
Safety Assessment of Polymerized Tetramethylcyclotetrasiloxanes as Used in Cosmetics

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All interested persons are provided 60 days from the above date to comment on this safety assessment and to identify additional published data that should be included or provide unpublished data which can be made public and included. Information may be submitted without identifying the source or the trade name of the cosmetic product containing the ingredient. All unpublished data submitted to CIR will be discussed in open meetings, will be available at the CIR office for review by any interested party and may be cited in a peer-reviewed scientific journal. Please submit data, comments, or requests to the CIR Director, Dr. Lillian J. Gill.

The 2015 Cosmetic Ingredient Review Expert Panel members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Ronald A. Hill, Ph.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; James G. Marks, Jr., M.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Director is Lillian J. Gill, D.P.A. This report was prepared by Lillian C. Becker, Scientific Analyst/Writer.

ABSTRACT

This is a safety assessment of 3 polymerized tetramethylcyclotetrasiloxanes as used in cosmetics. Industry reported that these ingredients are not used independently but are polymerized on the surface of metal oxide particles as particle surface coatings. This use does not reflect the functions listed in the *International Cosmetic Ingredient Dictionary and Handbook (Dictionary)* and it has not been verified that these ingredients are only used as particle surface coatings in cosmetics. The Cosmetic Ingredient Review (CIR) Expert Panel (Panel) reviewed the available relevant data related to these ingredients. The Panel concluded that polysilicone-2, -4, and -5 are safe in cosmetics when used as surface modifiers (i.e., encapsulating metal oxides), and that the available data or information are insufficient to make a determination that these ingredients are safe for use independently for other functions as listed in the *Dictionary* (e.g., antifoaming agents, hair conditioning agents, and viscosity increasing agents – nonaqueous).

INTRODUCTION

This is a safety assessment of polysilicone-2, polysilicone-4, and polysilicone-5 (i.e., polymerized tetramethylcyclotetrasiloxanes) as used in cosmetics. These ingredients are synthesized from tetramethylcyclotetrasiloxane and have a core chain of repeating $-O-Si(R)(CH_3)-$ moieties. According to the *Dictionary*, these polymerized tetramethylcyclotetrasiloxane ingredients are reported to function as antifoaming agents, hair conditioning agents, and viscosity increasing agents – nonaqueous in cosmetics (Table 1).¹ The monographs of these ingredients have been amended since the publication of the *Dictionary* and now include surface modifiers in the list of functions.² The new monographs also note that these ingredients may each be used as a coating agent polymerized *in situ* typically on metal oxides or other materials.

These ingredients are reportedly synthesized from the hydrosilation of vapor-deposited tetramethylcyclotetrasiloxane monomers, resulting in a network of repeating $-O-Si(R)(CH_3)-$ moieties, around the surface of a particle.³ It is reported that these ingredients are polymerized *in situ* as coatings for metal oxide particles, completely and durably encapsulating the particle in a shell of polysilicone. However, the data do not reflect the other cosmetic functions of these ingredients as recited by the *Dictionary*; this suggests that these ingredients may be used independently (not coating metal oxides) in cosmetics.

The CIR Panel previously reviewed other siloxane polymers, such as methicone and other related methicone-containing ingredients, and concluded that those ingredients were safe as used in cosmetic products.⁴ The Panel also reviewed cyclic-siloxanes, the cyclomethicones, and concluded that they were safe as used in cosmetic products.⁵ However, these previously reviewed silicone-based ingredients are used independent of particle coating.

CHEMISTRY

Definition, Structure, and Method of Manufacture

According to the *Dictionary* definition, it would appear that polysilicone-2, polysilicone-4, and polysilicone-5 are each ingredients, without including or encapsulating any other chemical(s).¹ Under that definition, the ingredients in this report could each be synthesized from tetramethylcyclotetrasiloxane (Figure 1). Typically, synthesis of these polymethylsiloxanes occurs via cationic ring-opening polymerization of the cyclic monomer tetramethylcyclotetrasiloxane, utilizing a Brønsted-Lowry type acid (e.g., triflic acid) as an initiator (and water). The result is a polymer that can easily be functionalized by the addition of vinyl-type monomers (e.g., glyceryl monoallyl ether or tetradecene; Figure 1).

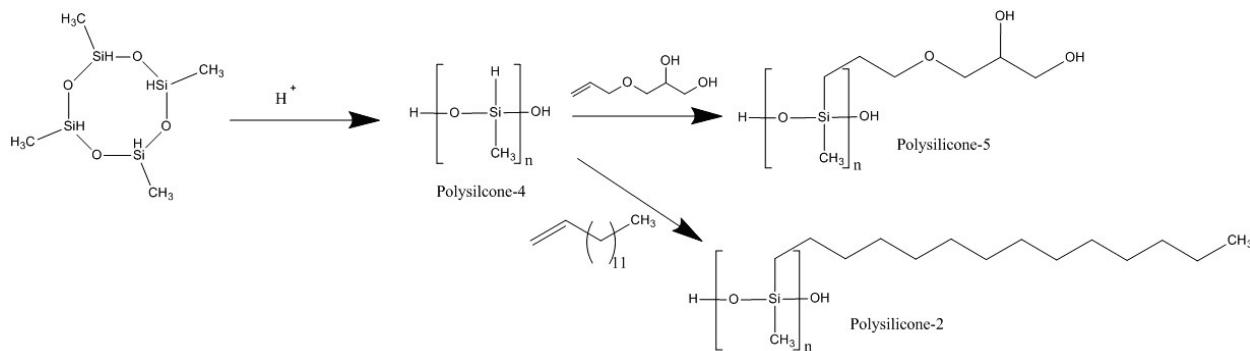


Figure 1. Synthesis of Polysilicones -2, -4, and -5.

Although these ingredients are depicted above as straight-chain polymers for the sake of simplicity, these polymers are most likely cross-linked to some degree because of the very highly labile silicone-hydrogen bonds, and the oxophilic

nature of silicone. These polymers can range from viscous liquids to hard rubber textures because of variations in temperature and duration of polymerization, and resultant variations of molecular weight and degree of cross-linking.

According to a submission from industry, it seems very likely that these 3 polysilicones are the result of: 1) vapor deposition on the surface of metal oxide particles, 2) polymerization *in situ*, via hydrosilation, to form a complete, covalently interlinked surface coating, and 3) in the case of polysilicones-2 and -5, further modification at reactive sites on this polymer shell with a vinyl-type monomer *before* use as cosmetic ingredients (Figure 2).³ These polysilicone surface coatings form complete shells around the metal oxide powder particles. These shells are covalently woven around the particle, and are durable and resistant to solubilization. Regardless of whether or not these polysilicones are covalently bonded to the surface of the particle, they are covalently bonded around the particle, and are *not simply mixtures*. Moreover, mixing a polymerized tetramethylcyclotetrasiloxane (polysilicone-2, -4, or -5 as *Dictionary* defined) with metal oxide particles, would not result in the same type of product (i.e., the polysilicone would not form a complete and durable shell around the metal oxide particle), thus failing the test for a mixture classification.

As described above, the manufacture of these coated materials begins with vapor deposition of tetramethylcyclotetrasiloxane onto metal oxide particles.³ The metal oxide used may be any one of the following: titanium dioxide, red iron oxide, yellow iron oxide, or black iron oxide. Via reaction with water (i.e., hydrosilation), these tetramethylcyclotetrasiloxane monomers are polymerized to form a polymethylsiloxane (i.e., polysilicone-4) coating on the surface of these particles. Modification of these coatings occurs by the addition of glyceryl monoallyl ether or tetradecene, and a catalyst.

Since this data submission, the monographs of all 3 of these ingredients in the *Dictionary* has been amended to include “surface modifier” in the functions and the note “...may be used as a coating agent polymerized *in situ* typically on metal oxides or other materials” has been added.² This new function and note are consistent with this method of manufacture for coated particles. However, the other functions, which have not been removed, are not consistent with coated particle ingredients and suggest that these ingredients are used independently of any metal oxide.

Physical and Chemical Properties

POLYMERIZED TETRAMETHYLCYCLOTETRASILOXANES

Data on the chemical and physical properties of polymerized tetramethylcyclotetrasiloxanes (independent of metal oxide particles) were not found in the published literature and no unpublished data were provided.

POLYMERIZED TETRAMETHYLCYCLOTETRASIOXANE/METAL OXIDE PARTICLES

According to an Industry submission, polysilicone-2-coated metal oxide particles are hydrophobic and have an estimated molecular weight >100,000 g/mol.^{3,6} The size of the coated particles was reported to be in the range of 0.2- 20 μm .

Impurities

POLYMERIZED TETRAMETHYLCYCLOTETRASILOXANES

Data on the impurities present in polymerized tetramethylcyclotetrasiloxanes independent of metal oxide particles were not found in the published literature and no unpublished data were provided.

POLYMERIZED TETRAMETHYLCYCLOTETRASIOXANE/METAL OXIDE PARTICLES

Residual levels of 1,3,5,7-tetramethylcyclotetrasiloxane (TS-4) and tetradecene were below the level of detection (<5 ppm for both) in 3 lots each of polysilicone-2-coated red iron oxide particles, polysilicone-2-coated yellow iron oxide particles, polysilicone-2-coated black iron oxide particles, and polysilicone-2-coated titanium dioxide.⁶

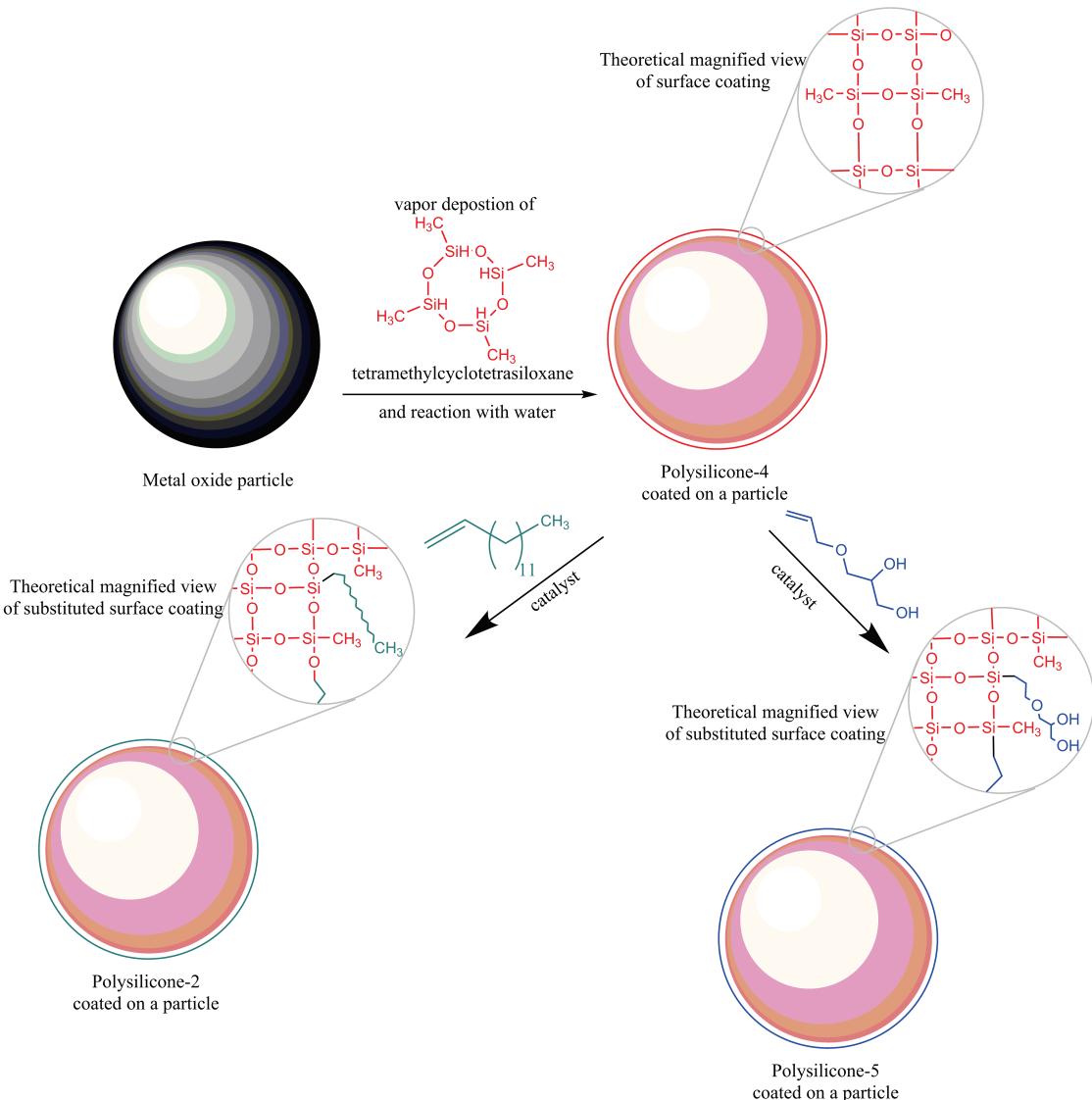


Figure 2. Particle Coating.

USE Cosmetic

The safety of the cosmetic ingredients included in this safety assessment is evaluated based on data received from the U.S. Food and Drug Administration (FDA) and the cosmetics industry on the expected use of these ingredients in cosmetics. The data received from the FDA are those it collects from manufacturers on the use of individual ingredients in cosmetics by cosmetic product category in its Voluntary Cosmetic Registration Program (VCRP), and those from the cosmetic industry are submitted in response to a survey of the maximum reported use concentrations by category conducted by the Personal Care Products Council (Council).

Because the actual forms of these ingredients are in question (independent polysilicone polymers, metal oxide particles coated with polysilicones, or both) it is impossible to know which form(s) was reported to the VCRP and the Council. The reported uses may be either or both of these. It is known that if the polysilicone-coated metal oxide form was used, the reported concentration of use is only for the polysilicone coating and does not include the encapsulated metal oxide.⁷ However, since it has not been confirmed by Industry that these ingredients are only used as metal oxide particle coatings, it is unknown which form or forms have been reported to the VCRP and the Council.

According to 2015 VCRP data, polysilicone-2 is reported to be used in 209 leave-on formulations and polysilicone-5 is used in 1 makeup fixative (Table 2).⁸ The VCRP has no reported uses for polysilicone-4.

The results of the concentration of use survey conducted by the Council in 2015 indicate polysilicone-2 had the highest reported maximum concentration of use; it is used at up to 1% in eye shadows and makeup products.⁹ Polysilicone-4 was used up to 0.6% in foundations and polysilicone-5 was used up to 0.84% in face powders.

For polysilicone-4, concentration of use data were received, but use information was not reported in the VCRP; concentrations of use were reported for 4 makeup product categories and 1 skin care product category. Therefore, it should be presumed that there is at least 1 use in every category for which a concentration of polysilicone-4 is reported.

Polysilicone-2 and polysilicone-5 are reported to be used in products that are applied around the eyes and all ingredients in this report are used in products that come in contact with mucus membranes including lipsticks.

Additionally, polysilicone-2 was reported to be used in cosmetic sprays and could possibly be inhaled; it is reported to be used at up to 0.00095% in perfumes. In practice, 95%-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.^{10,11} 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.^{12,13} Polysilicone-5 was reported to be used in face powders up to 0.84%. 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 established for talc particles and nuisance dusts in the workplace.¹⁴⁻¹⁶

These polymerized tetramethylcyclotetrasiloxanes are not restricted from use in any way under the rules governing cosmetic products in the European Union.¹⁷

TOXICOKINETICS

Absorption, Distribution, Metabolism, and Excretion

Data on the absorption, distribution, metabolism, and excretion of polymerized tetramethylcyclotetrasiloxanes were not found in the published literature and no unpublished data were provided.

TOXICOLOGICAL STUDIES

Acute Toxicity

Data on the acute toxicity of polymerized tetramethylcyclotetrasiloxanes were not found in the published literature and no unpublished data were provided.

Repeated Dose Toxicity

Data on the repeated dose toxicity of polymerized tetramethylcyclotetrasiloxanes were not found in the published literature and no unpublished data were provided.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

Data on reproductive and developmental toxicity of polymerized tetramethylcyclotetrasiloxanes were not found in the published literature and no unpublished data were provided.

GENOTOXICITY

Data on the genotoxicity of polymerized tetramethylcyclotetrasiloxanes were not found in the published literature and no unpublished data were provided.

CARCINOGENICITY

Data on the carcinogenicity of polymerized tetramethylcyclotetrasiloxanes were not found in the published literature and no unpublished data were provided.

IRRITATION AND SENSITIZATION

Data on dermal or ocular irritation of polymerized tetramethylcyclotetrasiloxanes were not found in the published literature and no unpublished data were provided.

Sensitization

Dermal - Human

In a human repeated insult patch test (HRIPT; n=52) of an eye shadow that contained polysilicone-2 coated on yellow iron oxide particles (1.54% after dilution in 70% squalene oil; 0.1-0.15 g), there were no signs of irritation during the induction phase and no signs of sensitization during the challenge phase.¹⁸

SUMMARY

This is a safety assessment of polysilicone-2, polysilicone-4, and polysilicone-5 (i.e., polymerized tetramethylcyclotetrasiloxanes) as used in cosmetics. These ingredients are synthesized from tetramethylcyclotetrasiloxane and have a core chain of repeating -O-Si(R)(CH₃)- moieties. According to the *Dictionary*, these polymerized tetramethylcyclotetrasiloxane ingredients are reported to function as antifoaming agents, hair conditioning agents, and viscosity increasing agents – nonaqueous in cosmetics. The monographs of these ingredients have been amended since the publication of the *Dictionary* and now include surface modifiers in the list of functions. The new monographs also note that these ingredients may be used as a coating agent polymerized *in situ* typically on metal oxides or other materials.

These ingredients are reportedly synthesized from the hydrosilation of vapor-deposited tetramethylcyclotetrasiloxane monomers and result in a network of repeating -O-Si(R)(CH₃)- moieties around the surface of a particle; they are polymerized *in situ* as coatings for metal oxide particles, completely and durably encapsulating the particle in a shell of a polysilicone. However, the data do not reflect the other cosmetic functions of these ingredients as recited by the *Dictionary*; this suggests that these ingredients may be used independently (not coating metal oxides) in cosmetics.

Polysilicone-2-coated metal oxide particles were reported to be hydrophobic and have an estimated molecular weight >100,000 g/mol. The size of the coated particles was reported to be in the range of 0.2- 20 µm.

According to 2015 VCRP data, polysilicone-2 is reported to be used in 209 leave-on formulations and polysilicone-5 is used in 1 makeup fixative. The VCRP has no reported uses for polysilicone-4 even though a maximum concentration of use was reported for polysilicone-4 in the Council survey. According to a 2015 survey conducted by the Council, polysilicone-2 had the highest reported maximum concentration of use, up to 1% in eye shadows and makeup products. Polysilicone-4 was used up to 0.6% in foundations and polysilicone-5 was used up to 0.84% in face powders.

Because the actual forms or use (independent polysilicone polymers, metal oxide particles coated with a polysilicone, or both) of these ingredients was not provided, it is impossible to know which form(s) was reported to the VCRP and the Council's survey. Each reported use may be as an independent polymer, a metal oxide particle coating, or both. It was reported that if the use was to coat the metal oxide particle with polysilicone, the reported concentration of use is for only the polysilicone coating and does not include the encapsulated metal oxide.

In a human repeated insult patch test of an eye shadow that contained polysilicone-2 coated on yellow iron oxide particles (1.54% after dilution in 70% squalene oil; 0.1-0.15 g), there were no signs of irritation during the induction phase and no signs of sensitization during the challenge phase. The polysilicone-2 was coating a yellow iron oxide powder.

There were no further toxicity data for these ingredients discovered in the literature and no other unpublished data were provided.

DISCUSSION

The Panel examined the available data on polymerized tetramethylcyclotetrasiloxanes. The available data on method of manufacture was inconsistent with the definitions and functions of these ingredients as described in the *Dictionary*. Recently amended monographs for these ingredients included “surface modifier” in the functions; the submitted data were consistent with the function of surface modifier on metal oxide particles. However, since the original definitions and functions (e.g., antifoaming agents, hair conditioning agents, and viscosity increasing agents – nonaqueous) have not been amended or removed from the monographs, it is still not clear whether or not these ingredients are used independent of metal oxide particles.

Additionally, it is not clear from the use information available, what form is being described. It is known that if the polysilicone-coated metal oxide form was used, the reported concentration of use is only for the polysilicone coating and does not include the encapsulated metal oxide. Additionally, the Council survey data did not differentiate whether or not the polymerized tetramethylcyclotetrasiloxanes were coating particles or used independently; therefore, use patterns with regards to which form (i.e., particle coating or not) of these ingredients were used, could not be discerned.

There were no repeated dose toxicity, reproductive and developmental toxicity, genotoxicity, or carcinogenicity studies available. Because the reported particle sizes of these ingredients as coated particles are very large and are unlikely to penetrate intact skin, the Panel stated that there should be little or no systemic exposure.

A negative HRIPT of a product containing polysilicone-2-coated on iron oxide particles was the only sensitization study and there were no irritation studies. The Panel was satisfied that these ingredients, as surface modifiers, were not

sensitizers or irritants because of the reported particle sizes of these ingredients when coating particles are very large, the unreactive nature of the polymer coating, and the negative HRIPT study. However, there is no information on the sensitizing or irritation potential of these ingredients when used independently.

Based on the data provided, the Panel concluded that any residual components from the manufacturing process, including allyl glycerol, would be volatized and would not be present in the ingredients. They stressed that Industry should continue to use good manufacturing practices to ensure that impurities are not present in these ingredients.

The Panel discussed the issue of incidental inhalation exposure from perfumes and face powders. There were no inhalation toxicity data available. The particle sizes of these ingredients, as surface modifiers, were reported to be >100,000 Da. The Panel believes that the sizes of a substantial majority of the particles of these ingredients are larger than the respirable range and/or aggregate and agglomerate to form much larger particles in formulation. These ingredients are reportedly used at concentrations up to 0.00095% in products that may be sprayed and aerosolized, and at up to 0.84% in loose-powder cosmetic products that may become airborne. The Panel noted that 95%-99% of droplets/particles from sprays would not be respirable to any appreciable amount. Furthermore, these ingredients are not likely to cause any direct toxic effects in the upper respiratory tract, based on the large size and lack of reactivity of polymerized tetramethylcyclotetrasiloxanes. 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 <http://www.cir-safety.org/cir-findings>.

The Panel concluded that these ingredients are safe when used as surface modifiers. However, the data are not conclusive that these ingredients are only used as coatings on metal oxides and are not used as independent polymers. No data were available on the use of these ingredients in the independent form. Therefore, the Panel concluded that the available data are insufficient to determine that these ingredients are safe to be used as independent polymers or for functions other than surface modifiers. The data needed for all 3 ingredients for all form or functions except for surface modifiers are:

- Chemistry, including average molecular weight and distribution, and method of manufacture
- Repeated dose inhalation
- Absorption/metabolism. If dermally absorbed: reproductive toxicity, 28-day dermal toxicity, and genotoxicity
- Impurity data for all 3 ingredients

CONCLUSION

The CIR Expert Panel concluded that polysilicone-2, polysilicone-4, and polysilicone-5 are safe in cosmetics when used as surface modifiers (i.e. encapsulating metal oxides), and that the available data or information are insufficient to make a determination that these ingredients are safe for their use independently or for other functions as listed in the *Dictionary* (e.g., antifoaming agents, hair conditioning agents, and viscosity increasing agents – nonaqueous).

TABLES

Table 1. Definitions, idealized structures, and functions of the ingredients in this safety assessment.^{1,2} CIR Staff

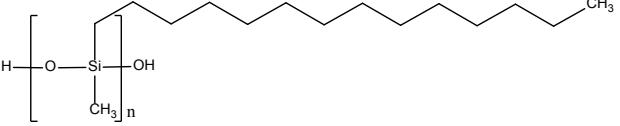
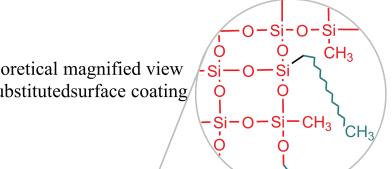
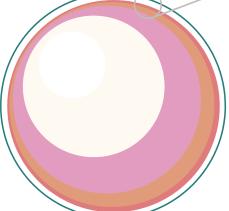
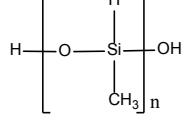
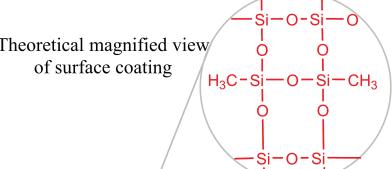
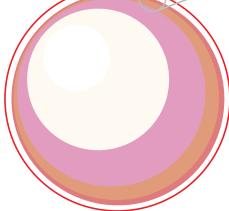
Ingredient CAS No.	Definition & Structures	Function(s)
Polysilicone-2 258521-91-4; 76684-67-8	<p>Polysilicone-2 is the polymer formed by the reaction of tetradecene [(1-tetradecene)] with polymerized tetramethylcyclotetrasiloxane [<i>a.k.a. Polysilicone-4</i>].</p>  <p style="text-align: center;">or</p>  <p>Theoretical magnified view of substituted surface coating</p> 	Antifoaming agent; hair conditioning agent; surface modifier
Polysilicone-4 9004-73-3	<p>Polysilicone-4 is the reaction product of the polymerization of tetramethylcyclotetrasiloxane [in the presence of moisture].</p>  <p style="text-align: center;">or</p>  <p>Theoretical magnified view of surface coating</p>  <p>Polysilicone-4 coated on a particle</p>	Hair conditioning agent; surface modifier; viscosity increasing agent – nonaqueous

Table 1. Definitions, idealized structures, and functions of the ingredients in this safety assessment.^{1,2}, CIR Staff

Ingredient CAS No.	Definition & Structures	Function(s)
Polysilicone-5 848302-17-0	<p>Polysilicone-5 is the reaction product of Polysilicone-4 and glyceryl monoallyl ether [(3-(2-propenyoxy)-1,2-propanediol)].</p> <p>Theoretical magnified view of substituted surface coating</p> <p>Polysilicone-5 coated on a particle</p>	Hair conditioning agent; surface modifier; viscosity increasing agent – nonaqueous

Table 2. Frequency of use according to duration and exposure of polymerized tetramethylcyclotetrasiloxanes.^{8,9}

Use type	Maximum Concentration Uses (%)	Maximum Concentration Uses (%)	Maximum Concentration Uses (%)	Maximum Concentration Uses (%)
	Polysilicone-2	Polysilicone-4	Polysilicone-5	
Total/range	209 0.00005-1	NR 0.0015-0.6	1 0.0015-0.84	
<i>Duration of use</i>				
Leave-on	209 0.00005-1	NR 0.0015-0.6	1 0.0015-0.84	
Rinse-off	NR 0.0003-0.06	NR NR	NR NR	
Diluted for (bath) use	NR NR	NR NR	NR NR	
<i>Exposure type^a</i>				
Eye area	27 0.0003-1	NR NR	NR 0.02-0.33	
Incidental ingestion	96 0.78	NR 0.33	NR 0.68	
Incidental Inhalation-sprays	1 ^b ; 10 ^c 0.00095; 0.00005 ^b	NR NR	NR NR	
Incidental inhalation-powders	2; 10 ^c 1; 0.091-0.94 ^d	NR 0.36; 0.0015 ^d	NR 0.84; 0.0015 ^d	
Dermal contact	107 0.0003-1	NR 0.0015-0.6	1 0.0015-0.84	
Deodorant (underarm)	NR NR	NR NR	NR NR	
Hair-noncoloring	NR 0.00005	NR NR	NR NR	
Hair-coloring	NR 0.06	NR NR	NR NR	
Nail	2 0.062-0.51	NR NR	NR NR	
Mucous Membrane	96 0.78	NR 0.33	NR 0.68	
Baby	NR NR	NR NR	NR NR	

NR = Not Reported; Totals = Rinse-off + Leave-on Product Uses.

Note: Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure type uses may not equal the sum total uses.

^a Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.^b It is possible these products may be sprays, but it is not specified whether the reported uses are sprays.^c Not specified whether a powder or a spray, so this information is captured for both categories of incidental inhalation.^d It is possible these products may be powders, but it is not specified whether the reported uses are powders.

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