Safety Assessment of Polymerized Tetramethylcyclotetrasiloxanes as Used in Cosmetics

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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, Polysilicone-4, and Polysilicone-5 are safe when used to coat metal oxide particles and that the data are insufficient to determine safety if these ingredients are used independently.

INTRODUCTION

This is a safety assessment of Polysilicone-2, Polysilicone-4, And Polysilicone-5 (i.e., polymerized tetramethyl-cyclotetrasiloxanes) 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 tetramethylcyclotetra-siloxane 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 tetramethylcyclotetra-siloxane 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 in 2003 concluded that those ingredients were safe as used in cosmetic products.[4] The Panel also reviewed cyclic-siloxanes and in 2011 concluded that the cyclomethicones were safe as used in cosmetic products.[5] However, these previously reviewed silicone-based ingredients were used independently of particle coating.

CHEMISTRY

Definition, Structure, and Method of Manufacture

The ingredients in this report are synthesized from tetramethylcyclotetrasiloxane upon a metal particle support (Figure 1). Typically, polymerization 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).

Although these ingredients can be depicted 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. Independently, 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.

However, 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 1).[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 an independently polymerized tetramethylcyclosiloxane (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 customary mixture classification (even though the *Dictionary* refers to such encapsulated materials are named as mixtures). Moreover, cosmetic product labels containing these coated particles will recite the name of the polysilicone ingredient and the name of the appropriate metal oxide separately (e.g., Polysilicone-4, Red Iron Oxide,…).

As described above, the manufacture of these coated materials begins with vapor deposition of tetramethylcyclo-tetrasiloxane onto metal oxide particles.[3] The metal oxide used may be any one of the following: Titanium Dioxide, Red

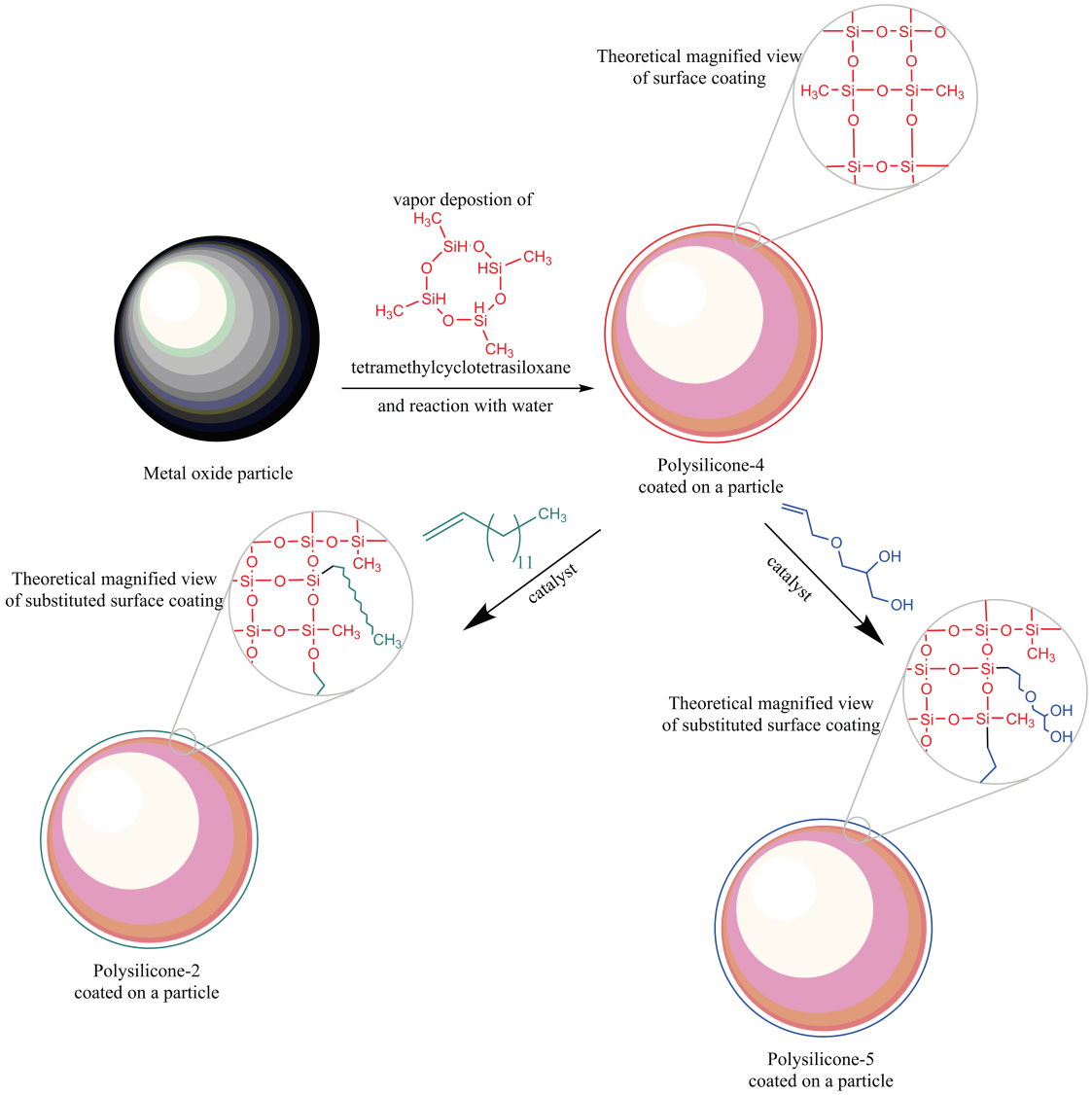


Figure 1. Synthesis of polymer-coated particles.

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. Chemical forms of these ingredients for other functions have not been defined and are not considered further in this report.

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 the surface-bound polymers 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]

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 FDA collects data 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 not known which form(s) was reported to the VCRP. Industry has stated that there are no known uses of these ingredients as anything other than surface modifiers; however, the *Dictionary* still contains other functions (i.e., antifoaming agent, hair conditioning agent, and viscosity increasing agent). The reported uses may be either or both of these. The Council, however, did report that all of their concentration of use data reflect the polysilicone-coated particle form, and that the reported concentration of use is only for the polysilicone coating itself and does not include the encapsulated particle.[7,8]

According to 2016 VCRP data, Polysilicone-2 is reported to be used in 219 leave-on formulations and Polysilicone-5 is used in 1 makeup fixative (Table 2).[9] 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.[7,10] 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.[11,12] 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.[13,14] Polysilicone-2 was reported to be used in face powders up to 1%. 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.[15-17]

These polymerized tetramethylcyclotetrasiloxanes are not restricted from use in any way under the rules governing cosmetic products in the European Union.[18]

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.[19]

SUMMARY

This is a safety assessment of Polysilicone-2, Polysilicone-4, and Polysilicone-5 (i.e., polymerized tetramethyl-cyclotetrasiloxanes) as used in cosmetics. According to the *Dictionary*, these polymerized tetramethylcyclotetra-siloxane 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 tetramethylcyclotetra-siloxane monomers and result in a network of repeating -O-Si(R)(CH_3)- 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 the surface-bound polymers 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 2016 VCRP data, Polysilicone-2 is reported to be used in 219 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 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. Industry has stated that there are no known uses of these ingredients as anything other than surface modifiers; however, the *Dictionary* still contains other functions (i.e., antifoaming agent, hair conditioning agent, and viscosity increasing agent). The reported uses may be either or both of these. The Council, however, did report that all of their concentration of use data reflect the polysilicone-coated particle form, and that the reported concentration of use is only for the polysilicone coating and does not include the encapsulated particle.

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 Oolysilicone-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 these ingredients are used in forms other than coatings for metal oxide particles.

Additionally, it is not clear from the use information available from the VCRP whether forms other than particle coatings were counted. However, it has been clarified that the data in the Council's concentration of use survey of the polymerized tetramethylcyclotetrasiloxanes referred only to particle coatings. It is also known that the reported concentration of use is only for the polysilicone coating and does not include the encapsulated metal oxide. Therefore, use patterns with regards to which form (i.e., particle coating or not) of these ingredients were clear for the concentration of use data but not for the VCRP data.

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, nor could these coatings be liberated should the particles be somehow internalized (e.g., by indidental oral or mucous membrane routes), 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, which also showed no irritation, was the only sensitization study, and there were no other irritation studies. The Panel was satisfied that these ingredients, as surface modifiers, were not sensitizers or irritants because the size of the coated particles are very large, the polymer coating is irreversibly-bound, and the negative result of the 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 eliminated during manufacture, and would not be present in the ingredients when added to formulations. They stressed that Industry should continue to use good manufacturing practices to ensure that impurities are absent in practicality 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 g/mol and the size of the coated particles were reported to be 0.2-20 μm. The Panel believes that the sizes of a substantial majority of the particles of these ingredients are larger than those in the respirable range and/or the particles would 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 1% in loose-powder cosmetic products that may become airborne. The Panel noted that droplets/particles from spray and loose-powder cosmetic products 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 complete insolubility of the coatings or the particles, the irreversibly-bound nature of the polymer coatings, and the 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 in other forms. No data were available on the use of these ingredients in independent forms, if they exist. Therefore, the Panel concluded that the available data are insufficient to determine that these ingredients are safe to be used for functions other than surface modifiers. The data needed for all three ingredients, for all 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 when used to coat metal oxide particles and that the data are insufficient to determine safety if these ingredients are used independently in cosmetics.

TABLES

Table 1. Definitions, idealized structures, and functions of the polymerized tetramethylcyclotetrasioxanes in this safety assessment.[1,2, CIR Staff]

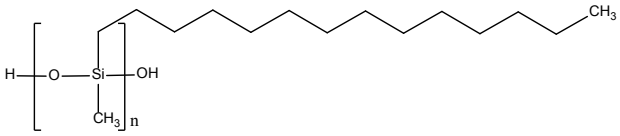
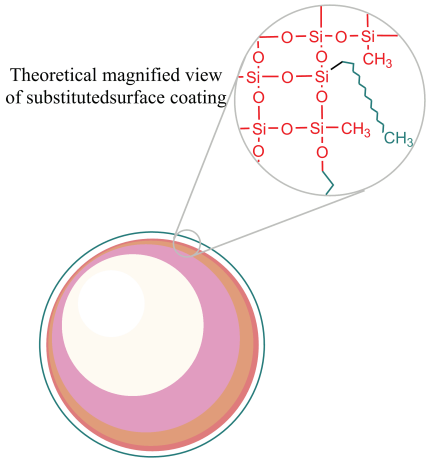
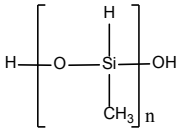
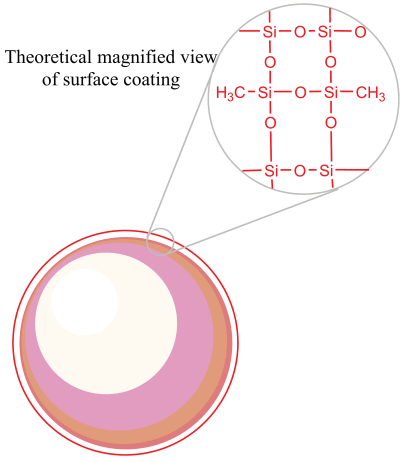
Ingredient CAS No.	Definition & Structures	Function(s)
Polysilicone-2 258521-91-4; 76684-67-8	Polysilicone-2 is the polymer formed by the reaction of tetradecene [(*1-tetradecene*)] with polymerized tetramethylcyclotetrasiloxane [(*a.k.a. Polysilicone-4*)].  or  Theoretical magnified view of substitutedsurface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

Table 1. Definitions, idealized structures, and functions of the polymerized tetramethylcyclotetrasioxanes in this safety assessment.[1,2, CIR Staff]

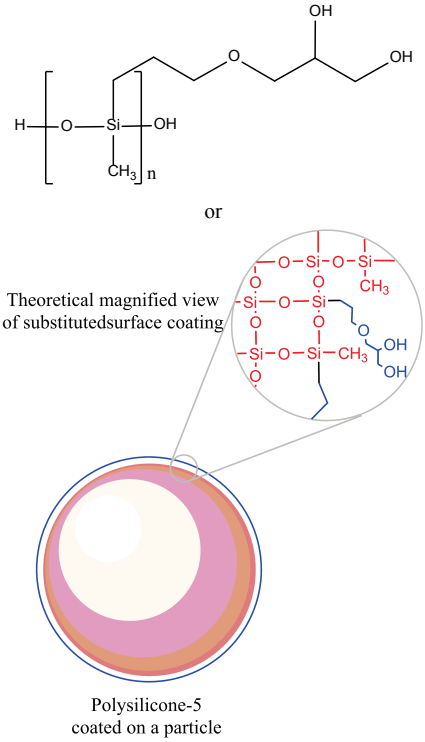
Ingredient CAS No.	Definition & Structures	Function(s)
Polysilicone-5 848302-17-0	Polysilicone-5 is the reaction product of Polysilicone-4 and glyceryl monoallyl ether [(*3-(2-propenyloxy)-1,2-propanediol*)].  	Hair conditioning agent; surface modifier; viscosity increasing agent – nonaqueous

Table 2. Frequency of use according to duration and exposure of polymerized tetramethylcyclotetrasiloxanes.[7,9,10]

Use type	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)
	Polysilicone-2		Polysilicone-4		Polysilicone-5			
Total/range	**219**	**0.00005-1**	**NR**	**0.0015-0.6**	**1**	**0.0015-0.84**		
Duration of use								
Leave-on	219	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		
Exposure type[a]								
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; Total = Rinse-off + Leave-on + Diluted 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.

REFERENCES

1. Nikitakis, J. International Cosmetic Ingredient Dictionary and Handbook. 16 *ed*. Washington, DC: Personal Care Products Council, 2016.

2. Nikitakis J. 12-3-2015. Memorandum on Polysilicone-2, -4, -5. Unpublished data submitted by Personal Care Products Council.

3. Anonymous. 2015. Data for the safety assessment of Polysilicone-2, -4, and -5. Unpublished data submitted by Personal Care Products Council.

4. Andersen, FA. Final report on the safety assessment of stearoxy dimenticone, dimethicone, methicone, amino bispropyl dimethicone, aminopropyl dimethicone, amodimethicone, amodimethicone hydroxystearate, behenoxy dimethicone, C24-28 alkyl methicone, C30-45 alkyl methicone, C30-45 alkyl dimethicone, cetearyl methicone, cetyl dimethicone, dimethoxysilyl ethylenediaminopropyl dimethicone, heyxyl methicone, hydroxypropyldimethicone, stearamidopropyl dimethicone, stearyl dimethicone, stearyl methicone, vinyldimethicone. *International Journal of Toxicology*. 2003;22(Suppl. 2):11-35.

5. Johnson Jr, W, Bergfeld, W, Belsito, D, Hill, R, Klaassen, C, Liebler, D, Marks Jr, J, Shank, R, Slaga, T, Snyder, P, and Andersen, F. Safety assessment of cyclomethicone, cyclotetrasiloxane, cyclopentasiloxane, cyclohexasiloxane, and cycloheptasiloxane. *International Journal of Toxicology*. 2011;30(Suppl. 3):149S-227S.

6. Anonymous. 2015. Certificates of analysis and infrared absorption spectrum of Polysilicone-2 containing ingredients. Unpublished data submitted by Personal Care Products Council.

7. Personal Care Products Council. 2-9-2016. Concentration of Use by FDA Product Category - Polysilicone-2, Polysilicone-4 and Polysilicone-5. Unpublished data submitted by Personal Care Products Council.

8. Anonymous. 2015. Polysilicone-2, -4, and -5 (additional information) with addendum (response to the insufficient data announcement). Unpublished data submitted by Personal Care Products Council.

9. Food and Drug Administration (FDA). Frequency of use of cosmetic ingredients; *FDA Database*. Washington, DC, FDA. 2016.

10. Personal Care Products Council. 3-6-2015. Concentration of Use by FDA Product Category: Polysilicone-2, Polysilicone-4 and Polysilicone-5. Unpublished data submitted by Personal Care Products Council.

11. Rothe H. Special aspects of cosmetic spray safety evaluation. 2011. Unpublished information presented to the 26 September CIR Expert Panel. Washington D.C.

12. Johnsen MA. The Influence of Particle Size. *Spray Technology and Marketing*. 2004;14(11):24-27. cir-safety.org.

13. Bremmer HJ, Prud'homme de Lodder LCH, and van Engelen JGM. Cosmetics Fact Sheet: To assess the risks for the consumer; Updated version for ConsExpo 4. 2006. http://www.rivm.nl/bibliotheek/rapporten/320104001.pdf. Date Accessed 8-24-2011. Report No. RIVM 320104001/2006. pp. 1-77.

14. Rothe H, Fautz R, Gerber E, Neumann L, Rettinger K, Schuh W, and Gronewold C. Special aspects of cosmetic spray safety evaluations: Principles on inhalation risk assessment. *Toxicol Lett*. 8-28-2011;205(2):97-104. PM:21669261.

15. CIR Science and Support Committee of the Personal Care Products Council (CIR SSC). 11-3-2015. Cosmetic Powder Exposure. Unpublished data submitted by the Personal Care Products Council.

16. Aylott RI, Byrne GA, Middleton, J, and Roberts ME. Normal use levels of respirable cosmetic talc: preliminary study. *Int J Cosmet Sci*. 1979;1(3):177-186. PM:19467066.

17. Russell RS, Merz RD, Sherman WT, and Sivertson JN. The determination of respirable particles in talcum powder. *Food Cosmet Toxicol*. 1979;17(2):117-122. PM:478394.

18. European Commission. Cosing database. http://ec.europa.eu/growth/tools-databases/cosing/. European Commission. Last Updated 2015.

19. Anonymous. 2015. Clinical safety evaluation repeated insult patch test of an eye shadow containing Polysilicone-2 (as tested 1.54%). Unpublished data submitted by Personal Care Products Council.