. Paakkulainen, H. and Kanerva, L. (1998) Occupational skin and respiratory diseases among hairdressers. Scandinavian Journal of Work, Environment & Health. Vol. 24, No. 5, pp: 398-406. 1998
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[5] Leino T., Tammilehto L, Luukkonen R, and Nordman H. (1997) Self reported respiratory symptoms and diseases among hairdressers. Occupational and Environmental Medicine. Vol. 54, pp: 452-455. 1997.
[6] Bradshaw L., Harris-Roberts J., Bowen J., Rahman S. and Fishwick D. (2011) Self-reported work-related symptoms in hairdressers. Occupational Medicine. Vol. 61, pp:328-334. 2011.
[7] Reutman SR., Rohs AM., Clark JC., Johnson BC., Sammons DL., Toennis CA., Robertson SA., MacKenzie BA. And Lockey JE. (2009) A pilot respiratory health assessment of nail technicians: Symptoms, lung function and airway inflammation. American Journal of Industrial Medicine. Vol. 52, pp: 868-875. 2009.

WOMEN'S VOICES FOR THE EARTH

November 16, 2021

Re: Comments on the Respiratory Exposure to Cosmetic Ingredients Resource Document To

the CIR:

I greatly appreciate that the CIR expert panel and staff are continuing to work on the Respiratory Exposure resource document to incorporate new information on cosmetic aerosols and powders. I have been concerned for a number of years that the boilerplate language frequently used in CIR safety assessments has under-estimated the potential hazards of inhaling cosmetic products. Part of this concern comes from generalizations made about the potential for inhalation of cosmetics based on data from just a few types of products. I think the new draft has made some definite improvements, but still has more to be done.

While some new data has been added, it is clear that there is still a relatively small body of particle size distribution data available from a limited assortment of types of cosmetic sprays - namely pump hair sprays, aerosol hair sprays, aerosol deodorant sprays and airbrush cosmetics. This data seems to be telling us is that there can be significant variation in the particle size distributions that can be emitted from these different kinds of spray products. I think the resource document needs to be more transparent that more data is still needed to understand the potential hazards of the large variety of different types of inhalation exposures created by diverse cosmetic use.

CIR staff annotation: The CIR Resource – Respiratory Exposure to Cosmetic Ingredients Document (previously known as Aerosols Precedents Document) was first submitted to the Panel in 2011. Since then, it has been revised in 2012, 2016, 2017, 2018, and 2019. The Panel determined to monitor data development regarding the aerosol inhalation exposure and deposited doses from various types of cosmetic sprays, and update this document ad hoc. The Panel last approved this document at the September 2019 meeting. As new data on characterization of diverse aerosol properties have been identified, the Panel recommended incorporating such into the Document, and consequently, to address the health challenges facing the public. Compared to the 2019 version, the number of references cited in the Document increased from 37 to 85. For example, data or findings identified from the following research papers and guidance literature, which were published after the September 2019 meeting and have been added to the updated Document:

Oh H-J, Kim J. Characterization of inhalable aerosols from cosmetic powders and sustainability in cosmetic products. *Sustainability.* **2020**;12(8187).

Laycock A, Wright MD, Romer I, Buckley A, Smith R. Characterisation of particles within and aerosols produced by nano-containing consumer spray products. *Atmos Environ X.* **2020**;8:100079.

Pearce K, Goldsmith WT, Greenwald R, Yang C, Mainelis G, Wright C. Characterization of an aerosol generation system to assess inhalation risks of aerosolized nano-enabled consumer products. *Inhal Toxicol.* **2019**;31(9-10):357-367.

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Pearce KM, Okon I, Watson-Wright C. Induction of Oxidative DNA Damage and Epithelial Mesenchymal Transitions in Small Airway Epithelial Cells Exposed to Cosmetic Aerosols. *Toxicol Sci.* **2020**;177(1):248-262.

Park J, Ham S, Kim S, et al. Physicochemical characteristics of colloidal nanomaterial suspensions and aerosolized particulates from nano-enabled consumer spray products. *Indoor Air.* **2020**;30(5):925-941.

Dreno B, Alexis A, Chuberre B, Marinovich M. Safety of titanium dioxide nanoparticles in cosmetics. *J Eur Acad Dermatol Venereol.* **2019**;33 Suppl 7:34-46.

Fytianos G, Rahdar A, Kyzas GZ. Nanomaterials in Cosmetics: Recent Updates. *Nanomaterials (Basel).* **2020**;10(5).

Oh HJ, Han TT, Mainelis G. Potential consumer exposure to respirable particles and TiO2 due to the use of eyebrow powders. *J Expo Sci Environ Epidemiol.* **2020.**

Tha EL, Canavez A, Schuck DC, Gagosian VSC, Lorencini M, Leme DM. Beyond dermal exposure: The respiratory tract as a target organ in hazard assessments of cosmetic ingredients. *Regul Toxicol Pharmacol.* **2021**;124:104976.

Scientific Committee on Consumer Safety (SCCS). *Guidance on the safety assessment of nanomaterials in cosmetics.* **2019**. SCCS/1611/19.

Please also note the following statement in the draft Inhalation Resource Document:

> The Panel will **continue to review all of the relevant** inhalation toxicity, use, and other data to determine the safety of cosmetic ingredients. The Panel will evaluate the importance of the inhalation route for assessing the safety of an ingredient or group of ingredients, and **evaluate data that may be available** to estimate potential respiratory doses from aerosolized products. **Factors to consider include** whether or how much of the spray products enter the breathing zone, the likely droplet/particle size distributions in the breathing zone, and the exposure durations that can be expected during product use.

(See pdf page 89 at https://www.cir-safety.org/sites/default/files/Inhalation.pdf)

Specifically, the inhalation resource document currently includes a number of assumptions that need to be challenged.

Assumption 1:

The particles emitted from most cosmetic sprays will be similar to those emitted from hair sprays (i.e, large and not respirable) with two exceptions 1) that deodorant sprays will emit a greater proportion of respirable particles, and 2) that the data is insufficient to characterize particle sizes from airbrush products.

Specifically p. 88 of the .pdf states this assumption by only pointing to deodorant sprays and airbrush products as cases that need further evaluation:

> *"Identifying the use of ingredients in deodorant spray and airbrush products may be especially important, because they potentially release the largest quantity of respirable droplets/ particulates among the products evaluated."*

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Challenge: While some additional data has been added to the most recent draft of the inhalation resource document, it still stands that the available data on particle size distribution from cosmetic sprays is quite limited. There are few studies available, and those that are available only have data on hair sprays, deodorant sprays and airbrush cosmetics. But there is a wide variety of cosmetic sprays on the market (that are neither deodorants, hair sprays or airbrush cosmetics). We have no data to tell us whether these other kinds of cosmetic sprays more commonly emit larger particles like hair sprays or finer respirable particles like deodorants, and shouldn't assume either of these categories to be representative of all other cosmetic sprays.

CIR staff annotation: It is necessary to clarify that the 2 assumptions made by WVE in the current comments do not represent CIR views or intention.

Notably, a tiered approach is outlined in the Document to assess inhalation exposure and risk assessment. As indicated in CIR Science and Support Committee (CIR SSC)'s memo dated October 30, 2018 (re-submitted in the current Wave2),

> While there may be some unique considerations in the evaluation of safety following exposure by the inhalation route, the **basic framework for risk assessment** - consisting of hazard assessment, exposure assessment, and risk characterization - **is fully applicable**. **Both local (lung) effects and systemic effects are considered in the process**. Data useful for the assessment, in addition to animal inhalation toxicity data (if available), include safety data generated using routes of exposure other than inhalation, physical/chemical properties, and data on mucosal membrane, skin, and eye irritation.

Thus, the following statements presented in the draft Inhalation Resource Document should be understood on the basis of full consideration of the risk assessment framework.

> The final particle size distribution of a spray product is the result of the composition of the formula, the concentration of individual ingredients, and other relevant spray parameters (e.g., spray nozzle, can size, propellant type and pressure). When **considered necessary**, **risk characterization** for spray products can **be carried out** to access the risk to human health at certain levels of exposure under real-use conditions (e.g., Risk Characterization Ratio (RCR) can be derived by comparison of the calculated exposure with the relevant derived no-effect level (DNEL) for an ingredient).

(See pdf page 89 of the draft Resource Document at https://www.cir-safety.org/sites/default/files/Inhalation.pdf)

> As more nanotechnology-based consumer products are being formulated and released into the market, in order to **determine safety for the discrete ingredient** used in aerosolized consumer products that are specially delivered through airbrush systems or other nano-enabled aerosol canisters, **data requirements for inhalation risk evaluation would include** characteristics of airborne particles, such as the final particle size (and size distribution) of a spray product, the maximum use concentration of ingredient, and information on methods of use and spray characteristics, e.g., exposure duration and frequency, and technical details of spray equipment, as well as **inhalation toxicity testing data**, if necessary.

(See pdf page 86 of the draft Resource Document at https://www.cir-safety.org/sites/default/files/Inhalation.pdf)

> If substances are meant to be included in sprays or aerosols, evaluation of consumer **exposure via inhalation** is **paramount** in the overall safety assessment. If inhalation toxicity data are absent or provide an insufficient basis to support the safety of an ingredient used in products that may be aerosolized, the Panel will evaluate the sufficiency of other data that may be available **on a case-by-case basis**. Such data would include, for example, the potential for the ingredient to **cause systemic toxicity**, ocular or dermal irritation or sensitization, or other effects after repeated exposures. Other factors to consider include whether the ingredient belongs to a class of toxicants recognized to have the potential to cause lung injury after exposure via inhalation or other routes, possesses structural alerts based on known structure-activity relationships, or has a noteworthy potential to yield reactive intermediates or other metabolites of concern in the lungs.

(See pdf page 89 - 90 at https://www.cir-safety.org/sites/default/files/Inhalation.pdf)

Additionally, it deserves to be re-emphasized that "the **purview** of the Panel is exclusive to **assessing the safety of ingredients** as used in cosmetics. Assessing the safety of **devices**, such as airbrush delivery systems, is obviously **outside of that purview**."

Assumption 2:

All cosmetic products in pump spray format will emit predominantly large particles that are not respirable.

Specifically p. 82 of the inhalation document states:

"*Typically, < 1% of the airborne droplets/particles released from pump sprays are in the range considered to be respirable (i.e., dae < 10 µm).*"

Challenge: The initial data on pump sprays (which has measured pump hair sprays only) indicate that the particles emitted are generally large and not respirable. However, there is data on a single cosmetic facial spray (in a pump spray format) that indicates otherwise. In the Laycock et.al. (2020) paper (citation #39 in the newest version of the respiratory resource document) there is data on particle size distributions of a cosmetic facial spray called M2Beaute. This facial spray is manufactured in a pump spray bottle. The researchers found for the M2 Beaute facial spray that "The largest aerosol particles produced were up to 4 µm in size." This means that, unlike the pump hair spray data, virtually all the particles measured from this cosmetic facial pump spray were smaller than 10 microns and therefore respirable.

CIR staff annotation: Such assumption does not represent CIR views. For instance, "typically" does not mean "all." Furthermore, the statement cited above clearly indicates that a fraction of airborne droplets/particles released from pump sprays are respirable (i.e., with aerodynamic equivalent diameter < 10 µm), though the

percentage is less than 1%.
Please take note that the following statement from citation 1 of the draft Inhalation Resource Document was once cited by WVE in their memo dated on September 9, 2021 (see pdf page 4 at https://www.cir-safety.org/sites/default/files/Inhalation.pdf)

"*Typically, propellant gas sprays may produce proportionate respirable particles or droplets < 10 µm particle size, whereas pump sprays emit larger droplets in a non-respirable range > 10 µm particle size.*"

In addition, the following statement is identified from the same reference (Rothe et al. 2011. *Toxicol Lett.*):

*"Typically, the mean diameter of primary droplets of a **pump spray** is in the range of **70 µm** diameter while **< 1%** is in the respirable range (unpublished industry data)."*

Here is a picture of the M2 Beaute product that was tested:

According to the M2 Beaute website the instructions for application are:

> "*Spray the ULTRA PURE SOLUTIONS PEARL & GOLD FACIAL NANO SPRAY onto clean skin 3–5 times, morning and evening, at a distance of 15–20 cm. Once it has been allowed to absorb, additional skincare products can be applied as desired.*
>
> *Tip: Thanks to its extremely fine spray mist, the active ingredient serum can be used over make-up over the course of the day for an extra bit of care*."

https://www.m2beaute.com/en/facial-care/ultra-pure-solutions-pearl-gold-facial-nano-spray

CIR staff annotation: Please note the following product introduction was quoted from the Laycock et.al. (2020) paper (i.e., citation 39 of the draft Inhalation Resource Document):

> Product 4 – M2 beaute
>
> M2 Beaute is a **Au nano-containing** beauty product that is intended to be sprayed directly onto the skin… The TEM images reveal the presence of a small number of nanoparticles (**NPs**) that are slightly irregular, typically **2 – 5 nm** in size with clusters in the region of **20 – 50 nm**… The **mean diameter size** from spICP-MS analysis was **70 nm**, suggesting that the smallest particles were not detected and only the larger particles and clusters were identified. The sizes and size distributions determined by DLS and NTA are relatively consistent with the respective Z-average and mean diameter sizes being **in the range of 107 – 151 nm**… These trends may be explained by the

> presence of a significant number of other particles of a similar, or slightly larger size, possibly due to the presence of '**pearl nanoparticles**' as claimed by the manufacturer but not confirmed here…Total metal quantification showed that **Au was present at 1.5 – 1.9 ppb**. The **largest aerosol particles** produced were up to **4 µm in size**. The **highest detected aerosol number concentrations** were in the 'fine' (**< 2.5 µm**) and submicron size range for the **APS**, and the ultrafine size range for the **SMPS** (500 - 750 cm^{-3} above background). The total aerosol mass concentration detected by the two techniques was ~ 55 µg m^{-3}, with approximately 1% of this being in the SMPS size range.

To be clear, M2 Beaute should be considered as a nano-enabled consumer product and citation 39 of the draft Inhalation Resource Document clearly indicates that "application of a nanomaterial in **loose powder or sprayable products** may pose a risk of inhalation of airborne particles into the consumer's lung airways." (see pdf page 84 at https://www.cir-safety.org/sites/default/files/Inhalation.pdf). Please note that in the updated Document, a whole section has been added to specifically discuss the increased engineered nanoparticles inhalation risks resulting from the aerosolization of common nano-enabled consumer products, titled *Inhalation Exposure of Engineered Metal Nanoparticles (ENPs) from Aerosolized Consumer Products.* For more details, please refer to the draft revised Inhalation Resource Document. (see pdf page 85 - 86 at https://www.cir-safety.org/sites/default/files/Inhalation.pdf)

Furthermore, the aerosol produced by M2 Beaute in the current study was characterized by scanning mobility particle sizer (SMPS) and aerodynamic particle sizer (APS), which cover an aerosol size range (**0.005 – 20 µm**). In this regard, please note the following discussion has already been presented in the document *annotated-WVEcomments_InhalationDocument_122021* (see pdf page 12 at https://www.cir-safety.org/sites/default/files/Inhalation.pdf):

> In addition, it is necessary to point out that, in both Pearce 2019 and 2020 papers, aerosols were monitored using both a scanning mobility particle sizer (SMPS), that measured particle size distributions between **~ 10 – 435 nm,** and an optical particle sizer (OPS), that measured size distributions between **0.3 – 10 µm**. In comparison, Dr. Rothe indicated in her 2011 presentation (second slide from her presentation as shown above) that "*The scale on the X-axis is going **only** to **20 microns**, so **it's not really the whole distribution pattern.** So, when you remember what I showed you at the beginning, **the distribution pattern which was going up to 150 microns.***" That is, the whole distribution pattern of aerosols resulting from application of airbrush makeup products have **not** been examined by two Pearce studies, while the potential particle deposition fraction and deposited mass flux in human lungs during airbrush makeup use were estimated by MPPD computational model in Pearce 2020 paper….

A similar consideration thus applies to M2 Beaute with regard to the particle size measurements: the whole distribution pattern of aerosols resulting from application of M2 Beaute spray has not been examined. Though the results showed "the largest aerosol particles produced were up to 4 µm in size. The highest detected aerosol number concentrations were in the 'fine' (< 2.5 µm)." It should be noted that only aerosol sized $\leq$ 20 µm was investigated in the current study.

While this was the only example, I could find in the literature of particle size data on a cosmetic pump spray that was not a hair spray, there is another paper on cleaning sprays that may also be illustrative. In this paper (Loven, et.al. 2021) seven different ready-to-use trigger cleaning sprays were tested. (These products had manual trigger sprays, none of them were aerosols with propellants.) The median particle sizes emitted by these sprays ranged from 1.9 – 3.7 microns. Here is the data for three of these products:

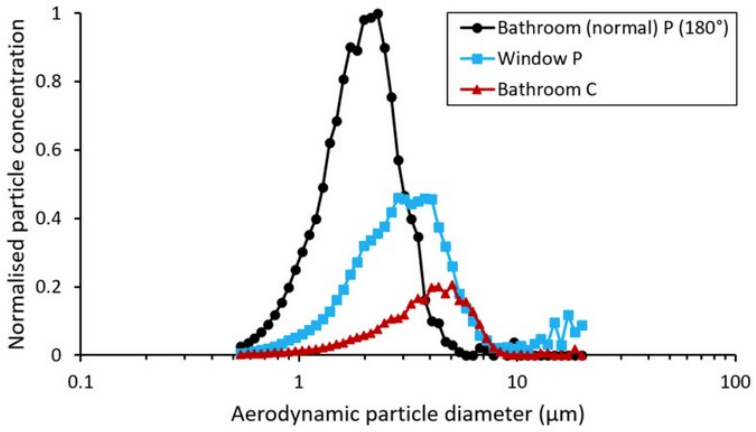

Figure 3. Particle mass size distributions for three of the seven cleaning sprays tested. The size distributions are based on APS measurements (0.5–20 μm). The particle mass concentration was normalized by the maximum concentration value.

While this study did not find any nano-sized particles emitted from the trigger sprays, it was clear that these products did emit the majority of particles smaller than 10 microns.

Source: Karin Lovén, Christina Isaxon, Aneta Wierzbicka & Anders Gudmundsson (2019) Characterization of airborne particles from cleaning sprays and their corresponding respiratory deposition fractions, Journal of Occupational and Environmental Hygiene, 16:9, 656-667, DOI: 10.1080/15459624.2019.1643466. Available at: https://www.tandfonline.com/doi/epub/10.1080/15459624.2019.1643466?needAccess=true

CIR staff annotation: It is not clear which paper "this paper (Loven, et.al. 2021)" mentioned above refers to, since the one listed by WVE was published in 2019. Again, please note the figure legend, particle number concentration and size distribution (**0.5 – 20 µm**) of the airborne particles from spraying products were measured using an aerodynamic particle sizer (APS). As discussed above, the whole distribution patterns of aerosols resulting from application of such trigger sprays have not been elucidated. WVE claims herein "it was clear that these products did emit **the majority** of particles smaller than 10 microns," which is **NOT** correct.

And there are numerous cosmetic products, particularly hair products like conditioners, that are marketed in trigger spray bottles.

It appears that the desired particle size distribution from a cosmetic spray can be specified by the manufacturer and engineered fairly precisely by their aerosol/pump/trigger spray packaging supplier. Different particle size distributions may have different functionality depending on the product. The CIR

might consider adding language to the resource document on safer recommended particle size specifications for manufacturers to adhere to, to account for the diversity of products available.

CIR staff annotation: CIR has recognized the particle/droplet size distribution is complex and depends on product formulation and the technical details of the applicator. Please note the following language has already been included in the Document:

"The final particle size distribution of a spray product is the result of the composition of the formula, the concentration of individual ingredients, and other relevant spray parameters (e.g., spray nozzle, can size, propellant type and pressure)." (See pdf page 89 at https://www.cir-safety.org/sites/default/files/Inhalation.pdf)

"Further reduction of incidental inhalation exposures to respirable particles from cosmetic products can be accomplished by utilizing use devices, ingredients, and formulations that enable minimized aerosol generation, and/or skew the size distributions, of the particles released from these products, outside of the respirable range." (See pdf page 84 at https://www.cir-safety.org/sites/default/files/Inhalation.pdf)

> As characteristics of nanoparticles, such as size distribution, shape, and surface area are **unique to each aerosol** and can **affect their regional deposition** in the lung airways, as well as their **interactions with biological organisms**, a novel aerosol generation system coupled with individual animal exposure pods for measuring particle concentration, has been developed to monitor and sample aerosols from various type of nano-enabled consumer products, and to **mimic real-world consumer exposures** to liquid powder consumer sprays. Such exposure platform provides reproducible aerosol generation and can be used for in vivo toxicological assessments to determine toxicological profiles of aerosol fractions as well as potential respiratory hazards for realistic application." (See pdf page 85 - 86 at https://www.cir-safety.org/sites/default/files/Inhalation.pdf)

Assumption 3:

Exposure to cosmetic sprays and powders are generally of short duration, involves only a very small amount of a cosmetic product, and/or are not directly applied within the breathing zone – leading to negligible exposure from incidental inhalation.

Specifically, p.87 &88 of the inhalation document .pdf include this assumption:

> "*The Panel noted that particle/droplet size data under simulated consumer use scenarios are generally not needed when conducting inhalation risk assessment due to the tiered approach to risk assessment, which provides an adequate margin of safety at the screening and modeling tiers. This is consistent with the very low product and ingredient exposures based on short exposure durations, ingredient content of product and total amount of product used.*[31]"
>
> "*In practice, exposure to aerosolized cosmetic ingredients is very low, due to low use quantities and very short exposure times*."

Challenge: Clearly the example of airbrush cosmetics challenges all of these assumptions in that it can take 20 minutes or more to apply these sprays directly to the user's face. Similarly, there are other types of cosmetic sprays that the CIR Expert panel should also consider that challenge these assumptions including:

a) Temporary hair color sprays which can involve spraying the hair with the entire contents of more than one can per application.
b) Dry shampoo spray which involves repeated spraying multiple sections of your hair.
c) Dry shampoo powder which involves considerably more loose powder application than a loose facial powder, and involves multiple applications of the powder on each section of hair. (This powder can also get resuspended as it is brushed out after application.)
d) Self tanning sprays –which can involve spraying the entire body, including the face, spraying for 10 minutes or more.
e) Makeup setting sprays which involve spraying the face at least daily, sometimes multiple times throughout the day.

CIR staff annotation: It is important to re-state that WVE's assumption does not represent CIR views or potential intention, and CIR does **NOT** encourage making such assumption. To avoid misinterpreting the language cited by WVE, it is necessary to read the draft revised Inhalation Resource Document both carefully and comprehensively. For instance, the comprehensive meaning of following paragraph under the section titled, *Measurement of Exposure under In-use Conditions,* should be meticulously considered before arriving at a conclusion:

> As for cosmetic products in spray form, the major targets are the skin and hair, but **spraying causes the partitioning of the product between the target and the surrounding air**. **For the risk assessment purpose, the use of spray products should be quantified not only in terms of the amount of product dispensed from the spray can, but also the product fraction reaching the skin and deep lung regions during application**. It is important to note that particle/droplet size data generated under experimental conditions may be significantly different from particle/droplet size under realistic consumer use conditions, in which exposure to droplets/particles from propellant sprays is highly affected by numerous critical factors, including nozzle size, spray distance, spray time, spray direction, temperature, humidity, ventilation, room size, propellant gas and the solvent applied, as well as physiological factors, such as respiratory rate, tidal volume and clearance mechanisms. Therefore, in most cases, a **refinement of spray characteristics is required** to achieve realistic consumer exposure measurements, which will provide a clear insight into the inhalable and respirable fractions that might be expected. One study, which performed exposure measurements with deodorants/antiperspirants in aerosol form, indicated that **experimentally measured exposure is generally many times lower than the that derived from the in silico models**, after inhaled doses are refined to adjust for the amount of material that ends up on skin/hair (and is therefore not available for respiration). In another study, inhalation exposure to aluminum from four antiperspirant sprays were estimated when the product was sprayed against a skin surrogate compared to spraying in the air ("free spraying"). **Findings suggests free spraying overestimated uptake by more than a factor of two**; i.e., calculating the systemic uptake using release data obtained for the free spray operation results is an overestimation of the uptake by more than a factor of two. Moreover, exposure estimates incorporating spray product use levels and ingredient concentrations and adjusted for distribution in two-box model result in highly conservative estimates of lung exposure. Thus, a safety assessor may expect that unintentional

exposure by inhalation during usage of some types of cosmetic powders, under realistic exposure conditions, can be very low to negligible.

In addition, as indicated by CIR SSC, while particle size impacts exposure, other exposure factors are key in assessing inhalation safety. The sample exposure calculations presented in the CIR SSC memo dated October 30, 2018 (re-submitted in the current Wave2), show the impact of other factors.

Temporary hair color spray application video example:

https://www.youtube.com/watch?v=zsiKMGR5bDA

Note: L'oreal Paris website has an article on "How to use a temporary hair color spray" which makes no recommendations on reducing inhalation of the product. It also confirms that the amount of product used per application can be considerable: "*…if you're looking for all-over color, you may need to use more than one can, depending on the length and thickness of your mane*."

https://www.lorealparisusa.com/beauty-magazine/hair-color/hair-color-trends/temporary-hair-color-spray

Dry shampoo spray application video example:

https://www.youtube.com/watch?v=y6Tab2ywdK0

Dry shampoo powder application video example:

https://www.youtube.com/watch?v=HOwk3RiTfPM

Makeup setting spray examples:

https://www.urbandecay.com/all-nighter-setting-spray-by-urban-decay/ud803.html

Urban Decay All Nighter Setting Spray

"Shake bottle well to activate the formula. Spray in an "X" and "T" formation repeatedly (about 3-5 times) until face is fully saturated."

https://www.onesizebeauty.com/products/on-til-dawn-setting-spray?variant=40781518438599

ON 'TIL DAWN MATTIFYING WATERPROOF SETTING SPRAY

"Shake well before each use, and keep eyes closed during application. Hold 10-12 inches away from

face, and spray in a circular motion for even distribution on skin."

(This product is an aerosol spray.)

https://www.sephora.com/product/milk-makeup-hydro-grip-set-refresh-spray-P463071?

MILK MAKEUP - Hydro Grip Setting + Refreshing Spray

-Press the hydro-fine mist pump for an all-over, even halo distribution onto skin.

-Hold bottle eight to 10 inches away from face and mist evenly onto skin two times. Close mouth and eyes while spraying.

-Use before makeup application to seal in skincare, prep, hydrate, and provide a natural-looking glow.

Use as a setting spray to lock in your look for up to 12 hours after makeup application. Allow formula one minute to set makeup.

-Reapply throughout the day as desired to refresh skin and revitalize makeup.

Self tanning spray application video example:

https://www.youtube.com/watch?v=T68IXR42gyY

Potential hazards from the inhalation of cosmetics are much more complex than the CIR has previously taken into account. Cosmetic products can be inhaled, and the cosmetic ingredients in them can lead to potential harm. Epidemiological studies of cosmetologists, hair and nail salon workers support this assertion, as they commonly show that people in these occupations have significantly higher risks of asthma[1,2,3] idiopathic pulmonary fibrosis[4], chronic bronchitis[5], work-related cough[6] and decreased lung function[7]. Strong recommendations from the CIR expert panel can help reduce these inhalation exposures and prevent possible disease is cosmetics users and salon workers alike.

CIR staff annotation: Science-based risk assessments rely on solid and reliable data generated from use studies. When new data for such diverse types of consumer sprayable products are identified from peer-reviewed research papers, those should definitely be considered by the Panel and incorporated to the Document. The Panel cares about the health and safety in cosmetics industries, and emphasizes that cosmetics production should meet standards of occupational health and safety. When data are available, the Panel should review the assessment of cosmetic safety, considering factors relevant to exposure duration, concentrations of application, work environment, and so forth, on a case-by-case basis.

Thank you for your careful consideration of these comments.

Alexandra Scranton
Director of Science and Research
Women's Voices for the Earth

[1] Kwok C., Money A., Carder M., Turner S., Agius R., Orton D. and Wilkinson M. (2014) Cases of occupational dermatitis and asthma in beauticians that were reported to The Health and Occupation Research (THOR) network from 1996 to 2011. Clinical and Experimental Dermatology. Vol. 39, pp:590- 595. 2014.

[2] Kreiss K., Esfahani RS., Antao VC., Odencrantz J., Lezotte DC. and Hoffman RE. (2006) Risk factors for asthma among cosmetology professionals in Colorado. Journal of Occupational and Environmental Medicine. Vol. 48, No. 10, pp: 1062-1069. October 2006.

[3] Leino, T., Tammilehto, L., Hytonen, M., Sala, E. Paakkulainen, H. and Kanerva, L. (1998) Occupational skin and respiratory diseases among hairdressers. Scandinavian Journal of Work, Environment & Health. Vol. 24, No. 5, pp: 398-406. 1998

[4] Baumgartner KB., Samet JA., Coultas DB., Stidley CA., Hunt WC., Colby TV., Waldron JA. and collaborating centers (2000) Occupational and environmental risk factors for idiopathic pulmonary fibrosis: A multicenter case-control study. American Journal of Epidemiology. Vol. 152, No. 4, pp: 307-315. 2000.

[5] Leino T., Tammilehto L, Luukkonen R, and Nordman H. (1997) Self reported respiratory symptoms and diseases among hairdressers. Occupational and Environmental Medicine. Vol. 54, pp: 452-455. 1997.

[6] Bradshaw L., Harris-Roberts J., Bowen J., Rahman S. and Fishwick D. (2011) Self-reported work-related symptoms in hairdressers. Occupational Medicine. Vol. 61, pp:328-334. 2011.

[7] Reutman SR., Rohs AM., Clark JC., Johnson BC., Sammons DL., Toennis CA., Robertson SA., MacKenzie BA. And Lockey JE. (2009) A pilot respiratory health assessment of nail technicians: Symptoms, lung function and airway inflammation. American Journal of Industrial Medicine. Vol. 52, pp: 868-875. 2009.

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Christina L. Burnett, Senior Scientific Analyst/Writer, CIR
Jinqiu Zhu, PhD, DABT, ERT, CIR Toxicologist
Date: November 22, 2021
Subject: Annotated WVE's comments on reopening MCI/MI

Enclosed are the comments received from Women's Voices (WVE) dated November 16, 2021, on the concerns of sensitization to Methylchloroisothiazilionone (MCI)/ Methylisothiazilionone (MI). For clarification purpose, annotations have been added to the WVE memo to indicate the missing exposure data in the figure presented by WVE. The annotations are highlighted in yellow therein for the Panel's consideration.

WVE
WOMEN'S VOICES FOR THE EARTH

November 16, 2021

To the CIR,

While I realize that neither of the Safety Assessments for methylisothiazolinone (MI) or methylchloroisothiazilionone (MCI) are currently open – I am writing to bring your attention to recent data on the trend in sensitizations to these ingredients in the United States which indicate a stark departure from what is being seen in the rest of the world. The CIR has the opportunity to re-open ingredients, and there appears to be a compelling public health reason to do so.

Brief history:

In 2013, Cosmetics Europe issued a bold recommendation that **the use of MI in leave-on cosmetic products be discontinued**. This recommendation was enacted following discussions with the European Society of Contact Dermatitis, which raised concerns about the rapidly growing numbers of reactions to MI seen in patients in Europe.[1] This recommendation was largely heeded by manufacturers and **eventually resulted in 2017 in a formal regulatory ban on MI in leave-on cosmetic products**, and a strict restriction in rinse-off products in the EU. This ban effectively **banned the use of MCI/MI in cosmetic products as well**.

As a result of these actions, sensitizations to MI in the EU have decreased dramatically – beginning almost immediately after the 2013 Cosmetics Europe recommendation was issued. Most studies show that sensitizations to MI have decreased by half from their epidemic-high levels in the EU.

In Australia, action on MI in cosmetics was enacted a few years later than in the EU – with an official ban on MI in leave-on cosmetics promulgated officially in 2017. The trend in sensitizations to MI in Australia, while still high, is also declining rapidly from its peak in 2015 based on the most recently available data.

In contrast, **in the United States**, in September 2014, the CIR came to a different decision than Cosmetics Europe and issued a final safety assessment on MI with the conclusion that MI is **safe for use in rinse-off cosmetic** products at concentrations up to 100 ppm **and safe in leave-on cosmetic products** when they are formulated to be non-sensitizing, which may be determined based on a QRA. More recently in September 2020, despite awareness of the declining trends in the EU and Australia, the CIR reconfirmed their 2014 decision. No regulatory action or ban on MI has been made in the United States.

As a result, **sensitizations to MI and MCI in the United States are at their highest level ever,** on a trend that is continuing to increase. The most recent data is now available from the North American Contact Dermatitis Group Patch Test Results (NACDG) for 2017-2018 – which reflects a considerable increase over the 2015-2016 numbers. We are not seeing the same public health benefits here as experienced in the EU and Australia, which resulted from the removal of MI from most cosmetic products. This means that in the past decade thousands (possibly tens of thousands?) of Americans have been (and are continuing to be) unnecessarily sensitized to MI and MCI due to their exposure from

[1] https://cosmeticseurope.eu/files/3614/7634/5470/Recommendation_on_MIT.pdf

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cosmetics. Compared to a ban, the less-specific CIR recommendation to allow MI in leave-on products "when they are formulated to be non-sensitizing" **is not working**. The clear evidence of success of the bans in other countries cannot be ignored. The CIR can make a different choice and take steps which will reverse the adverse trend in sensitizations in the US as well.

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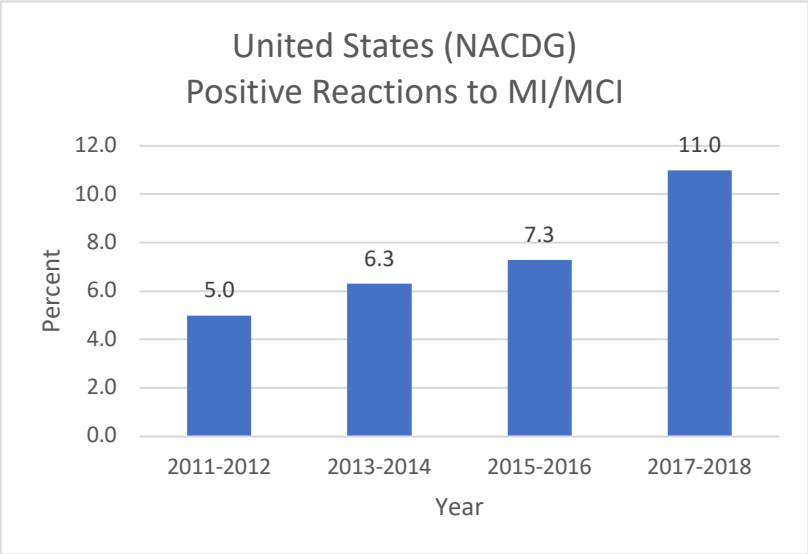

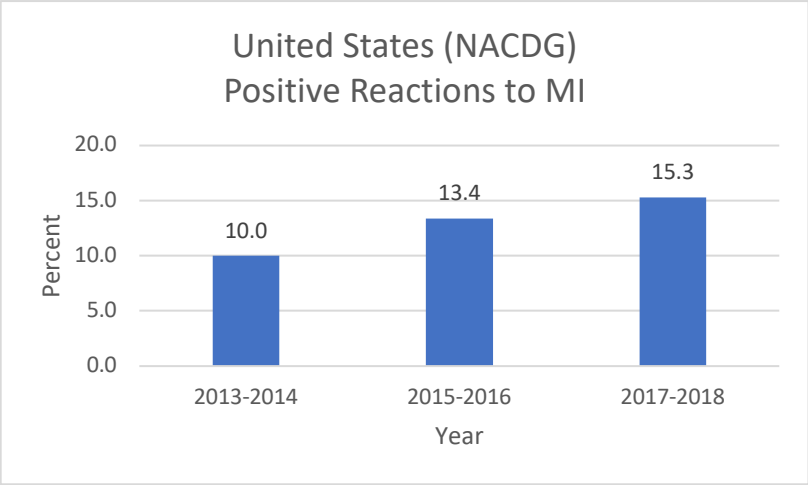

Sources:

Zirwas MJ, Hamann D, Warshaw EM, Maibach HI, Taylor JS, Sasseville D, DeKoven JG, Fransway AF, Mathias CGT, Zug KA, DeLeo VA, Fowler JF, Marks JG, Pratt MD, Belsito DV. Epidemic of Isothiazolinone Allergy in North America: Prevalence Data From the North American Contact Dermatitis Group, 2013-2014. Dermatitis. 2017 May/Jun;28(3):204-209

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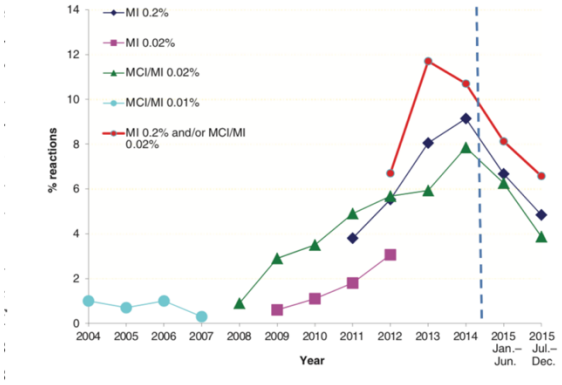

Fig. 1. Incidence of contact allergy to methylchloroisothiazolinone (MCI)/methylisothiazolinone (MI) and MI by year. Our new data are to the right of the blue line.

Source: Urwin R, Craig S, Latheef F, Wilkinson M. Methylisothiazolinone: the epidemic is declining - but not gone. Contact Dermatitis. 2017 May;76(5):301-302. doi: 10.1111/cod.12750.

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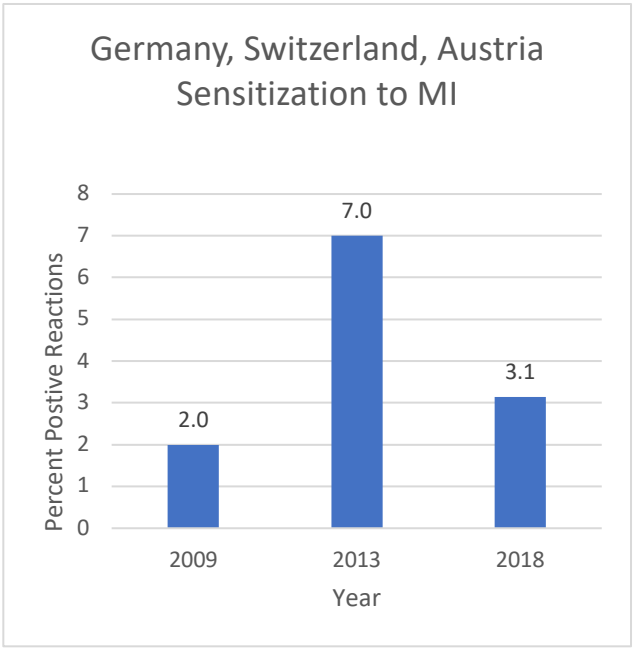
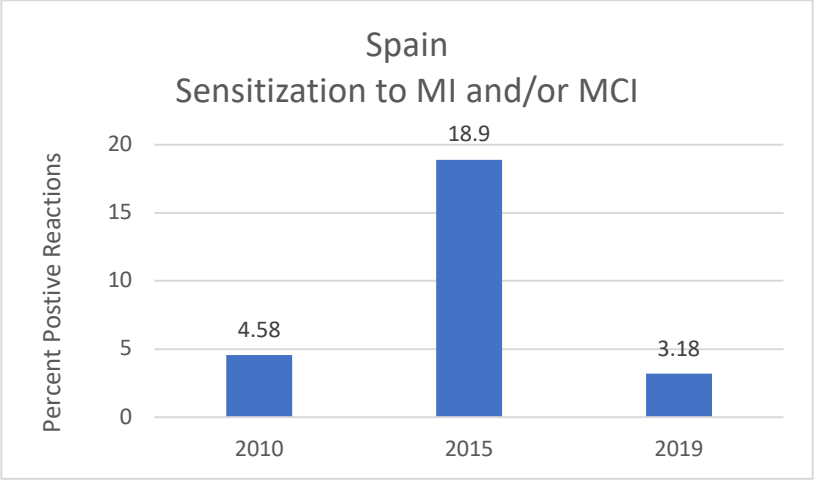


Source: Schnuch, A., Schubert, S., Lessmann, H., & Geier, J. (2019). The methylisothiazolinone epidemic goes along with changing patients' characteristics – After cosmetics industrial applications are the focus. Contact Dermatitis. doi:10.1111/cod.13414

Data from Spain:



Source: Magdaleno-Tapial, J., Valenzuela-Oñate, C., Ortiz-Salvador, J. M., García-Legaz-Martínez, M., Martínez-Domenech, Á., Alonso-Carpio, M., ... Zaragoza-Ninet, V. (2019). Contact allergy to isothiazolinones epidemic: Current situation. Contact Dermatitis. doi:10.1111/cod.13396

Data from Belgium:

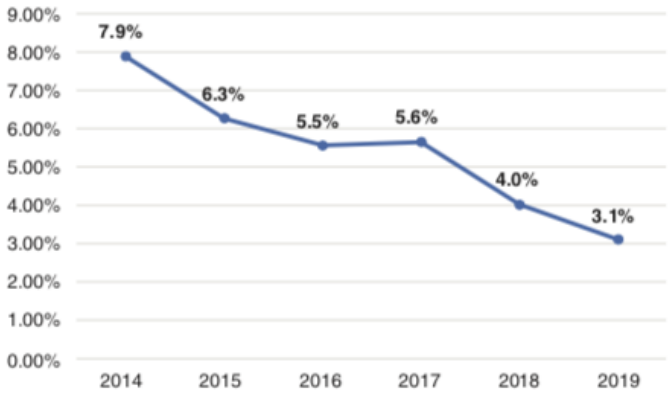


FIGURE 1 Evolution of the sensitization rate to methylisothiazolinone in Belgium between January 2014 and December 2019 (2014-2017, data from five university centres; 2017-2019, data from four university centres; and 2019, data from three university centres)

Source:

Herman A, Aerts O, Jacobs MC, Scheers C, Gilissen L, Goossens A, Baeck M. Evolution of methylisothiazolinone sensitization: A Belgian multicentric study from 2014 to 2019. Contact Dermatitis. 2021 Aug 13. doi: 10.1111/cod.13956.

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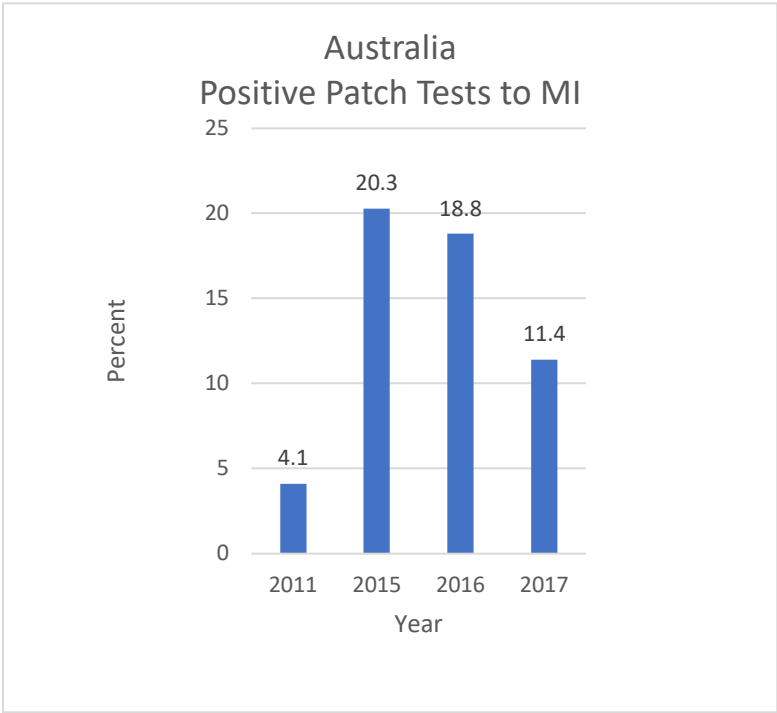

Source: Flury, U., Palmer, A., & Nixon, R. (2018). The methylisothiazolinone contact allergy epidemic in Australia. Contact Dermatitis, 79(3), 189-191. doi:10.1111/cod.13025

WOMEN'S VOICES FOR THE EARTH

November 16, 2021

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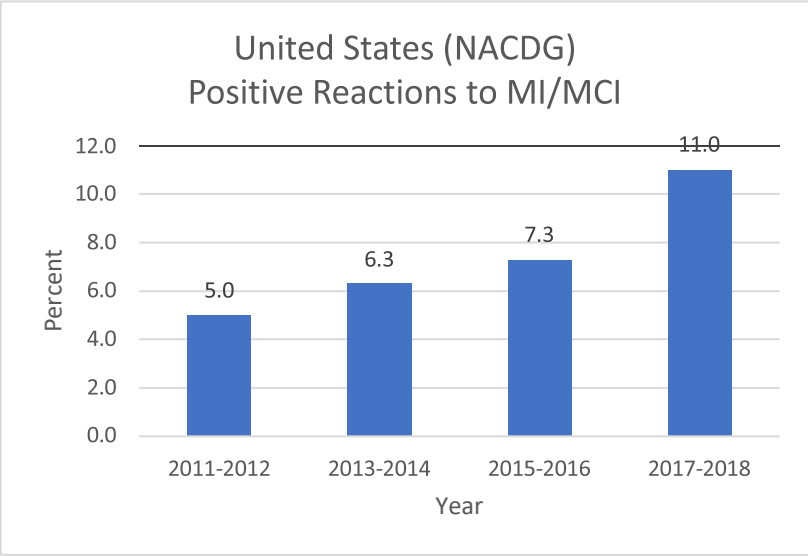

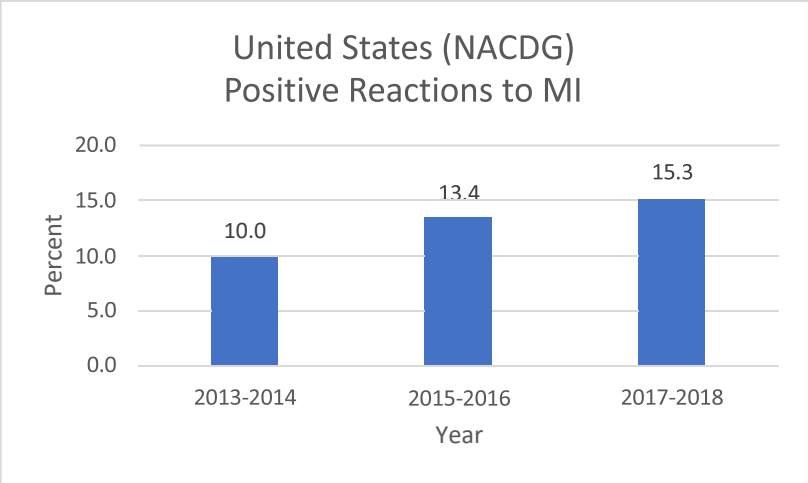

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CIR staff annotation: To clarify, the graph shown above does not appear in the original paper, but is drawn by WVE, which misrepresents the concentrations of MI or MCI/MI that are **NOT** marked therein. Please note the original data clearly indicate that in all of the tested cycle, as shown in the figure (i.e., 2011-2018 for MCI/MI, as well as 2013-2018 for MI), MI entered the North American Contact Dermatitis Group (NACDG) patch screening test at a concentration of **2000 ppm (0.2% aqueous)**, while MCI/MI entered at a concentration of **200 ppm (0.02% aqueous)**. The original data may be found in Table 3 of the following reference: DeKoven JG, Silverberg JI, Warshaw EM, Atwater AR, Reeder MJ, Sasseville D, Taylor JS, Zug KA, Belsito DV, Maibach HI, Pratt MD, Cgt M, DeLeo VA, Fowler JF Jr. North American Contact Dermatitis Group Patch Test Results: 2017-2018. *Dermatitis*. 2021 Mar-Apr 01;32(2):111- 123

Importantly, such doses **exceed** the Panel's recommendation by **more than a factor of ten or twenty**.

Please note the conclusion of CIR MI report (Burnett et al., *Int J Toxicol*., 2021, 40(1_suppl):5S-19S) states that "Methylisothiazolinone is safe for use in rinse-off cosmetic products at concentrations up to **100 ppm** (**i.e. 0.01%**) and safe in leave-on cosmetic products when they are formulated to be non-sensitizing, which may be determined based on a quantitative risk assessment (QRA) or similar methodology."

Further, the following language presented in the Discussion section of CIR MI report should be paid much attention:

> As discussed in the previous report on Methylisothiazolinone, the Panel reviewed the results of QRAs performed by Cosmetics Europe and the CIR Science and Support Committee. Those results supported the safety of the use of Methylisothiazolinone in **rinse-off product** categories at concentrations **up to 100 ppm**. However, the QRA indicated that Methylisothiazolinone use in several **leave-on product** categories, such as wet wipes, would be **safe only at concentrations lower than 100 ppm**. Using the QRA results, the Panel reaffirmed the limitation of 100 ppm Methylisothiazolinone in rinse-off products. However, they also determined that the original limitation for leave-on products needed to be modified, and that **leave-on cosmetic products should be formulated to contain Methylisothiazolinone at concentrations below 100 ppm and to be non-sensitizing**, as demonstrated, for example, by QRA estimates of safe exposures (typically expressed in $\mu g/cm^2/d$) for the relevant cosmetic product category.
>
> The Panel's recommendations for Methylisothiazolinone in rinse-off and leave-on cosmetic products are intended to prevent the induction of sensitization to Methylisothiazolinone. However, the Panel cautioned that following these recommendations may not necessarily prevent the elicitation of allergic reactions in individuals who are already allergic to Methylisothiazolinone. **Individuals sensitized to Methylisothiazolinone should avoid products that contain Methylisothiazolinone.**

In addition, please also note the conclusion of CIR MCI/MI report (Burnett et al., *Int J Toxicol*., 2021, 40(1_suppl):20S-33S) states that "MCI/MI is safe in cosmetics when **formulated to be non-sensitizing**, based on the results of a quantitative risk assessment (QRA) or similar methodology; however, **at no point should concentrations exceed 7.5 ppm in leave-on products or 15 ppm in rinse-off products**"

And the following language is presented in the Discussion section of CIR MCI/MI report:

> The Panel noted the results of a QRA for skin sensitization performed by the CIR Science and Support Committee. The results indicated that some leave-on products comprising MCI/MI at the

recommended maximum safe concentration of **7.5 ppm** may yet increase the risk of inducing dermal sensitization. In most rinse-off products, **15 ppm** MCI/MI was not associated with a potential increased risk of skin sensitization induction. Individuals previously sensitized to MCI/MI should avoid products that contain this ingredient mixture.

MCI/MI is a useful and necessary preservative system in cosmetic products. The Panel is **aware** that the **conclusion herein differs from** that reached by counterparts in the European Union. In part, the differing conclusions are based on interpretation of earlier LLNA data on which the hazard assessments were determined. However, the Panel supports managing sensitization risks by the use of valid assessment tools and strategies, such as a QRA system (or similar methodology). **Instead of banning ingredients that may pose a risk under certain conditions (e.g., formulation, body-part exposure), the Panel has proposed that such risk-mitigating tools and strategies can be applied by formulators, and thus avoid exhausting available preservative systems. Such systems are necessary to protect consumers from microbial contaminations that would otherwise occur in cosmetic products.**

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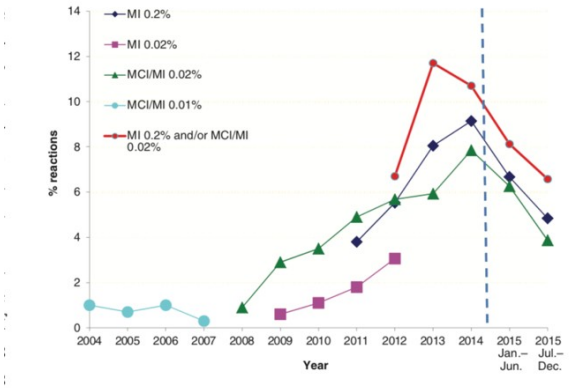

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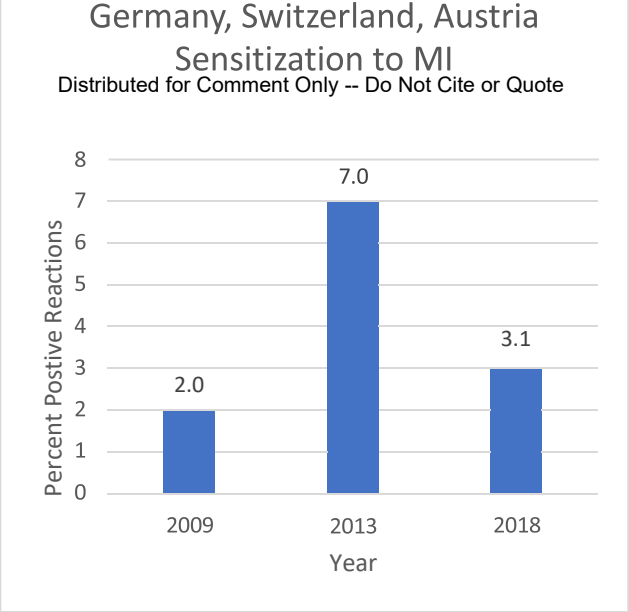

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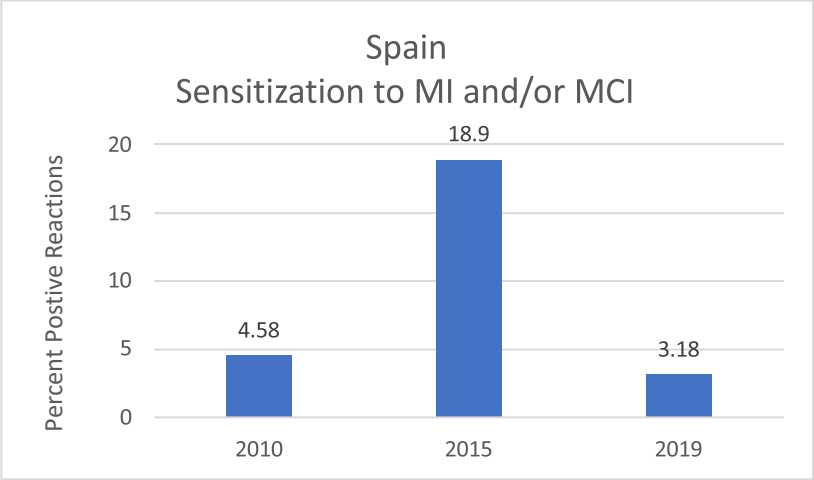

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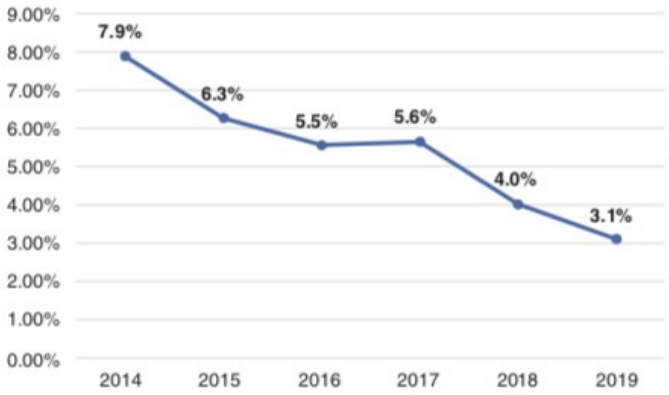

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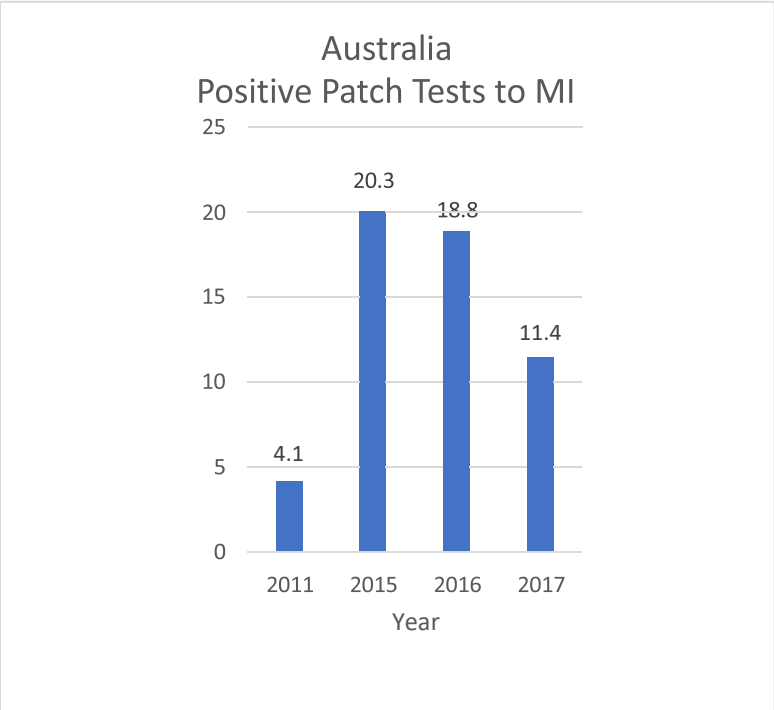

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Memorandum

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From: Christina L. Burnett, Senior Scientific Analyst/Writer, CIR
Jinqiu Zhu, PhD, DABT, ERT, CIR Toxicologist
Date: November 22, 2021
Subject: Annotated WVE's comments on Silicates report

Enclosed are the comments received from Women's Voices (WVE) dated November 16, 2021, on the Amended Safety Assessment of Silicates as Used in Cosmetics. Annotations have been added to WVE's memo to clarify concerns with regard to misunderstanding on concentration of use, as well as inhalation exposure to sprayable products, as highlighted in yellow therein.

WOMEN'S VOICES FOR THE EARTH

November 16, 2021

Re: Comments on the Safety Assessment of Silicates

To the CIR:

These comments on the Amended Safety Assessment of Silicates as used in Cosmetics are submitted on behalf of Women's Voices for the Earth.

1.) Inconsistent concentrations of use

In the Cosmetic use section (p.283 of .pdf) it states:

> "*For example, Calcium Silicate is used at up to 0.005% in hair color sprays and Lithium Magnesium Silicate is used at up to 0.4% in face and neck sprays, and Calcium Silicate and Magnesium Aluminum Silicate are reported to be used at up to 5% and 1% in face powders, respectively*.[27]".

The data on powders appear to be use concentrations from older VCRP data. The 2018 VCRP data indicates higher percentages at which these ingredients are used as reported in the Summary section on p.288.

> "*The results of the concentration of use survey conducted in 2018 by the Council indicate Aluminum Calcium Sodium Silicate has the highest reported maximum concentration of use for leave-on products; it is used at up to 26.3% in eye shadows. Magnesium Silicate is reported to have a maximum concentration of use for leave-on products of 21.6% in eye shadows.*"

2) Hazards of synthetically manufactured silicates

The conclusion of the safety assessment currently states that present practices and uses of silicates are safe except that data are insufficient for incidental inhalation of silicates that are naturally sourced. But on p.285, inhalation studies of synthetically manufactured silicates in animals are discussed. These studies showed significant inflammatory results, fibrosis, pulmonary lesions and emphysema from exposure to synthetically-manufactured amorphous and hydrated silica. Some silicate ingredients, such as magnesium aluminum silicate are found in spray products that may be incidentally inhaled, including in some deodorant sprays – which we understand can emit a significant proportion of respirable particles.

Does the CIR panel feel this research supports the safety of exposures to silicates from deodorant sprays which could be deeply inhaled into the lungs if the silicates are synthetically manufactured?

Thank you for your consideration of these comments.

Alexandra Scranton
Director of Science and Research

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CIR staff annotation: Data presented on pdf page 283 of the report refer to ingredients that are formulated **in sprayable products** while data on pdf page 288 show the maximum use concentration of ingredients **in leave-on products**.

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Does the CIR panel feel this research supports the safety of exposures to silicates from deodorant sprays which could be deeply inhaled into the lungs if the silicates are synthetically manufactured?

CIR staff annotation: Based on the Council's survey, there are **zero** spray deodorant uses reported for Silicates, i.e., the two uses reported by the VCRP for Magnesium Aluminum Silicate that fall into the "may be used in sprays" have use concentrations that were reported by Council to **not be** sprays. However, the Panel noted in WVE's comments, dated January 21, 2021, Magnesium Aluminium Silicate was presented in formulations of several types of airbrush makeup foundation, coupled with engineered metal nanoparticles, such as titanium dioxide (TiO_2) and iron oxide (Fe_2O_3). Safety concerns regarding inhalation exposure to constituent metal nanoparticles during the use of airbrush makeup devices have been discussed in the draft revised CIR Resource – Respiratory Exposure to Cosmetic Ingredients Document. (See pdf page 85 - 86 at https://www.cir-safety.org/sites/default/files/Inhalation.pdf.)

Thank you for your consideration of these comments.

Alexandra Scranton
Director of Science and Research

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Christina L. Burnett, Senior Scientific Writer/Analyst, CIR
Date: November 22, 2021
Subject: Safety Assessment on Zeolites as Used in Cosmetics – Wave 2

Enclosed are updated concentration of use data for both natural and synthetic Zeolite (*data1_Zeolites_Wave2_1222021*). According to the new data, the maximum concentration of use for synthetic Zeolite is 0.9% in aerosol hair spray. The maximum concentration of use for natural Zeolite is 0.6% in face powders and foundations.

Additionally, unpublished data on zeolite A, a synthetic subtype of Zeolite, were submitted by W.R. Grace & Co. in response to the IDA (*data2_Zeolites_Wave2_122021*). These data include chemical properties, method of manufacturing, particle size, and impurities.

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Concentration of Use by FDA Product Category – Zeolites*

Zeolite
Ammonium Silver Zeolite
Gold Zeolite
Silver Copper Zeolite
Titanium Zeolite
Zinc Zeolite

Ingredient	Product Category	Maximum Concentration of Use
Zeolite	Other eye makeup preparations	0.6%
Zeolite	Hair sprays Aerosol	 0.25%, 0.9%#
Zeolite	Face powders	0.6%**
Zeolite	Foundations	0.42%#, 0.5%#, 0.6%**
Zeolite	Skin cleansing (cold creams, cleansing lotions, liquids, and pads)	0.0043%
Zeolite	Body and hand products Not spray	 0.03%#

*Ingredients included in the title but not found in the table were included in the concentration of use survey, but no uses were reported.

#Synthetic Zeolite

**Natural Zeolite

Type of Zeolite used in other products not stated

Information collected in 2021
Table prepared: November 15, 2021

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November 11, 2021

The Expert Panel for Cosmetic Ingredient Review
Dr. Cohen and Dr. Heldreth
1620 L St NW Suite 1200
Washington, DC 20036-4702

Re: Insufficient Data Announcement (IDA) for zeolite

Dear Dr. Cohen and Dr. Heldreth:

The following responds to the Insufficient Data Announcement (IDA) for zeolite ingredients issued by the Cosmetic Ingredient Review's (CIR) Expert Panel after its September 13-14, 2021 Meeting.

The Panel issued an IDA for six zeolites used as cosmetic ingredients, including "zeolite," an ingredient that encompasses a diverse group of substances. This submission provides information on zeolite A, which was identified in the CIR's March 2003 *Final Report on the Safety Assessment of [...] Zeolite* as one of the most common zeolites (Ref.1). Grace manufactures synthetic Zeolite A for use in cosmetic formulations, primarily for face masks due to its heat-releasing properties when contacting water.

The Expert Panel identified four items of additional data needed to determine safety; this submission responds to the first two identified items:

- Method of Manufacturing and/or source data; and
- Chemical characterization, including specific framework(s), and composition and impurities data.

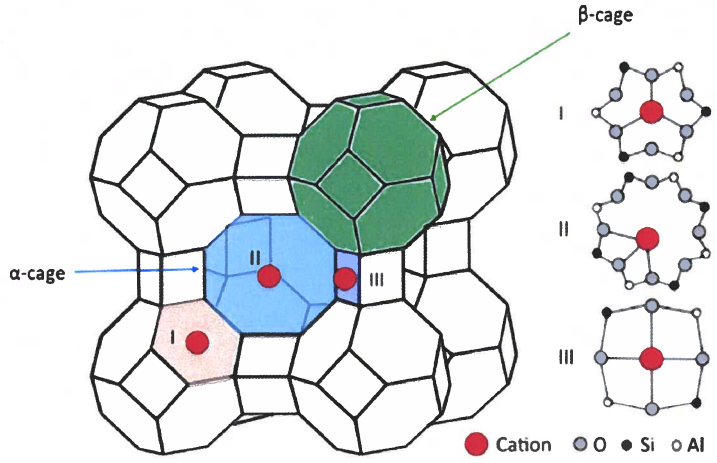
GENERAL CHEMISTRY

As the CIR recognizes, zeolites are a diverse group of materials. To understand the broad range of structures encompassed with zeolites, the International Zeolite Association has published a Database of Zeolite Structures, which provides structural information on the Zeolite Framework Types that have been approved by its Structure Commission (Ref.2). Zeolite A is identified in this framework as Linde Type A, LTA.

ZEOLITE TYPE A CHEMISTRY

Zeolite A is a well characterized, three-dimensional, aluminosilicate based crystalline solid. Silicon, aluminum and oxygen form the structural framework with cations and water located in the pores. These

cations can be exchanged. The silicon and aluminum atoms are connected via an oxygen atom and they are both in a tetrahedral coordination. The framework of Zeolite A is shown below (Ref. 3)



The unit cell of hydrated zeolite A contains 12 AlO_4 and 12 SiO_4 tetrahedra along with 27 water molecules, and it can be represented by the formula: $Na_{12}[(AlO_2)_{12}(SiO_2)_{12}]\cdot 27H_2O$ (Ref. 3)

The chemical composition of Zeolite A can also be written in the following oxide form: $(Na_2O)\cdot(Al_2O_3)\cdot 2(SiO_2)\cdot 4.5H_2O$ (Ref. 4)

METHOD OF MANUFACTURE

Grace manufactures Zeolite A as a sodium salt, where the sodium ion may then be exchanged with potassium or calcium ions to form their respective salts, as follows.

Synthesis of Zeolite A (sodium form)

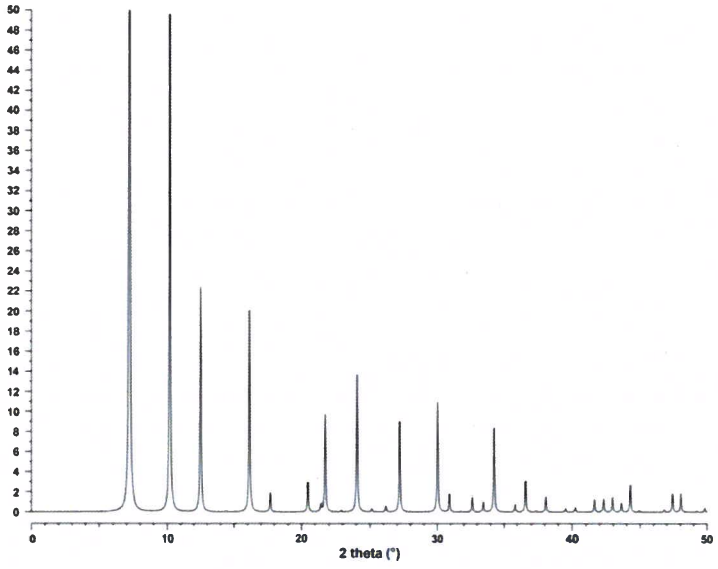
- Raw materials:
  - Water
  - Sodium Silicate
  - Sodium Aluminate
  - Sodium Hydroxide
- All raw materials are combined and heated to promote the formation of Zeolite A, which precipitates out of the solution. The pure Zeolite A particles are recovered via filtration and washing with water.
- The Zeolite A produced using this synthetic scheme has the following formula (expressed as the oxides of the sodium, aluminum and silicon): $(Na_2O)\cdot(Al_2O_3)\cdot 2(SiO_2)\cdot wH_2O$ (where w represents the variable amount of water in the material). This is the hydrated form of the Zeolite A.
- The materials can be dehydrated via exposure to high temperatures. After the majority of water is removed, Zeolite A (sodium form) has the following composition: $(Na_2O)\cdot(Al_2O_3)\cdot 2(SiO_2)\cdot wH_2O$ where w is less than 1.
- A representative synthesis procedure can be found in Refs. 5 and 6.

Synthesis of Zeolite A (sodium, potassium, calcium forms)

- Raw materials:
  - Water
  - $(Na_2O)\cdot(Al_2O_3)\cdot 2(SiO_2)\cdot wH_2O$ (as described above)
  - Potassium salt (e.g. potassium chloride)
  - Calcium salt (e.g. calcium chloride)
- The hydrated form of Zeolite A is added into a water solution of the potassium and/or calcium salts. Potassium and/or calcium ions exchange with the sodium ions present in the Zeolite A. Sodium ions leave the Zeolite A structure and potassium and/or calcium take its place in order to maintain neutrality. Finally, the material is washed with water to remove free salts
- This ion exchange step produces materials with the following compositions: $x(Na_2O)\cdot y(K_2O)\cdot z(CaO)\cdot(Al_2O_3)\cdot 2(SiO_2)\cdot wH_2O$ where $x+y+z=1$.
- Similarly to the sodium form, the ion exchanged materials can be heated to produce the dehydrated form with the formula $x(Na_2O)\cdot y(K_2O)\cdot z(CaO)\cdot(Al_2O_3)\cdot 2(SiO_2)\cdot wH_2O$ where $x+y+z=1$ and $w<1$.

IDENTIFICATION

Zeolites are well defined crystalline materials which exhibit a characteristic X-Ray Diffraction (XRD) pattern. Thus, the identity of commercial Zeolite A is verified by comparison of its XRD pattern to published reference patterns. The XRD pattern for Zeolite A is shown below (Ref. 7):



PARTICLE SIZE

Typical particle sizes of Grace-supplied Zeolite A have a D_{50} (by volume) in the 6-10 micron range.

IMPURITIES:

Residual levels of free sodium, potassium and calcium salts remain in the finished product from the raw materials. Synthetic zeolites are tested for the presence of heavy metals, such as Zn, Ni, Cd, Pb, Cr, As, Hg, Mo, Co, Sb and Se.

Thank you for your attention.

Sincerely,

Demetrius Michos, Ph.D.
Senior Principal Scientist

SOURCE DATA

1. Final Report on the Safety Assessment of Aluminum Silicate, Calcium Silicate, Magnesium Aluminum Silicate, Magnesium Silicate, Magnesium Trisilicate, Sodium Magnesium Silicate, Zirconium Silicate, Attapulgite, Bentonite, Fuller's Earth, Hectorite, Kaolin, Lithium Magnesium Silicate, Lithium Magnesium Sodium Silicate, Montmorillonite, Pyrophyllite, and Zeolite." International Journal of Toxicology, vol. 22, no. 1_suppl, Jan. 2003, pp. 37–102, Table 2.
2. For general information, see http://www.iza-structure.org/databases/; the https://america.iza-structure.org/IZA-SC/ftc_table.php
3. Reprinted with permission from Ronghong Lin et. al. Ind. Eng. Chem. Res. 2015, 54, 42, 10442-10448. Copyright 2015 American Chemical Society
4. Breck, Donald W. (1974). Zeolite Molecular Sieves – Structure, Chemistry, and Use. John Wiley & Sons. Pg. 133, 274 and 725
5. Cejka, Jiri van Bekkum, Herman Corma, Avelino Schuth (2007). Introduction to Zeolite Science and Practice, Volume 168 (3rd Edition). Pg. 39 and 45
6. Harry Robson, Karl Petter Lillerud (2001). Verified Synthesis of Zeolitic Materials. Pg. 19 and 179
7. Reprinted from M.M.J. Treacy, J.B. Higgins, John B. Higgins (2001). Collection of Simulated XRD Powder Patterns for Zeolites. Pg. 215. Copyright (2001), with permission from Elsevier