Amended Safety Assessment of Dimethicone, Methicone, and Substituted-Methicone Polymers as Used in Cosmetics

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All interested persons are provided 60 days from the above release date (i.e., March 13, 2021) to comment on this safety assessment and to identify additional published data that should be included or provide unpublished data which can be made public and included.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 All unpublished data submitted to the Cosmetic Ingredient Review (CIR) will be discussed in open meetings, will be available at the CIR office for review by any interested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 Executive Director, Dr. Bart Heldreth.

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ABSTRACT

The Expert Panel for Cosmetic Ingredient Safety (Panel) assessed the safety of 30 dimethicone, methicone, and substituted-methicone polymers; 20 of these ingredients were previously reviewed by the Panel. Most of these ingredients are reported to function as skin and hair conditioning agents. The Panel reviewed relevant new data, including frequency and concentration of use, as well as exposure type, and considered data from the previous report. The Panel concluded that these ingredients are safe in cosmetics in the present practices of use and concentration as described in this safety assessment when formulated to be non-irritating, and that the available data are insufficient to make a determination of safety for use of these ingredients in airbrush cosmetics.

INTRODUCTION

In 2003, the Expert Panel for Cosmetic Ingredient Safety (Panel) published a final report on the safety assessment of 20 dimethicone, methicone, and substituted-methicone polymers.[1] Based on the available data, the Panel concluded that the ingredients named in that report are safe as used in cosmetic products. According to the Cosmetic Ingredient Review (CIR) Procedures, the Panel evaluates the conclusions of previously-issued reports approximately every 15 years. In December 2019, the Panel determined that this safety assessment should be re-opened due to an increase in the overall frequency of use for ingredients in this group. The Panel also determined that it is appropriate to include an additional 10 alkyl dimethicone and methicone ingredients (denoted in red below); the complete family of 30 ingredients comprises:

Amino Bispropyl Dimethicone
Aminopropyl Dimethicone
Amodimethicone
Amodimethicone Hydroxystearate
Behenoxy Dimethicone
C20-24 Alkyl Dimethicone
C20-24 Alkyl Methicone
C24-28 Alkyl Dimethicone
C24-28 Alkyl Methicone
C26-28 Alkyl Dimethicone
C26-28 Alkyl Methicone
C30-45 Alkyl Dimethicone
C30-45 Alkyl Methicone
C30-60 Alkyl Dimethicone
C32 Alkyl Dimethicone
Capryl Dimethicone
Caprylyl Methicone
Cetearyl Methicone
Cetyl Dimethicone
Dimethicone
Dimethoxysilyl Ethylenediaminopropyl Dimethicone
Hexyl Dimethicone
Hexyl Methicone
Hydroxypropyldimethicone
Methicone
Stearamidopropyl Dimethicone
Stearoxy Dimethicone
Stearyl Dimethicone
Stearyl Methicone
Vinyl Dimethicone

According to the web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI; *Dictionary*), the majority of the ingredients included in this assessment are reported to function as skin and/or hair conditioning agents.[2] Additional functions are also reported for some ingredients (Table 1).

Excerpts from the summary of the 2003 report are included throughout the text of this re-review document, as appropriate, and are *identified by italicized text.* (This information is not included in the Summary section.) For complete and detailed information, please refer to the original report on the methicone polymer ingredients, which can be accessed on the CIR website (https://www.cir-safety.org/ingredients).

This safety assessment includes relevant published and unpublished data that are available for each endpoint that is evaluated. Published data are identified by conducting an exhaustive search of the world's literature. A listing of the search engines and websites that are used and the sources that are typically explored, as well as the endpoints that the Panel typically evaluates, is provided on the CIR website (https://www.cir-safety.org/supplementaldoc/preliminary-search-engines-and-websites; https://www.cir-safety.org/supplementaldoc/cir-report-format-outline). Unpublished data are provided by the cosmetics industry, as well as by other interested parties. Much of the data included in this safety assessment was found in an European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC) report, on the European Chemicals Agency (ECHA) website, and in Australian Industrial Chemicals Introduction Scheme (AICIS) assessments.[3-7] Please note that most of the toxicology studies described in these documents were summaries, and it is these summary data that are reported when cited in this safety assessment.

CHEMISTRY

Definition and Structure

The ingredients in this report are all siloxane polymers. Each silicone atom is further substituted with hydrogen, methyl, or other substituents (Figure 1). For Methicone (CAS No. 9004-73-3), most of the silicone atoms in the polymer

backbone each have 1 methyl group and 1 hydrogen atom, while for Dimethicone (CAS No. 9006-65-9), most silicone atoms in the polymer back bone have 2 methyl substituents. The remaining ingredients in this report have 1 or 2 of the substituents on the silicone atoms replaced with an alternative functional group (e.g., Hexyl Methicone (CAS No. 1873-90-1) is substituted with hexyl (C6) chains). The definitions and idealized structures of all the ingredients included in this report are provided in Table 1.

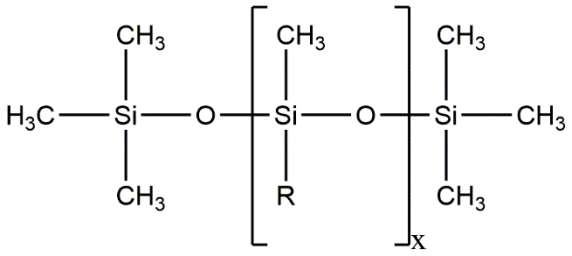


Figure 1. Methicones, wherein R is hydrogen, methyl, or other substituents

The polymerization of linear methicones, however, often results in a mixture of polymers (chains of variable lengths and molecular weights, including oligomers) and cyclic compounds.[8] Dimethicone is a mixture of fully methylated linear siloxane polymers end-blocked with trimethylsiloxy units.[2] Methicone is a linear monomethyl polysiloxane. The other ingredients included in this review are siloxane polymers of Dimethicone and Methicone.

Viscosity is expressed in both dynamic and kinematic measurements, and is directly correlated with molecular weight and the degree of polymerization of a molecule, i.e., the longer the polymer chains, the more viscous the liquid polymer.[3] Most of the viscosities reported in previous and current data have been described in kinematic centistokes (cSt; cm^2/s), and are converted to the standard, dynamic, Pascal*second (Pa·s; kg/m·s), where specific gravity, or relative density, values were available. To do this, the product of centistoke and specific gravity, or relative density, values, was divided by 1000, to attain Pa·s values. Specifically, a median reported relative density value of 950 has been used for the conversion of Dimethicone samples described in the ECETOC report.[3]

Chemical Properties

Dimethicone is a white, almost odorless fluid polymer.[1] Specifications for Dimethicone stated that the color and odor are specified by the buyer. Also specified by the buyer are the refractive index at 25℃ (within the range of 1.4000 to 1.4035), and the kinematic viscosity (provided that the specified mean viscosity at 25℃ is not less than 20 centistokes [cs] and not greater than ± 5% of the specified mean). It contains 98.5% to 101.1% Dimethicone and the total acid number is 0.01 maximum. One supplier of Dimethicone noted that 100 and 350 cs fluids are generally used for cosmetics.

C30-45 Alkyl Dimethicone

C30-45 Alkyl Dimethicone is a an off-white solid, which occurs in small pellets, at standard temperature and pressure.[4] This ingredient has a melting point of 63 - 74 °C and is considered insoluble in water.

Caprylyl Methicone

At atmospheric pressure, Caprylyl Methicone is a liquid at 20 °C, has a melting/freezing point at -20 °C, a boiling point at 263 °C, and a calculated partition coefficient (log P_{ow}) of 9 at 20 °C.[6] This ingredient also has a molecular weight of 335 g/mol, a relative density of 0.84 at 20 °C, a viscosity of 0.0027 kg/m·s at 20 °C, a vapor pressure of 0.64 Pa at 25 °C, and a water solubility of 2.8 x 10^{-5} mg/l.

Hexyl Methicone

At atmospheric pressure, Hexyl Methicone is a liquid at 20 °C, has a melting/freezing point at < -20 °C, a boiling point at 232 °C, and a log P_{ow} > 6.2 at 40 °C.[7] Additionally, Hexyl Methicone has a relative density of 0.83 at 20 °C and a water solubility of 0.011 mg/l at 20 °C.

Method of Manufacture

Stearoxy Dimethicone is produced by the reaction of dichloropolydimethylsiloxane with stearyl alcohol.[1] Dimethicone is produced by polymerization/equilibration. Cetyl Dimethicone is produced by hydrosilylation of C_{16} alpha-olefins. Stearyl Dimethicone is produced by hydrosilylation of C_{18} alpha-olefins.

No additional methods of manufacture data were found in the published literature, and unpublished data were not submitted.

Impurities

One supplier of these ingredients noted that Stearoxy Dimethicone, Dimethicone, Cetyl Dimethicone, and Stearyl Dimethicone contain no antioxidants or preservatives.[1] Heavy metals are at 5 ppm maximum, and D4/D5 cyclomethicone is at less than 1%.

C30-45 Alkyl Dimethicone

The Australian National Industrial Chemicals Notification and Assessment Scheme (NICNAS) noted that C30-45 Alkyl Dimethicone can potentially contain residual monomers which are classified as hazardous according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS)*.[4] As per Australian chemical manufacturing guidelines, however, these are not present above the cut off concentrations for classification.

No additional impurities data were found in the published literature, and unpublished data were not submitted.

USE

Cosmetic

The safety of the cosmetic ingredients addressed in this assessment is evaluated based on data received from the US Food and Drug Administration (FDA) and the cosmetics industry on the expected use of these ingredients in cosmetics. Use frequencies of individual ingredients in cosmetics is collected from manufacturers and reported by cosmetic product category in the FDA Voluntary Cosmetic Registration Program (VCRP) database. Use concentration data are submitted by the cosmetic industry in response to a survey, conducted by the Personal Care Products Council (Council), of maximum reported use concentrations by product category.

Frequency and concentration of use has generally increased for these ingredients since they were originally reviewed, with some of the increases being quite significant. According to VCRP survey data, the frequency of use of Dimethicone has increased from 1659 reported uses in 1998 to 14,050 reported uses in 2020, and the number of uses reported for Methicone increased from 0 reported uses in 1998 to 654 uses reported in 2020 (Table 2).[1,9] Of the ingredients newly added to this report, Caprylyl Methicone has the highest overall frequency of use (234).[9]

Although the overall increase in the reported maximum concentration of use of Dimethicone is not substantial (from 80% to 85%), increases in concentration according to exposure type are notable.[1,10,11] For example, increases in maximum use concentrations of Dimethicone for products resulting in dermal contact increased from 30% in 1999 to 85% in 2019, application to the eye area increased from 13% (in eyebrow pencils) in 1999 to 37.8% (in eyeliners) in 2019, incidental ingestion via lipstick formulations increased from 20% in 1999 to 71.3% in 2019, and incidental inhalation increased from 16% (in perfume sprays) in 1999 to 85% (in moisturizing sprays) in 2019, and from 30% in 1999 to 53% in 2019 for face powders. Caprylyl Methicone has the highest reported maximum concentration of use for the newly added ingredients; it is reported to be used at up to 16% in eye lotions.[12] The 8 ingredients which are not reported to be in use, according to VCRP and survey data, are listed in Table 3.

As mentioned above, some of the ingredients named in this report are used in cosmetic sprays and powders, and could possibly be inhaled. 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.[13,14] 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.[15,16] There is some evidence indicating that deodorant spray products (Dimethicone is reported to be used in spray deodorants at up to 18.6%) can release substantially larger fractions of particulates having aerodynamic equivalent diameters in the range considered to be respirable.[15] 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. Additionally, 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 air.[17-19]

Toxicological simulations have demonstrated the potential for nano-enabled delivery of cosmetic products, such as airbrush makeup, to produce a fraction of particles/agglomerates that are within the respirable range of 1-10 μm.[20] It has come to the attention of the Panel that Dimethicone and Methicone are listed as ingredients being used in consumer products which are applied via aerosolized airbrush devices. However, information regarding this type of use was not reported to the Panel in response to the industry survey, and would not be evident in the VCRP; therefore, details of this type of use (e.g., classification as a cosmetic, drug, device, etc.) are unknown.

The ingredients named in this report are not restricted from use in any way under the rules governing cosmetic products in the European Union.[21]

Non-Cosmetic

Dimethicone

The allowable concentration of use of Dimethicone as an active ingredient in the formulation of skin protectant drug products for over-the-counter human use is 1 - 30%. [21 CFR § 347.10] Dimethicone has been used as a physical barrier method of eradicating head lice and eggs.[22,23] Dimethicone use is also prevalent in condom lubricants.[3,24] Dimethicone is also used industrially, in various construction sealants, rubber, and paints.[3]

In 2008, at the Joint Expert Committee on Food Additives (JECFA) of the World Health Organization (WHO), the established acceptable daily intake (ADI) level for Dimethicone of 0 - 1.5 mg/kg was withdrawn due to variability in safety data, and was temporarily replaced with 0 - 0.8 mg/kg, while concerns about ocular toxicity resulting from molecular weight and viscosity-dependent absorption and toxicity were evaluated.[25] As of 2011, the original ADI of 0 - 1.5 mg/kg was reinstated.[25]

TOXICOKINETIC STUDIES

Penetration

Caprylyl Methicone

The dermal penetration of Caprylyl Methicone is deemed unlikely due to a low water solubility and an estimated log P_{ow} of 9.[6]

Dimethicone

Penetration of Dimethicone (9.5 kg/m·s and 332.5 kg/m·s) was examined in female human abdominal skin and vaginal tissue.[3] Both viscosities were applied in infinite doses for 96 h to the donor side of split-thickness human abdominal skin sections (reference standard) and full-thickness human vaginal tissue mounted in Franz in vitro diffusion cells. (The identification of the vehicle and receptor fluid was not provided.) The dermal flux rate for Dimethicone (332.5 kg/m·s) in abdominal skin was 0.3 ng/cm^2/h, compared to 2 ng/cm^2/h for vaginal tissue; while the flux rates for Dimethicone (9.5 kg/m·s) in abdominal skin were 0.2 ng/cm^2/h and 6 ng/cm^2/h for vaginal tissue. The authors concluded that there was a low penetration rate, which occurred more rapidly in vaginal tissue, for both viscosities.

In a dermal penetration study, the authors sought to determine if Dimethicone interacts with and alters the stratum corneum lipid microstructure.[26] Excised human stratum corneum tissue samples were obtained from the inner thigh of a healthy 50 yr-old woman and the abdomen of a healthy 26 yr-old man. An in vitro model lipid system containing stratum corneum fatty acids was also used to mimic the skin barrier. These tissue samples were rinsed with 0.001% m/m trypsin inhibitor and stored for 48 h in 76% humidity, at ambient temperature, to achieve an approximately 20% hydration level. The hydrated samples were then treated for 20 min in various viscosities of excess Dimethicone (332.5, 475, 950, or 19,000 kg/m·s) at 37 ºC, removed with a cellulose tissue, and analyzed for change using thermal profile, x-ray diffraction, polarized light microscopy, and transmission electron microscopy. All results indicated that Dimethicone did not disturb or interact with the liquid crystalline structure of the upper layer of the epidermis, and hence is not likely to penetrate the skin barrier.

Absorption, Distribution, Metabolism, and Excretion (ADME)

Several acute pharmacokinetic studies in dogs, rats, and a monkey reported minimal gastrointestinal absorption of Dimethicone and up to 99.99% recovery of the administered dose via excretion.[1] In a repeated dose study, beagle dogs were fed 91% Dimethicone at a dose of 300 mg/kg/d for 120 d in the diet. Although one female showed atrophy of the spleen, and another female had slightly reddened rugae near the stomach and mucus in the intestine, Dimethicone was not detected in any organs or considered absorbed.

Animal

Dimethicone

In a study examining dermal absorption and distribution, an occlusive patch containing [^{14}C]Dimethicone (332.5 kg/m·s) was applied to male CD rats (number not provided) for 24 h.[3] After the initial 24-h exposure period, animals were removed from the metabolism cages, the occlusive patch was removed, and the exposure site was washed. The animals were re-wrapped with a non-occlusive bandage and returned to metabolism caging for continued monitoring and collection of biologic samples. The animals were killed 72 h after their initial exposure and the exposure sites were carefully excised. Radioactivity tracing demonstrated that 70% of the administered dose was found on the patch materials, 11.4% was present at the site of application, and none was found in the blood. Minimal amounts were found in the feces (0.01%) and carbon dioxide traps (0.001%).

Human

In human studies, absorption was seen in humans following ingestion of a Dimethicone sample containing low-molecular-weight polymers.[1] Dermal upper back exposure to Dimethicone for 10 d did not increase blood or urine silicone concentrations in men.

Caprylyl Methicone

According to an estimated blood: air partition coefficient of 1.7×10^{-4}:1 for human inhalation, systemic circulation of Caprylyl Methicone is not likely.[6,27] Based on an algorithm,[28] the soluble fraction of Caprylyl Methicone in the blood is << 1%, suggesting the minimal likelihood of this ingredient being excreted in urine as water-soluble metabolites.

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

Dermal

The dermal LD_{50} for Dimethicone was > 2000 mg/kg in rats and rabbits.[1] The dermal LD_{50} for Methicone was > 20 ml/kg in rabbits. The dermal LD_{50} for Vinyldimethicone was > 16 ml/kg in rabbits.

C30-45 Alkyl Dimethicone

An acute dermal exposure study with C30-45 Alkyl Dimethicone was performed, in rats, according to the US Toxic Substances Control Act (US TSCA) [40 CFR § 798.1100] Test Guideline (TG).[4] The LD_{50} in rats was reported to be > 2000 mg/kg bw.[4] (No further details, including viscosity, were provided.)

Caprylyl Methicone

In an acute dermal exposure study, performed in accordance with Organization for Economic Cooperation and Development (OECD) TG 402, undiluted Caprylyl Methicone was tested on 5 male and 5 female Wistar rats at a dose of 2000 mg/kg bw.[6] The test substance was spread over approximately 10% of the back area, and covered with an occlusive dressing for 24 h. Test sites were rinsed with water at the end of the application period; animals were examined daily for 14 d, before necropsy. No mortality or signs of systemic toxicity were observed. The dermal LD_{50} of Caprylyl Methicone was determined to be > 2000 mg/kg bw in rats.

Dimethicone

A single, 2008 mg/kg bw dermal application of Dimethicone (332.5 kg/m·s) was made on 5 male and 5 female Sprague Dawley (SD) rats, in accordance with the OECD TG 402.[3] The test substance was spread over approximately 10% of the total body surface and was held in place with a bandage for 24 h. Test sites were rinsed with lukewarm water at the end of the application period; animals were monitored for mortality and clinical signs for 14 d, before necropsy. No mortality or noticeable abnormalities were observed. The dermal LD_{50} in this study was determined to be > 2008 mg/kg bw.

Undiluted Dimethicone (54,150 kg/m·s) was applied to the shaved backs of 5 male and 5 female adult New Zealand White rabbits at a dose of 2000 mg/kg bw.[3] The test site was occluded and Dimethicone was in contact with the skin for 24 h. After exposure, the residual test material was removed with Dimethicone (332.5 kg/m·s)-moistened gauze. The rabbits were frequently observed on the day of treatment, and at least once a day during a 14-d observation period. No signs of systemic toxicity were observed during the study, and no rabbits died during this study. Under the conditions of this study, the acute LD_{50} of Dimethicone in adult male and female rabbits was considered to be > 2000 mg/kg bw.

Oral

Dimethicone, Methicone, and Vinyldimethicone were not acutely toxic following oral exposure.[1] Methicone had an oral LD_{50} of > 64 ml/kg in male albino rats. Vinyldimethicone had an oral LD_{50} of > 16.0 ml/kg in Sprague Dawley rats. Greasy-textured fur was noted in the rats, while one rat had pneumonia and pleuritis observed at necropsy.

Caprylyl Methicone

In accordance with OECD TG 423, 3 female Wistar rats were administered a single dose of 2000 mg/kg bw Caprylyl Methicone, via gavage.[6] No signs of systemic toxicity were observed over the course of a 14-d post-dose observation period. An expected increase in body weight was observed in all animals, none died prior to necropsy, and no gross pathological changes were observed. The acute oral LD_{50} of Caprylyl Methicone was determined as > 2000 mg/kg bw in female rats.

Dimethicone

Five male and 5 female Sprague-Dawley rats were administered a single dose of 2000 mg/kg bw Dimethicone (57,000 kg/m·s) in corn oil by gavage.[3] No overt signs of systemic toxicity were observed over the course of a 14-d post-dose

observation period. All of the rats gained weights, no animals died during the study, and no gross necropsy lesions were observed. The acute oral LD_{50} of Dimethicone in male and female rats was determined as > 2000 mg/kg bw.

Inhalation

Two dogs, 7 guinea pigs, and 7 rats were exposed to a "200 fluid" aerosol of Dimethicone at a concentration of 2.12 mg/l for 6 h.[1] Three guinea pigs died during the study, and all necropsied animals had hyperemic lungs with hemorrhagic areas. Vapor exposure to Methicone, at a concentration of 0.78 mg/l for 8h, and Vinyldimethicone, at a near-saturation concentration (no further details provided) for 6 h, did not cause mortality or lesions in rats. Aerosolized Hexyl Methicone was administered by whole-body inhalation exposure to Fischer F344/N rats for 4 h, at varied target concentrations ranging from 1.0 mg/l - 5.0 mg/l with particles having a mass median aerodynamic diameter (MMAD) of 0.27µm - 0.29µm. All rats exposed to the 5.0 mg/l concentration (0.27 µm MMAD) died, while a portion died at the other concentrations. Lesions at necropsy of the rats who died included dark red or mottled lungs and/or fluid filled trachea. The calculated LC_{50} for both sexes was 1.8 mg/l.

Dimethicone

An acute aerosol inhalation study of Dimethicone (95,000 kg/m·s)was performed in a similar fashion to OECD TG 403.[3] Groups of 5 Wistar rats were exposed for 4 h, nose-only, to solutions of 25% Dimethicone dissolved in petroleum ether, or to two other solvents in separate control groups (control solvents not named). Rats were exposed to mean Dimethicone concentrations of 4315 mg/m^3 at a MMAD of 1.55 µm, or 11,582 mg/m^3 and a MMAD of 0.846 µm. During, and after, the 14-d observation period, no mortality or clinical symptoms were attributed to Dimethicone exposure. The LC_{50} was determined to be > 11,582 mg/m^3.

Dimethicone (9500 kg/m·s) dissolved in dichloromethane was used to perform an acute aerosol inhalation toxicity study, in accordance with OECD TG 403.[3] Groups of 5 Wistar rats were tested with concentrations of either 153.3, 322.0, 445.6, or 694.8 mg/m^3 Dimethicone, with a MMAD up to 1.8 µm. Duration of exposure was not provided; however, according to OECD TG 403, exposure can be up to 6 h (nose-only) in rats. No mortality or toxic effects were observed during the 14-d observation period or at necropsy. The LC_{50} was determined to be > 695 mg/m^3.

Short Term Toxicity Studies

Dermal

No adverse reactions were found in rabbits following short-term dermal dosing with 6% to 25% Dimethicone.[1] Rats were dermally dosed with either 0.04% Dimethicone (18.92 kg/m·s), or a solution containing 5% each of four linear/cyclic dimethylpolysiloxanes for 4 wk. No macroscopic changes were noted. Changes were seen in serum total cholesterol concentrations, and dermal dosing resulted in less silicon accumulation in the fat when compared to oral administration.

Dimethicone

Three groups of 10 New Zealand white rabbits (number per sex not specified) were dermally administered Dimethicone (332.5 kg/m·s) via an occlusive patch for 4 wk (28 d) at doses of 0, 100, 300, or 1000 mg/kg/d.[3] On a daily basis, rabbits were examined for dermal irritation prior to application, and were exposed to the test material for 6 h prior to patch removal. Body weight was measured twice a week, and blood samples were taken for hematology and blood chemistry evaluations on day 29 for males and day 30 for females. No deaths or adverse events related to the treatment occurred. Body weight, hematology, blood chemistry, and gross and microscopic evaluation of selected organs showed no changes that were considered of toxicological significance. The no-observable-adverse-effect-level (NOAEL) for dermal application of Dimethicone in rabbits in this study was therefore considered to be 1000 mg/kg/d.

Oral

Mongrel dogs were fed with up to 3.0 g/kg/d of 83% Dimethicone for 12 wk.[1] The liver of dosed dogs had bile pigment deposits in Kupfer and hepatic cells, which were proportional to the daily dose received.

Caprylyl Methicone

Seven groups of 10 male and 10 female Crl: WI (Han) rats were dosed with 0, 100, 300, or 1000 mg/kg bw/d Caprylyl Methicone, in corn oil, by gavage, for 28 d.[6] Four recovery groups of 5 male and 5 female rats were selected from the control and 1000 mg/kg bw/d group, to be observed for 14 d after exposure. No mortality or clinical abnormalities occurred during observation. An elongated mean activated partial thromboplastin time in the 1000 mg/kg bw/d males became similar to controls at the end of the recovery period. A statistically significant lower red blood cell count in the 300 mg/kg females, an absent pupillary reflex and white stain on the eye of a 100 mg/kg male, slight vacuolation in the adrenal glands of 1 male each from the 100 mg/kg and 1000 mg/kg groups, and 2 males from the 1000 mg/kg/d recovery group, and a statistically significant minimal increase in the liver weights of 300 and 1000 mg/kg females, were all considered unrelated to treatment or toxicologically irrelevant. The reported NOAEL of Caprylyl Methicone was determined to be > 1000 mg/kg bw/d.

Eight groups of 10 male and 10 female Sprague-Dawley rats were dosed with 0, 500, 1000, or 5000 mg/kg bw/d Caprylyl Methicone, via gavage, for 28 d.[5] Two females treated with 500 mg/kg bw, 1 male and 2 females treated with 1000 mg/ kg bw, and 3 males and 1 female treated with 5000 mg/kg bw died prior to sacrifice. The unscheduled animal deaths were attributed to aspiration of the test substance, and not the test substance itself. Besides dark, mottled, and congested lungs, enlarged livers, and sores, alopecia, and rough, stained fur in the posterior regions of animals in the 5000 mg/kg bw group, no statistically significant differences were observed in the laboratory and clinical findings. Statistically significant lower mean organ and body weights were only observed in 5000 mg/kg bw males and females; organ to brain weight ratios of the treated groups were not significantly different from controls. The NOAEL was determined to be 1000 mg/kg bw/d and the no-observed-effect-level (NOEL) was deemed to be 500 mg/kg bw/d.

Dimethicone

In a 28-d oral toxicity study, Dimethicone (9.5 kg/m·s and 332.5 kg/m·s) was administered to groups of 10 CDF-(F344)-CrlBr rats in the diet, at concentrations of 10,000 to 100,000 ppm (1 - 10%).[3] No mortality or adverse clinical signs of toxicity were noted during observation or upon necropsy. Test article related symptoms consisted of dose-related increase in matting of male and female rat fur, increased incidence of corneal opacity and inflammation, and significantly decreased mean triglycerides and low-density-lipoprotein levels (LDL) at higher doses (≥ 2.5%). These symptoms were not regarded as adverse effects and the NOAEL of Dimethicone in the rat diet was determined to be > 100,000 ppm.

Inhalation

A cat, rabbit, guinea pig, 2 rats, and 4 mice were sprayed for 4 h with an atomizer containing 10 ml/kg of a sample of Dimethicone (140 cm^2/s; dynamic viscosity or specific gravity values were not available) for 29 d.[1] During the 6-wk post-dosing observation period, no exposure-related adverse effects were seen in the cat, rabbit, guinea pig, and rats. All 4 mice died – one after the 20th exposure, and the 3 others during the post-dosing period. The link between treatment and death was uncertain and the authors concluded that Dimethicone inhalation is harmless.

Subchronic Toxicity Studies

Oral

Mice and rats were dosed for 90 d with up to 10% Dimethicone, via diet.[1] No signs of systemic toxicity were seen during the study or during post-study pathologic examination. Anal leakage of Dimethicone was detected in the high dose groups and in those rats that were fed more viscous Dimethicone. Observations of slight chronic corneal inflammation, opacity, and neovascularization was observed in the eyes of the rats, regardless of dosage, and was regarded as a local ocular effect resulting from contact with the feed. In another rat study, in which animals were fed an antifoam compound containing 0.1%, 0.3%, or 1.0% Dimethicone for 120 d, changes in body weight or spleen weight were observed in the 1.0% Dimethicone dose group.

Chronic Toxicity Studies

Oral

No significant differences were observed in the organ weights of Wistar rats that were fed 0.3% Dimethicone in the diet for 2 yr, compared to controls.[1] Upon pathologic examination, pulmonary lesions, changes in the ovaries and uterus, and mild fatty changes in the liver and tubular epithelium of the kidneys was observed in all treated rats. Rats and rabbits which were fed 1% Dimethicone in the diet (50 or 350 cm^2/s; dynamic viscosity or specific gravity values were not available) for up to 1 yr did not exhibit signs of systemic toxicity.

Dimethicone

Four groups of 30 male and 30 female Fischer 344 were administered Dimethicone (9.5 kg/m·s) in the diet at doses of 0 (control), 100, 300, or 1000 mg/kg bw/d for 12 mo.[3,29] Four groups of 10 males and 10 females from each treatment group were necropsied after 12 mo of Dimethicone administration. The remaining animals (20 male and 20 female rats from each group) were observed for chronic recovery for 12 mo after the 12-mo treatment period. Test article-related toxicological effects in necropsied rats were limited to increased incidence of ocular opacities in ≥ 300 mg/kg bw/d females and 1000 mg/kg bw/d males. Similarly, in the chronic recovery group, there was an increase in eye opacity for all treated male groups, without dose correlation. This result was further supported by microscopic findings of keratitis and corneal dystrophy. The NOEL for systemic toxicity of Dimethicone was determined to be equal to the highest tested dose, 1000 mg/kg bw/d.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY (DART) STUDIES

Dimethicone was tested in numerous oral-dose (using rats) and dermal-dose (using rats, rabbits, monkeys) reproductive and developmental toxicity studies.[1] In an oral study with rats, 3.3 ml/kg/d Dimethicone was administered directly to the stomach for 6 d. Males treated with 1 of 3 Dimethicone samples (no further details provided) had significantly decreased body weight and/or decreased testes or seminal vesicles weights. No treatment-related adverse findings were noted in

pregnant females or fetuses, dosed orally, via diet, and dermally. In an intergenerational study, a motor oil containing an unspecified amount of Dimethicone was applied undiluted in doses of 0.1, 0.4, and 1.5 ml/kg, to the shaved backs of the parental (P_1) and first generation (F_1) of Sprague-Dawley rats, daily for an 8-wk premating period, 3-wk mating period, and throughout gestation and lactation. Mortality was significantly increased on day 0 in the 0.4 ml/kg group, and absolute testes weight was significantly reduced in the adult F_1 male rats of the 1.5 ml/kg group, beginning wk 7, but the relative testes to body weight ratio was not significantly different from controls.

Caprylyl Methicone

Six groups of 10 male and 10 female Crl: WI (Han) rats were dosed with 0, 100, 300, or 1000 mg/kg bw/d Caprylyl Methicone, in corn oil, by gavage, for 28 d; 2 groups of 5 male and 5 female rats served as recovery animals from the control and 1000 mg/kg bw/d group.[6] The animals were cohoused to facilitate impregnation, after a minimum of 14 d of exposure, for a maximum time period of 14 d. Fertility and conception parameters were not affected and no maternal abnormalities were observed; no changes or differences in fetal or pup body weights, number of live offspring, sex ratios, litter size, and skeletal, visceral, or external malformations were observed. The NOAEL for Caprylyl Methicone maternal toxicity and developmental effects was determined to be > 1000 mg/kg bw/d.

GENOTOXICITY STUDIES

Dimethicone tested negative for genotoxic effects in multiple Ames tests, at up to 5000 µg/plate, bacterial reverse mutation assays, at up to 79% in formulation, micronucleus tests, at up to 5 g/kg, and in mouse cell and Chinese hamster ovary (CHO) assays, at up to 10,000 µg/ml, both with and without metabolic activation.[1]

In Vitro

C30-45 Alkyl Dimethicone

A bacterial reverse mutation assay was performed with C30-45 Alkyl Dimethicone in accordance with OECD TG 471.[4] The test substance was found to be non-mutagenic. (No further details were provided.)

Caprylyl Methicone

In accordance with OECD TG 471, *Salmonella typhimurium* strains TA97s, TA98, TA100, TA102, and TA 1535 were tested with up to 5 mg/plate Caprylyl Methicone (in ethanol), in a bacterial reverse mutation assay, in the presence and absence of metabolic activation.[6] No precipitates or cytotoxicity were observed and the test substance was determined to be non-mutagenic to bacteria, under these study conditions.

Dimethicone

S. typhimurium strains TA98, TA100, TA1535, TA1537, and *Escherichia coli* strains WP2 uvrA and WP2 uvrA (pKM 101) were tested with Dimethicone (57,000 kg/m·s) in a bacterial reverse mutation assay, in the presence and absence of metabolic activation.[3] The assay was performed in two stages, in which a range-finding study, and consequent initial and independent repeat assays were used to evaluate the mutagenic potential of Dimethicone. Based on the toxicity assay, the maximum dose tested was 5000 µg per plate. Although precipitate was observed at ≥ 500 or at ≥ 1500 µg/plate, no appreciable toxicity was observed; Dimethicone was considered non-mutagenic under these study conditions.

In Vivo

Caprylyl Methicone

Groups of 5 ICR mice were intraperitoneally dosed with 0, 1253, 2505, or 5010 mg/kg bw Caprylyl Methicone, or given 80 mg/kg bw of cyclophosphamide (positive control) via gavage, in a mammalian erythrocyte micronucleus test.[5,6] Bone marrow cells were harvested 24, 48, and 72 h after dose exposure. No significant increase in the micronucleated polychromatic erythrocytes (PCEs) was observed in any of the test animals at all harvest times. Caprylyl Methicone was deemed non- genotoxic under the conditions of this study.

CARCINOGENICITY STUDIES

Dimethicone tested negative for carcinogenicity in both an oral (up to 2.5% Dimethicone in diet for 76 wk) and a dermal carcinogenicity study (lifetime application; 50 µl of the test article (motor oil) that contained an unspecified amount of Dimethicone) using mice.[1] One treated mouse in the dermal study had a palpable skin mass at the application site during wk 65, which regressed by wk 67; no application site dermal neoplasms were microscopically confirmed in either treated or control mice.

Dimethicone

The carcinogenic potential of a silicone resin containing 92% Dimethicone and 8% silica (300-1050 cm^2/s; dynamic viscosity or specific gravity values were not provided (similar to the cosmetic ingredient "Simethicone," the safety of which is assessed elsewhere) was evaluated using groups of 50 male and 50 female F344/DuCrj rats.[30] The rats were given diets containing 0, 1.25, or 5.0% of the test article for 104 wk. Animals were monitored twice daily for signs of toxicity, and body weight was measured alternate weeks. During the study, there were no significant differences in appearance or behavior between the control and treatment groups. Survival rates were also not significantly different between both groups. The relative organ weight percentage for livers in male rats that received 5.0% test article in the diet were significantly lower than those of the livers in male control rats. Lower relative kidney, brain, and heart organ weight percentages were also considered to be statistically significant in treated female rats compared to female control rats. There was a statistically significant, 2 - 18%, increase in the incidence of parafollicular cell (C-cell) adenomas in female rats within the highest dose group (5.0%); however, according to previous carcinogenic assays done by the National Toxicology Program, the naturally occurring incidence of C-cell adenomas ranges from 0 - 34%. The males of the 5.0% dose group experienced a decreased incidence of prostate cancer (8% vs. 22% in controls); however, values for prostatic intraepithelial neoplasias (PINs) were similar across groups. The prostate cancer incidence of the control group was relatively high (compared to historical results elsewhere); thus, the difference between treatment and control groups were considered incidental.

In a long-term toxicity study, 3 groups of 20 male and 20 female F344 rats were observed for oncogenic effects associated with oral administration of Dimethicone (9.5 kg/m·s) at doses of 100, 300, or 1000 mg/kg bw/d for up to 24 mo.[29] Slightly increased incidence of corneal opacity was observed in male rats dosed at 1000 mg/kg bw/d and in female rats dosed at 100 and 1000 mg/kg bw/day, as well as an overall increase in minimal to mild keratitis in all male and female rats (statistical significance not mentioned). A statistically significant increase in the incidence of islet cell adenomas was observed in the 100 mg/kg bw male dose group; however, the lack of an effect in female groups, and high incidence of islet cell adenomas in controls (even when assigned to recover for 12 mo), suggested that that these effects were independent of Dimethicone exposure. No neoplastic changes were observed and the NOEL for oncogenicity of Dimethicone was determined to be 1000 mg/kg bw/d.

OTHER RELEVANT STUDIES

Immunotoxicity

Dimethicone

Four groups of 20 female A.SW (*H-2^s-T18^b-/SnJ*) mice received a single 0.5-ml intraperitoneal (i.p.) injection of one of the following: phosphate-buffered saline (PBS) as the negative control, pristane (2,6,10,14-tetramethylpentadecane) as the positive control, silicone gel (taken from a mammary implant), or Dimethicone (970 kg/m·s).[31] A pretest bleed was taken via orbital puncture prior to injection, after which blood samples were obtained post-injection once a month for 6 mo. The mice were killed after 6 mo of observation, and peritoneal macrophages were collected by lavage. Additionally, immuno-precipitation, fluorescent antinuclear antibody (FANA) microscopy, macrophage culture, kidney pathology, and enzyme-linked immunosorbent assay (ELISA) immunoglobin analyses were performed. Although Dimethicone-treated mice did not produce lupus-associated antinuclear antibodies (observed only in positive controls) various antibody isotopes were observed within 2 mo of injection. Immunoglobulin M (IgM) levels remained elevated compared to controls, and IgG1 and IgE serum levels were significantly elevated at 4 mo in comparison to 5 - 6 mo for the controls. Macrophages from negative control mice secreted little interleukin-6 (IL-6), a pro-inflammatory cytokine, while pristane-, silicone gel-, and Dimethicone-treated mice spontaneously secreted IL-6 and also produced greater, dose-dependent amounts of IL-6 when cultured with lipopolysaccharide. Suspected silicone droplets and expanded vacuoles within the glomeruli of treated mice kidneys also indicated capacity for systemic accumulation.

DERMAL IRRITATION AND SENSITIZATION STUDIES

Irritation

Most dermal irritation studies using rabbits classified Dimethicone as a minimal irritant.[1] Studies that scored reactions according to the Draize scale reported primary irritation indices of ≤ 2.8(with test samples containing 5% to 100% Dimethicone). Vinyl Dimethicone was not irritating to rabbits following a 4-h exposure.

Animal

C30-45 Alkyl Dimethicone

A skin irritation test using C30-45 Alkyl Dimethicone was performed in rabbits, in accordance with US TSCA [40 CFR § 798.4470].[4] The test substance was determined to be non-irritating. (No further details were provided).

Caprylyl Methicone

In a skin irritation test, performed in accordance with OECD TG 404, 0.5 ml Caprylyl Methicone was applied neat for 4 h under semi-occlusion to a 25 cm^2 patch of closely shaven skin of 3 female New Zealand white rabbits.[6] After patch removal, the exposure sites were washed with water and scored using the Draize scale for up to 72 h. No signs of irritation were observed in any of the animals, and the test substance was deemed non-irritating.

In a dermal toxicity study, also performed in accordance with OECD TG 404, 3 male and 3 female New Zealand white rabbits were exposed to an occlusive application of 97%, undiluted Caprylyl Methicone (dose not specified).[5] No deaths or clinical signs were noted during the study period. Minor erythema was observed in 4 rabbits within 1 h following the contact period, but had subsided within 24 h in 3 of the 4 animals and 48 h for the last animal. Minor edema was apparent in 1 animal within 1 h, but subsided by 24 h. Desquamation developed in 1 rabbit after 7 d of testing; no other signs of irritation were observed, and the test substance was deemed slightly irritating to the skin.

Dimethicone

Three rabbits and 3 guinea pigs were exposed to non-occlusive, daily applications of 0.5 ml of Dimethicone (100 cm^2/s; dynamic viscosity or specific gravity values were not provided) to a 2.5 cm^2 patch of closely shaven skin for 10 d.[32] No erythema or signs of skin irritation or inflammation were noted in the animals.

In an acute dermal toxicity study, undiluted, Dimethicone (57,000 kg/m·s) was applied to the shaved backs of 5 male and 5 female adult New Zealand White rabbits, under occlusion, for 24 h, at a dose of 2000 mg/kg bw.[3] Erythema was observed at the application site in all 10 rabbits, but resolved by the 7th day of observation.

Sensitization

Dimethicone (tested undiluted and at 79%) was not a sensitizer in 4 assays using mice and guinea pigs.[1] It was not a sensitizer at 5.0% in a clinical HRIPT using 83 subjects.

Animal

Caprylyl Methicone

The sensitization potential of Caprylyl Methicone was evaluated with a Buehler test, according to OECD TG 406.[6] During induction, 20 male guinea pigs were patched with 100% Caprylyl Methicone (in acetone) once a week, via 6-h occlusive patches, for 3 wk. After a 2-wk rest period, a one-time, challenge application of 0.75% Caprylyl Methicone (in acetone) held in place by an occlusive dressing for a 6-h exposure period was made. Two groups of 10 guinea pigs served as the negative and positive control groups. The test article was not a sensitizer.

In a guinea pig maximization test (number of animals not specified), intradermal injections of Freund's Complete Adjuvant/saline (1:1), with and without 5% Caprylyl Methicone, did not cause ulceration of the injection sites and was well-tolerated.[5] During topical induction, administration sites treated with 5% Caprylyl Methicone showed minor dermal irritation; however, sites treated with 5% Caprylyl Methicone in mineral oil did not show signs of irritation. Challenge applications were made with 5% Caprylyl Methicone in mineral oil, and were observed at 24 and 48 h after patch removal (occlusion not specified). No dermal reactions were seen in either the test or control groups at 48 h, and the test substance was deemed a non-sensitizer.

Dimethicone

Five groups of 8 female B6C3F1 mice were tested for contact hypersensitivity to Dimethicone.[33] Dimethicone was determined to be a non-irritant during a primary dermal irritancy study, and was applied undiluted during both the induction and challenge phases. Eight induction applications of either saline, Dimethicone (dose not specified), acetone/olive oil, or 0.5% 1-fluoro-2,4-dinitrobenzene, in acetone: olive oil, were made to a 0.5 cm^2 shaved and debrided region of the upper back. After a 6-d rest period, mice were injected with 0.2 ml of 125-iododeoxyuridine to measure radioisotopic hypersensitivity. Challenge applications were made 7 d after the rest period to the left ear using a cotton swab, and mice were examined for contact hypersensitivity via the mouse ear swelling test (MEST) for 2 d. All mice, except for 8 treated with Dimethicone, were killed after the first MEST; after 7 d, the surviving mice, and an additional 8 mice were tested in a second MEST. No statistically significant hypersensitivity was observed in the mice sensitized with Dimethicone, from the radioisotopic or MEST measurements. Subsequent challenge of previously sensitized mice also did not produce any change in the occurrence of ear swelling, and the test substance was determined a non-sensitizer.

Human

Dimethicone

In a human repeat insult patch test (HRIPT), Dimethicone (11,875 kg/m·s) was tested neat as a negative control, and was used as a vehicle for a 5% (v/v) solution of an unspecified test substance.[3] Sodium lauryl sulfate (0.1% aqueous

solution) was used as a positive control. Of the 115 subjects enrolled, 106 completed the study; no subjects withdrew due to adverse reactions to the test substance. Induction consisted of 9 consecutive applications, where 0.2 ml of Dimethicone was applied under a semi-occlusive dressing for 24 h. The test sites were evaluated in the following 48 - 72 h. After the 9th application, there was a 10 to 15-d non-treatment period. Challenge occurred in the sixth week of the study; the substance was applied to an unexposed site for 24 h, and graded after 24 - 48 h. No evidence of sensitization to Dimethicone, as a control or vehicle, was observed.

OCULAR IRRITATION STUDIES

Most ocular irritation studies using rabbits classified Dimethicone, ranging in concentration from 10% to 35%, as a mild to minimal irritant.[1] The most common finding was a conjunctival reaction. However, instillation of 0.005 ml 15% Dimethicone produced minor to moderate conjunctival irritation in all 6 rabbits; the irritation cleared in 5 of the 6 rabbits within 72 h. Additionally, a few studies reported conjunctival reactions, chemosis, and persisting redness, especially when the eyes were unrinsed. Similar to Dimethicone, Methicone and Vinyldimethicone also produced conjunctival reactions.

C30-45 Alkyl Dimethicone

The ocular irritancy potential of C30-45 Alkyl Dimethicone was tested in rabbits, in accordance to US TSCA [40 CFR § 798.4500].[4] Slight conjunctival effects were observed, but resolved within 24 h of exposure. The test substance was determined to be non-irritating. (No further details were provided).

Caprylyl Methicone

In an ocular irritation study, performed in accordance with OECD TG 405, 3 female New Zealand white rabbits were treated with 0.1 ml Caprylyl Methicone in one eye for 24 h (the second eye serving as control).[6] The treated eyes were thoroughly washed with saline after 24 h, and were examined at 1, 24, 48, and 72 h post-application. A 0.01% fluorescein-sodium solution was used to examine the treated eyes for corneal lesions at 24 and 72 h. Dilated blood vessels were observed in 2 of the 3 animals, as well as colorless eye discharge with moistening of the lids 1 h after instillation. All signs of irritation disappeared within 24 h of treatment, and the test substance was deemed not irritating to the eye.

In a similar study, also performed in accordance with OECD TG 405 (dose not specified), 3 male and 3 female New Zealand white rabbits did not exhibit corneal injury or iritis.[5] Minor conjunctival redness and minor (in 5 animals) to moderate (in 1 animal) ocular discharge occurred in all rabbits. Ocular irritation subsided within 24 h in 5 animals, and 48 h in the last animal. The test substance was deemed slightly irritating to the eye.

Dimethicone

Sixteen adult pigmented rabbits were tested for corneal tolerance of Dimethicone.[34] One eye of each animal was treated (the other eye served as a control) by forming a hanging suture in the lid which allowed 0.7 - 1.0 ml of generically produced, as well as medical-grade, Dimethicone at varying viscosities (485 - 12,125 kg/m·s) to remain on the eye for 3 - 6 h. Medical-grade Dimethicone (970 kg/m·s), which is produced with higher manufacturing, biocompatibility, and safety standards for use in pharmaceuticals and medical devices, was included to assess if it would elicit a variable eye irritation response. The oil was only replaced if the eye cup leaked or if the animal moved. The eyes were examined with fluorescein by slit lamp immediately after treatment, and were either enucleated immediately or 3 - 7 d later. Compared to the control eye, which was treated with a saline balanced salt solution, the eyes treated with Dimethicone exhibited increased epithelial and whole corneal thickness, which persisted for several days and was most noticeable ≥ 3 d post-treatment. Although there appeared to be better ocular tolerance for the medical-grade Dimethicone, it also caused some corneal changes; under light microscopy, all eyes treated with Dimethicone showed various degrees of intracellular epithelial and stromal edema. The authors concluded that both non-medical grade and medical-grade Dimethicone are mildly irritating to the corneal epithelium.

The ocular irritancy of Dimethicone was evaluated in a study using groups of either 3 mice, 3 guinea pigs, or 3 rabbits to test 5 separately-manufactured samples of Dimethicone (100 cm^2/s; dynamic viscosity or specific gravity values unavailable).[32] For the test, a drop of Dimethicone was instilled once daily for 10 d into the lower eyelid of the animals, and conjunctival irritancy and reflex response to light and touch were observed for 15 d. The first sample did not produce inflammation or ocular opacity; however, all tested guinea pigs died by day 8 - 10. The second sample caused inflammation in the eye of one rabbit after 10 d, while 2 guinea pigs and 1 rabbit died. The eyes of animals treated with the second sample were also opaque. No adverse effects were observed in the eyes of the rabbits or guinea pigs treated with 3 remaining samples; the researchers opined that the ocular irritancy and inflammatory effects of silicone fluids may be dependent upon the acidity of the samples.

MUCOUS MEMBRANE IRRITATION STUDIES

A mucoadhesive paste (53% Dimethicone) was introduced (0.5 g) via syringe into the vaginal cavity of 6 albino rabbits.[1] Two control rabbits were dosed with a sodium chloride solution. Tissue was scored according to the Draize scale

(maximum score of 8) at 24, 48, and 72 h post dosing. Erythema was noted in 3 rabbits at 24 h, and in one rabbit at 48 h after treatment. None had erythema at 72 h. No edema or signs of toxicity were observed. The irritation score for the paste was 0.22.

Dimethicone

Five samples of Dimethicone (100 cm^2/s; dynamic viscosity or specific gravity values unavailable), each not requiring more than 0.1 ml of 0.05 N alcoholic KOH to neutralize 15 g of the fluid, were tested for irritation of vaginal mucosa.[32] A sample of 0.05 ml of Dimethicone was instilled into the vagina of rats (number of animals not specified) daily for 8 d, the vaginal mucous membrane was observed to determine irritancy, and the effect on leukocyte count was determined. A 77.8 - 88% increase in leukocytes was observed in the vaginal smears of rats treated with two samples of Dimethicone. A similar increase was observed for rats instilled with formaldehyde as the reference irritant. Leukocyte increases in the rats treated with the 3 remaining samples was markedly lower. The authors concluded that 2 of the silicone samples with a higher acidity (0.17) and acid value of 0.3 were more likely to be mucous membrane irritants than the other 3 samples, in which the increase of leukocytes was relatively low (0.05 - 0.10 acidity; acid values were not provided).

CLINICAL STUDIES

Case Reports

Dimethicone

A 23-d old, premature twin male infant suffering with nasal congestion was accidentally sprayed intranasally with diaper rash protectant spray (instead of nasal saline spray), which listed 10% Dimethicone as the only active ingredient.[35] The child went into a choking and coughing spell, and was rushed to the emergency department. After 2 h, he was still in respiratory distress, wherein his oxygen saturation had dropped to 85% and his chest x-ray showed diffuse bilateral infiltrates, suggestive of bilateral chemical pneumonitis. By the 3rd day, he developed an eosinophilia of 31 - 37%, with an absolute eosinophilic count of 3100 - 4250 per µl. He was treated with frequent saline bronchial lavages and chest physical therapy to remove mucus plugs blocking his endotracheal tube and was weaned off the ventilator by the 7th day after exposure. Referring to the Expert Panel evaluation that Dimethicone is safe for cosmetic use and when inhaled short term,[1] the researchers were of the opinion that Dimethicone did not cause the patient's symptoms. They found that the inactive ingredients of the product were aloe oil extract, caprylic/capric triglyceride, mineral oil, Peruvian balsam oil, shea liquid, and tocopheryl acetate/vitamin E. The authors concluded that the massive dose of mineral oil exposure was the most likely cause for acute pneumonitis, as was the Peruvian balsam oil for eosinophilia.

SUMMARY

According to the *Dictionary*, these 30 methicone ingredients are reported to function in cosmetics as skin conditioning agents, hair conditioning agents, and/or viscosity increasing agents. Of the ingredients in this report, Dimethicone and Methicone have the greatest frequency of use, according to 2020 VCRP data. Reported use for Dimethicone increased from use in 1659 formulations in 1998 to 14,050 in 2020, and reported frequency of use of Methicone increased from no reported uses in 1998 to use in 654 formulations in 2020. The highest concentration of use reported in 2019 was for Dimethicone, at a concentration of 85% in moisturizing products; the maximum concentration of use reported previously for Dimethicone was 80%. Although the overall maximum concentration of use did not increase notably, the maximum concentration of use for several exposure categories did.

Penetration of Dimethicone (9.5 kg/m·s and 332.5 kg/m·s) in human abdominal and vaginal tissue was examined after a 96-h application. A low penetration rate was observed for both viscosities, with more rapid penetration in vaginal tissue. Based on an estimated, low blood: air partition coefficient and an algorithm, the soluble fraction of Caprylyl Methicone is << 1% in the blood, minimizing the possibility of systemic circulation. In a dermal penetration study, the interaction of Dimethicone with the stratum corneum lipid microstructure in healthy excised human tissue was evaluated. All results indicated that Dimethicone did not disturb or interact with the upper layer of epidermis, and is not likely to penetrate the skin barrier. Male rats were exposed to both occlusive and non-occlusive patches of [^{14}C]Dimethicone to observe dermal absorption and excretion over 3 days. Radioactivity tracing demonstrated that 70% of the applied dose remained on the patches, 11.4% of the applied dose was at the site of application, and minimal amounts were found in feces and carbon dioxide traps.

The acute dermal LD_{50} of C30-45 Alkyl Dimethicone was determined to be > 2000 mg/kg bw in rats. In two separate acute dermal studies, undiluted Caprylyl Methicone and Dimethicone (54,150 kg/m·s) were applied, under occlusion, to the shaved backs of 10 Wistar rats and 10 New Zealand white rabbits, respectively, at doses of 2000 mg/kg bw for 24 h. No mortality and signs of toxicity were observed in either study and the acute dermal LD_{50} for each ingredient was determined to be > 2000 mg/kg bw in rats and rabbits, respectively. A single, 2008 mg/kg bw dermal application of Dimethicone did not cause mortality or noticeable abnormalities in 5 male and 5 female Sprague-Dawley rats; under these study conditions the

acute dermal LD_{50} was determined to be > 2008 mg/kg bw. Three groups of 10 New Zealand white rabbits were exposed to an occlusive patch of Dimethicone (332.5 kg/m·s) for 28 d at doses up to 1000 mg/kg/d. No deaths or adverse events related to the exposure occurred, and the NOAEL for dermal application in rabbits was determined to be 1000 mg/kg/d.

Three female Wistar rats were administered a single dose of 2000 mg/kg bw Capryl Methicone, via gavage; no mortality or signs of systemic toxicity were observed, and the acute LD_{50} was determined to be > 2000 mg/kg bw. Five male and female Sprague-Dawley rats were administered a single oral dose of 2000 mg/kg bw Dimethicone in corn oil. No toxic effects or gross necropsy lesions were observed, and the acute LD_{50} was determined to be > 2000 mg/kg bw in rats. Caprylyl Methicone was administered in corn oil, via gavage, at doses of 0, 100, 300, or 1000 mg/kg bw/d to groups of 10 male and 10 female Han rats for 28 d. No mortality or clinical abnormalities occurred during observation; statistically significant lower blood cell count in the 300 mg/kg females, slight vacuolation in the adrenal glands of males in the main study, and recovery group, dosed with 1000 mg/kg/d, and minimal increases of the liver weights of females in the 300 and 1000 mg/kg groups, were all considered toxicologically irrelevant. The NOAEL of Caprylyl Methicone was determined to be > 1000 mg/kg bw/d. In another 28-d oral toxicity study of Caprylyl Methicone, groups of 10 male and 10 female Sprague-Dawley rats were orally dosed with 0, 500, 1000, or 5000 mg/kg bw/d, via gavage. Deaths of 2 females in the 500 mg/kg group, 1 male and 2 females in the 1000 mg/kg group, and 3 males and 1 female in the 5000 mg/kg group were attributed to aspiration of the test substance. Congested lungs, enlarged livers, and lower mean organ and body weights in the 5000 mg/kg group were statistically significant, and the NOAEL was determined to be 1000 mg/kg bw/d, while the NOEL was determined to be 500 mg/kg bw/d. In a 28-d oral toxicity study, Dimethicone was administered at up to 10% (100,000 ppm) in the diet of CDF-(F344)-CrlBr rats. Test article related symptoms included matted fur, increased incidence of corneal opacity, and significantly decreased mean triglycerides and LDL levels at higher doses. These symptoms were not considered adverse effects and the NOAEL of Dimethicone was determined > 100,000 ppm. Four groups of 30 male and 30 female Fischer 344 rats were orally administered Dimethicone (9.5 kg/m·s), in their diet, at doses up to 1000 mg/kg bw/d for 12 mo. Amongst the treated rats, four groups of 10 male and 10 female rats were necropsied after 12 mo, while a remaining 20 male and 20 female rats per group were observed for recovery for 12 mo after the treatment period. In both necropsied and recovery groups there was an increase in ocular opacity, and the NOEL for systemic toxicity was determined to be 1000 mg/kg bw/d.

Groups of 5 Wistar rats were exposed for 4 h, nose-only, to solutions of 25% Dimethicone (95,000 kg/m·s) dissolved in petroleum ether, or to two other solvents in separate control groups (control solvents not named). No mortality or clinical symptoms were attributed to Dimethicone exposure, and the LC_{50} was determined to be > 11,582 mg/m^3. Dimethicone (9500 kg/m·s) dissolved in dichloromethane was tested for acute inhalation toxicity, at doses up to 694.8 mg/m^3, in Wistar rats. No mortality or toxic effects were observed, and the LC_{50} was determined to be > 695 mg/m^3.

In a reproductive and developmental toxicity study, 6 groups of 10 male and 10 female Han rats were orally dosed with 0, 100, 300, or 1000 mg/kg bw/d Caprylyl Methicone, in corn oil, via gavage for 28 d. Fertility, maternal, birth, and fetal outcomes were not adversely affected; the NOAEL for Caprylyl Methicone was determined to be > 1000 mg/kg bw/d.

Bacterial reverse mutation assays were performed with C30-45 Alkyl Dimethicone and Caprylyl Methicone; the test substances were not found to be non-mutagenic. In a bacterial reverse mutation assay, *S. typhimurium* tester strains TA98, TA100, TA153, TA1537, and *E. coli* strains WP2 uvrA and WP2 uvrA (pKM 101) were tested with Dimethicone (57,000 kg/m·s), at a maximum dose of 5000 µg per plate, in the presence and absence of metabolic activation. Although precipitate was observed at ≥ 500 or ≥ 1500 µg per plate, Dimethicone was considered non-mutagenic under these study conditions. In vivo, Caprylyl Methicone was intravenously administered at up to 5010 mg/kg bw to groups of 5 ICR mice in a micronucleus test; no significant increases in PCEs were observed and the test substance was deemed non-genotoxic.

The carcinogenic potential of a silicone resin containing Dimethicone and silica was evaluated by feeding 50 male and 50 female F344/DuCrj rats diets containing up to 5.0% of the test article for 104 wk. There was a statistically significant, 2 - 18% increase in the incidence of C-cell adenomas in female rats in the highest dose group, while the male rats in the highest dose group experienced a decreased incidence of prostate cancer compared to the control group. The incidence of prostate cancer in the control group was relatively high, and thus the difference between treatment and control groups was considered incidental.

Three groups of 20 male and 20 female F344 rats were observed for oncogenic effects upon oral administration of Dimethicone (10 cm^2/s; dynamic viscosity or specific gravity unavailable) at doses of 100, 300, or 1000 mg/kg bw/d for up to 24 mo. Slightly increased incidence of corneal opacity was observed at the maximum dose, as well as a statistically significant increase in islet adenomas among males in the 100 mg/kg bw group. However, the lack of increased islet adenomas in female rats and the high incidence amongst control rats suggested that these effects were independent of Dimethicone exposure. The NOEL for oncogenicity of Dimethicone was determined to be 1000 mg/kg bw/d.

Twenty female A.SW mice received a single 0.5-ml i.p. injection of Dimethicone, while 3 groups of 20 mice were injected with either saline, pristane or silicone gel, to evaluate immunological reactions over 6 mo. Dimethicone-treated mice produced various antibody isotopes within 2 mo of injection, spontaneously secreted and produced greater, dose-dependent

amounts of IL-6, and showed silicone droplets and expanded vacuoles within kidney glomeruli, indicating the possibility for systemic accumulation.

A skin irritation test using C30-45 Alkyl Dimethicone (test concentration not specified) was performed in rabbits; the test substance was determined to be non-irritating. Two studies evaluating the dermal irritation potential of a neat, 4-h, occlusive application of Caprylyl Methicone to New Zealand white rabbits were performed; the test substance was deemed non-irritating at a dose of 0.5 ml, while it was deemed slightly irritating at an unspecified dose of 97%, undiluted Caprylyl Methicone. Dimethicone did not cause dermal irritation or inflammation in rabbits and guinea pigs. Caprylyl Methicone was determined to be a non-sensitizer in guinea pigs. Dimethicone did not cause sensitization or irritation in a contact sensitization study of female mice. In an HRIPT, Dimethicone was tested neat (as a negative control), and as used as a vehicle for a 5% solution of an unspecified test substance, in 106 subjects. No evidence of sensitization to Dimethicone, as a control or vehicle, was observed.

The ocular irritancy potential of C30-45 Alkyl Dimethicone was tested in rabbits; slight conjunctivae were observed, but resolved in within 24 h of exposure, and the test substance was deemed non-irritating. Caprylyl Methicone (0.1 ml) was not deemed irritating to rabbit eyes; an unspecified dose of Caprylyl Methicone was considered slightly irritating to rabbit eyes in another study. Sixteen rabbits were exposed for to up to 6 h with 0.7 - 1.0 ml of generic or medical-grade Dimethicone, in one eye, to test for variance in ocular irritancy. All eyes treated with either generic or medical-grade Dimethicone evidenced mild irritation corneal epithelium. In a study using groups of 3 mice, guinea pigs, or rabbits, 5 separately manufactured samples of Dimethicone (100 cm^2/s; dynamic viscosity or specific gravity values unavailable) were instilled into the lower eyelid of the animals once daily for 10 d. All guinea pigs exposed to the first sample died by days 8 - 10, and the second sample caused corneal inflammation in one rabbit after 10 d, and death in another rabbit and 2 guinea pigs. No adverse effects were observed with exposure to the 3 remaining samples. Both Dimethicone samples with positive results had a slightly more acidic profile, suggesting that the ocular irritancy and inflammatory effects of silicone fluids may be acidity-dependent.

The potential for five samples 0.5 ml of Dimethicone (100 cm^2/s; dynamic viscosity or specific gravity values unavailable) to cause vaginal mucosa irritation was tested in rats for 8 d. An ~88% increase in leukocytes was observed in the vaginal smears of rats treated with two Dimethicone samples. A similar increase was observed in rats treated with formaldehyde. The leukocyte increase in the rats treated with the 3 remaining Dimethicone samples was markedly lower. Irritation outcomes for each Dimethicone sample were deemed to be affected by higher acidity and acid values.

A 23-d old, premature twin male infant experienced severe respiratory distress, acute pneumonitis, and eosinophilia as a result of intranasal exposure to a 10% Dimethicone spray. Although Dimethicone was listed as the active ingredient, mineral oil and Peruvian balsam oil were considered to be causative agents for the severe reaction.

DISCUSSION

In accordance with the CIR Procedures & Support to the Expert Panel for Cosmetic Ingredient Safety, the Panel evaluates the conclusions of previously-issued reports approximately every 15 years. In 2003, the Panel published a final report on the safety assessment of 20 dimethicone, methicone, and substituted-methicone polymers, and concluded that the ingredients named in that report were safe as used in cosmetic products. Due to dramatic increases in frequency of use, and increases in concentrations of use for certain exposure types, especially for Dimethicone in products that could result in incidental inhalation, the Panel reopened this safety assessment. In addition to the ingredients previously reviewed, the Panel Clustering and Read-Across Working Group considered related polymers for inclusion in this report; the Working Group determined it was appropriate to include 10 additional polymers that have not yet been reviewed, due to chemical similarity and similarity of use.

The Panel noted that Dimethicone is now reported to be used at 85% in moisturizing spray formulations; in the original assessment, the greatest reported maximum use concentration in spray products was 16% in perfumes. Additionally, the Panel noted that some of these polymers are used in powders, which could also possibly be inhaled. Nevertheless, the Panel found that the absence of exposure-related effects from a study reported in the original assessment, in which several species of animals were sprayed with an atomizer containing 10 ml/kg Dimethicone for 29 d, mitigated concern for use of these ingredients in cosmetic products that could be incidentally inhaled. Also, 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 ingredient is 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.

The Panel was made aware, through alternative sources, that Dimethicone and Methicone are used in consumer products which are applied via aerosolized airbrush devices. The Panel considered information suggesting that a fraction of airborne particles resulting from airbrush delivery are respirable (i.e., aerodynamic equivalent diameter < 10 μm), according to one toxicological simulation study. However, the Panel noted a lack of information on aerosol particle size distributions when these ingredients are used with cosmetic airbrush devices. In addition, the Panel noted particle characteristics such as size, morphology, and surface chemistry are unique to each aerosol and can affect their deposition in the respiratory tract and their interactions with biological organisms. Therefore, the Panel considered the available data are insufficient to determine safety for ingredients in products delivered via airbrush technology. Consequently, the additional data needed to determine safety for use in airbrush cosmetics are:

- particle size distribution, present concentrations of use, and if the particles are considered of respirable size, respiratory toxicity data
- information on methods of use, including exposure duration and frequency (e.g., daily, brief foundation application, compared to periodic, but longer suntan spray exposure).

Furthermore, the Panel noted that Dimethicone is now being used at, or above, concentrations at which ocular irritation was observed in studies cited in the original assessment. Subsequently, the Panel distinguished the difference between instilling 35% Dimethicone in the eye, as described in an animal ocular irritation study from the original report, compared to using a cosmetic product containing 37.8% Dimethicone, in which ocular contact is not intended. However, the Panel stated that manufacturers should be cognizant of incidental/accidental exposure to the eye, and specified that products containing the ingredients included in this report should be formulated to be non-irritating to the eye. Additionally, the Panel discussed the validity of results from an ocular irritation study included in the present assessment, in which test animals died following instillation of 100% Dimethicone (970 kg/m·s) in the eye for 10 d. The Panel remarked that mortality occurring during an ocular irritation study is very unusual, and toxicologically implausible.

The Panel was also concerned that the potential exists for dermal irritation with the use of products formulated using dimethicone, methicone, and substituted-methicone polymers. The Panel specified that products containing these ingredients should be formulated to be non-irritating.

CONCLUSION

The Expert Panel for Cosmetic Ingredient Safety concluded that the following 30 dimethicone, methicone, and substituted-methicone polymers are safe in cosmetics in the present practices of use and concentration described in this safety assessment when formulated to be non-irritating, and that the available data are insufficient to make a determination of safety for the use of these ingredients in airbrush cosmetics.

Amino Bispropyl Dimethicone
Aminopropyl Dimethicone
Amodimethicone
Amodimethicone Hydroxystearate*
Behenoxy Dimethicone
C20-24 Alkyl Dimethicone
C20-24 Alkyl Methicone*
C24-28 Alkyl Dimethicone*
C24-28 Alkyl Methicone
C26-28 Alkyl Dimethicone
C26-28 Alkyl Methicone*
C30-45 Alkyl Dimethicone
C30-45 Alkyl Methicone
C30-60 Alkyl Dimethicone
C32 Alkyl Dimethicone*
Capryl Dimethicone
Caprylyl Methicone
Cetearyl Methicone
Cetyl Dimethicone
Dimethicone
Dimethoxysilyl Ethylenediaminopropyl Dimethicone
Hexyl Dimethicone
Hexyl Methicone*
Hydroxypropyldimethicone*
Methicone
Stearamidopropyl Dimethicone*
Stearoxy Dimethicone
Stearyl Dimethicone
Stearyl Methicone
Vinyl Dimethicone

**Not reported to be in current use. Were ingredients in this group not in current use to be used in the future, the expectation is that they would be used in product categories and at concentrations comparable to others in this group.*

TABLES

Table 1. Definitions, idealized structures, and functions

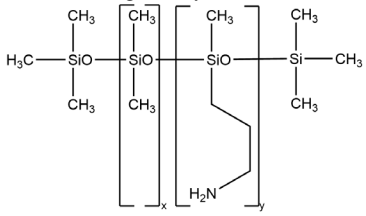
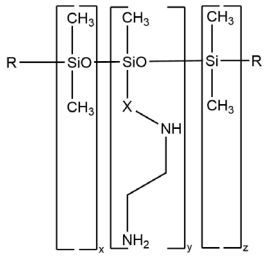
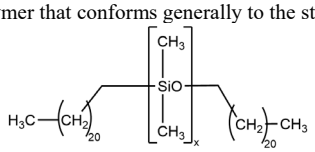
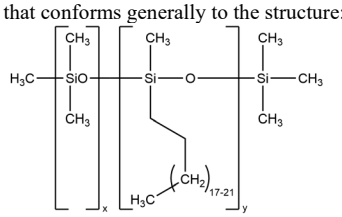
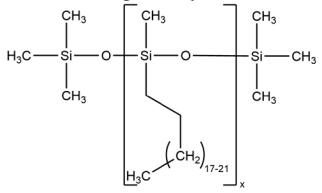
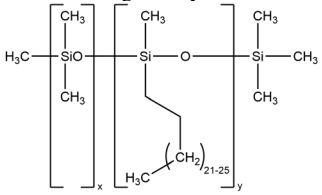
Name & CAS No.	Definition & Structure	Function(s)
Amino Bispropyl Dimethicone 189959-16-8	a complex three-dimensional siloxane polymer formed by the reaction between dimethiconol and 3-(trimethoxysilyl)-*N*-[3-(trimethoxysilyl)propyl]-1-propanamine.	Hair-conditioning agent
Aminopropyl Dimethicone 99363-37-8	the siloxane polymer that conforms generally to the structure: 	Hair-conditioning agent Skin-conditioning agent—miscellaneous
Amodimethicone 106842-44-8 68554-54-1 71750-79-3	a siloxane polymer that contains amino functional groups. It conforms generally to the structure:  where R=OH or CH_3, and X represents the propyl, isopropyl, or isobutyl group.	Hair-conditioning agent
Amodimethicone Hydroxystearate	the salt of Amodimethicone and Hydroxystearic Acid.	Hair-conditioning agent
Behenoxy Dimethicone	a dimethyl siloxane polymer that conforms generally to the structure: 	Skin-conditioning agent—emollient
C20-24 Alkyl Dimethicone 200074-76-6	is the siloxane polymer that conforms generally to the structure: 	Skin-conditioning agent—occlusive Viscosity increasing agent—nonaqueous
C20-24 Alkyl Methicone 200074-77-7	is the siloxane polymer that conforms generally to the structure: 	Skin-conditioning agent – emollient Viscosity increasing agent-- nonaqueous
C24-28 Alkyl Dimethicone 192230-29-8	is the siloxane polymer that conforms generally to the structure: 	Skin-conditioning agent—occlusive Viscosity increasing agent--nonaqueous

Table 1. Definitions, idealized structures, and functions

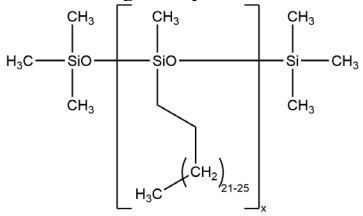
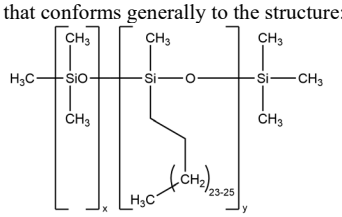
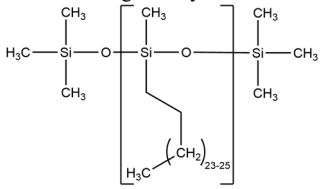
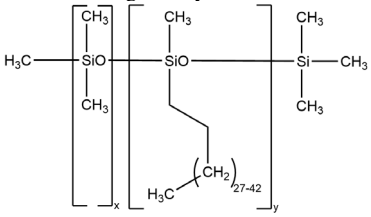
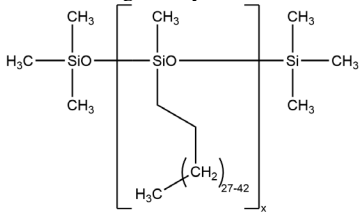
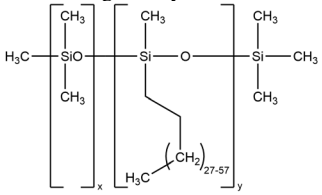
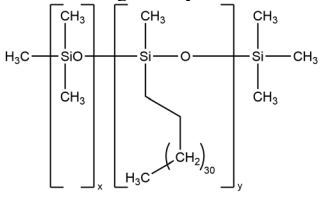
Name & CAS No.	Definition & Structure	Function(s)
C24-28 Alkyl Methicone 189378-12-9	the siloxane polymer that conforms generally to the structure: 	Skin-conditioning agent—emollient Viscosity increasing agent—non-aqueous
C26-28 Alkyl Dimethicone	is the siloxane polymer that conforms generally to the structure: 	Hair-conditioning agent Skin conditioning agent--occlusive
C26-28 Alkyl Methicone 189378-12-9	is the siloxane polymer that conforms generally to the structure: 	Skin-conditioning agent -- occlusive
C30-45 Alkyl Dimethicone	the siloxane polymer that conforms generally to the structure: 	Skin-conditioning agent—occlusive
C30-45 Alkyl Methicone 189378-12-9 246864-88-0	the siloxane polymer that conforms generally to the structure: 	Skin-conditioning agent—occlusive Viscosity increasing agent—non-aqueous
C30-60 Alkyl Dimethicone	the siloxane polymer that conforms generally to the structure: 	Skin-conditioning agent—occlusive Viscosity increasing agent – non-aqueous
C32 Alkyl Dimethicone	is the silicone polymer that conforms generally to the structure: 	Skin- conditioning agent--emollient

Table 1. Definitions, idealized structures, and functions

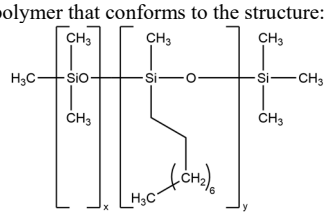
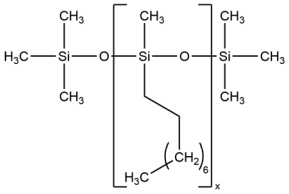
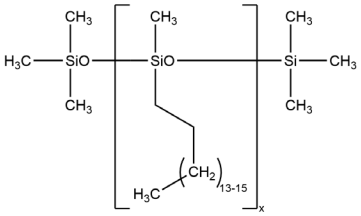
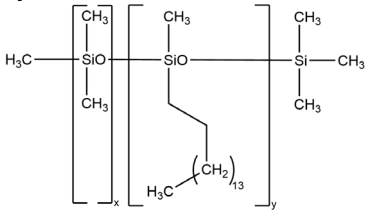
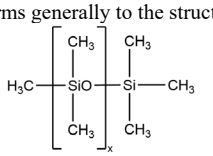
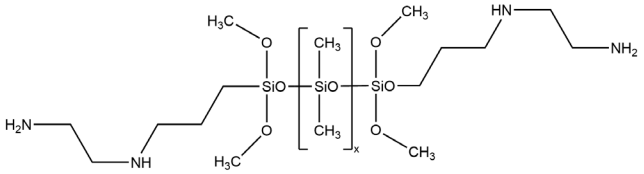
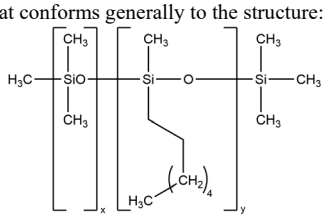
Name & CAS No.	Definition & Structure	Function(s)
Capryl Dimethicone	is a dimethyl siloxane polymer that conforms to the structure: 	Skin-conditioning agent--emollient
Caprylyl Methicone 17955-88-3	is the siloxane polymer that conforms to the structure: 	Skin-conditioning agent--occlusive
Cetearyl Methicone	a siloxane polymer that conforms to the structure: 	Skin-conditioning agent—occlusive
Cetyl Dimethicone 191044-49-2	a dimethyl siloxane polymer that conforms to the structure: 	Antifoaming agent Skin-conditioning agent—emollient and occlusive
Dimethicone 141-62-8 141-63-9 63148-62-9 9006-65-9 9016-00-6 107-52-8	a mixture of fully methylated linear siloxane polymers end blocked with trimethylsiloxy units. It conforms generally to the structure: 	Antifoaming agent Skin protectant Skin-conditioning agent—occlusive Solvent
Dimethoxysilyl Ethylenediaminopropyl Dimethicone 71750-80-6	the siloxane polymer that conforms generally to the structure: 	Hair conditioning agent
Hexyl Dimethicone	the siloxane polymer that conforms generally to the structure: 	Hair conditioning Skin conditioning agents - - miscellaneous

Table 1. Definitions, idealized structures, and functions

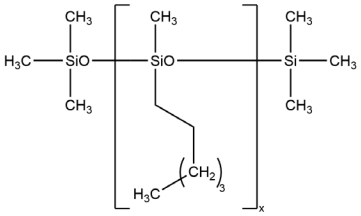
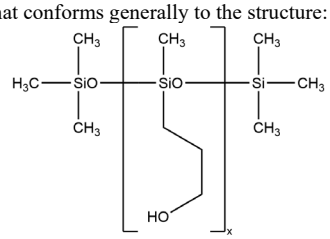
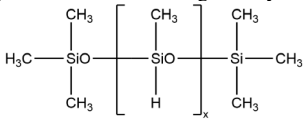
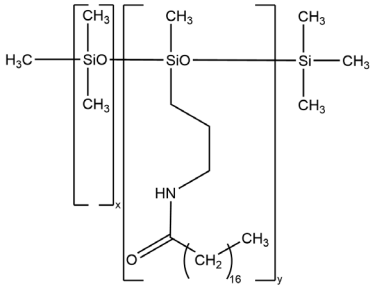
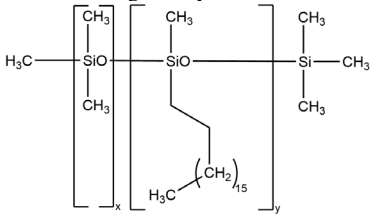
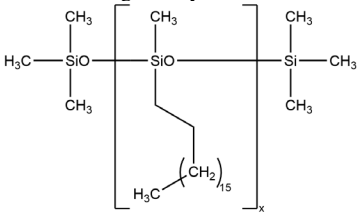
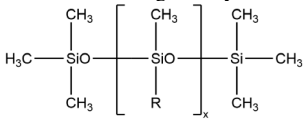
Name & CAS No.	Definition & Structure	Function(s)
Hexyl Methicone 1873-90-1	the siloxane polymer that conforms to the structure: 	Skin-conditioning—emollient
Hydroxypropyldimethicone 102782-61-6	the siloxane polymer that conforms generally to the structure: 	Hair-conditioning Skin-conditioning—miscellaneous
Methicone 63148-57-2 9004-73-3	a linear monomethyl polysiloxane. It conforms generally to the structure: 	Skin-conditioning agent—occlusive Surface modifier
Stearamidopropyl Dimethicone	the siloxane polymer that conforms to the structure: 	Corrosion inhibitor Film former
Stearoxy Dimethicone 68554-53-0	a polymer of dimethylpolysiloxane with some methyl groups replaced by stearoxy groups.	Skin-conditioning agent—emollient
Stearyl Dimethicone 67762-83-8	the siloxane polymer that conforms generally to the formula: 	Skin-conditioning agent—occlusive
Stearyl Methicone	the siloxane polymer that conforms generally to the structure: 	Skin-conditioning agent—occlusive
Vinyl Dimethicone 67762-94-1	a derivative of Dimethicone where some of the methyl groups have been replaced with vinyl groups. The vinyl groups can occur at the ends of the siloxane chain or pendant to the siloxane chain. It conforms generally to the structure:  wherein R is a methyl or vinyl group, and at least one vinyl group is present.	Not reported

Table 2. Current and historical frequency and concentration of use according to duration and exposure

	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	Amino Bispropyl Dimethicone				**Aminopropyl Dimethicone**			
	2020[9]	**1998[1]**	**2019[10]**	**1999[1]**	**2020[9]**	**1998[1]**	**2019[10]**	**1999[1]**
Totals*	**1**	**NR**	**NR**	**NR**	**57**	**NR**	**0.001-3**	**NR**
Duration of Use								
Leave-On	*1*	*NR*	*NR*	*NR*	*36*	*NR*	*0.001-3*	*NR*
Rinse-Off	*NR*	*NR*	*NR*	*NR*	*21*	*NR*	*0.3-0.66*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	NR	NR	NR	NR	1	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	NR	NR	NR	16[a]; 6[b]	NR	0.1-0.5[a]	NR
Incidental Inhalation-Powder	NR	NR	NR	NR	6[b]	NR	NR	NR
Dermal Contact	NR	NR	NR	NR	15	NR	0.001-3	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	Not spray: 0.001	NR
Hair - Non-Coloring	1	NR	NR	NR	36	NR	0.1-0.66	NR
Hair-Coloring	NR	NR	NR	NR	5	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR
	Amodimethicone				**Behenoxy Dimethicone**			
	2020[9]	**1998[1]**	**2019[10]**	**1999[1]**	**2020[9]**	**1998[1]**	**2019[10]**	**1999[1]**
Totals*	**1387**	**166**	**0.0051-5**	**0.0004-3**	**13**	**3**	**0.5**	**2-3**
Duration of Use								
Leave-On	*449*	*29*	*0.0051-4*	*0.0004-0.7*	*12*	*2*	*0.5*	*2*
Rinse-Off	*937*	*137*	*0.06-5*	*0.6-3*	*1*	*1*	*NR*	*3*
Diluted for (Bath) Use	*1*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	1	NR	NR	NR	5	NR	NR	NR
Incidental Ingestion	2	NR	NR	NR	2	NR	NR	NR
Incidental Inhalation-Spray	11; 208[a], 10[b]	3; 9[a]	0.3-2; 0.15-4[a]	0.0004-0.7[a]	4[a]; 1[b]	NR	NR	2[a]; 2[b]
Incidental Inhalation-Powder	1; 10[b]	NR	0.05[c]	NR	1[b]	NR	0.5[c]	2[b]
Dermal Contact	77	1	0.0051-0.49	NR	11	NR	0.5	2-3
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	1240	121	0.06-5	0.0004-3	NR	3	NR	NR
Hair-Coloring	68	44	0.18-1.3	2	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	43	NR	NR	NR	2	NR	NR	NR
Baby Products	2	NR	NR	NR	NR	NR	NR	NR
	C20-24 Alkyl Dimethicone				**C24-28 Alkyl Methicone**			
	2020[9]	**1998[1]**	**2020[12]**	**1999[1]**	**2020[9]**	**1998[1]**	**2019[10]**	**1999[1]**
Totals*	**38**	**NA**	**8**	**NA**	**NR**	**NR**	**NR**	**2**
Duration of Use								
Leave-On	*38*	*NA*	*8*	*NA*	*NR*	*NR*	*NR*	*2*
Rinse-Off	*NR*	*NA*	*NR*	*NA*	*NR*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NA*	*NR*	*NA*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	1	NA	8	NA	NR	NR	NR	NR
Incidental Ingestion	29	NA	NR	NA	NR	NR	NR	2
Incidental Inhalation-Spray	3[a]; 4[b]	NA	NR	NA	NR	NR	NR	NR
Incidental Inhalation-Powder	4[b]	NA	NR	NA	NR	NR	NR	NR
Dermal Contact	9	NA	8	NA	NR	NR	NR	NR
Deodorant (underarm)	NR	NA	NR	NA	NR	NR	NR	NR
Hair - Non-Coloring	NR	NA	NR	NA	NR	NR	NR	NR
Hair-Coloring	NR	NA	NR	NA	NR	NR	NR	NR
Nail	NR	NA	NR	NA	NR	NR	NR	NR
Mucous Membrane	29	NA	NR	NA	NR	NR	NR	2
Baby Products	NR	NA	NR	NA	NR	NR	NR	NR

Table 2. Current and historical frequency and concentration of use according to duration and exposure

	# of Uses		Max Conc of Use (%)		# of Uses		Max Conc of Use (%)	
	C26-28 Alkyl Dimethicone				C30-45 Alkyl Dimethicone			
	2020[9]	1998[1]	2020[12]	1999[1]	2020[9]	1998[1]	2019[10]	1999[1]
Totals*	**13**	**NA**	**0.8-2.8**	**NA**	**66**	**NR**	**0.16-5.1**	**2**
Duration of Use								
Leave-On	*11*	*NA*	*0.8-2.8*	*NA*	*64*	*NR*	*0.16-5.1*	*2*
Rinse-Off	*2*	*NA*	*NR*	*NA*	*2*	*NR*	*0.5*	*NR*
Diluted for (Bath) Use	*NR*	*NA*	*NR*	*NA*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	10	NA	0.8-2.8	NA	13	NR	0.16-5.1	NR
Incidental Ingestion	1	NA	NR	NA	36	NR	0.4-2.9	NR
Incidental Inhalation-Spray	NR	NA	NR	NA	3[a]; 5[b]	NR	2.3[a]	2[a]
Incidental Inhalation-Powder	NR	NA	NR	NA	5[b]	NR	4; 0.5-4[c]	NR
Dermal Contact	9	NA	2-2.8	NA	24	NR	0.16-5.1	2
Deodorant (underarm)	NR	NA	NR	NA	NR	NR	NR	NR
Hair - Non-Coloring	2	NA	NR	NA	2	NR	0.5-2.3	NR
Hair-Coloring	NR	NA	NR	NA	NR	NR	NR	NR
Nail	NR	NA	NR	NA	NR	NR	NR	NR
Mucous Membrane	1	NA	NR	NA	36	NR	0.4-2.9	NR
Baby Products	NR	NA	NR	NA	NR	NR	NR	NR
	C30-45 Alkyl Methicone				C30-60 Alkyl Dimethicone			
	2020[9]	1998[1]	2019[10]	1999[1]	2020[9]	1998[1]	2020[12]	1999[1]
Totals*	**71**	**NR**	**0.0054-2.2**	**NR**	**2**	**NA**	**NR**	**NA**
Duration of Use								
Leave-On	*50*	*NR*	*0.0054-2.2*	*NR*	*2*	*NA*	*NR*	*NA*
Rinse-Off	*21*	*NR*	*NR*	*NR*	*NR*	*NA*	*NR*	*NA*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NA*	*NR*	*NA*
Exposure Type								
Eye Area	12	NR	NR	NR	NR	NA	NR	NA
Incidental Ingestion	13	NR	NR	NR	NR	NA	NR	NA
Incidental Inhalation-Spray	7[a]; 5[b]	NR	NR	NR	2[b]	NA	NR	NA
Incidental Inhalation-Powder	5[b]	NR	0.0054-2.2[c]	NR	2[b]	NA	NR	NA
Dermal Contact	52	NR	0.0054-2.2	NR	2	NA	NR	NA
Deodorant (underarm)	NR	NR	NR	NR	NR	NA	NR	NA
Hair - Non-Coloring	3	NR	NR	NR	NR	NA	NR	NA
Hair-Coloring	NR	NR	NR	NR	NR	NA	NR	NA
Nail	2	NR	NR	NR	NR	NA	NR	NA
Mucous Membrane	13	NR	NR	NR	NR	NA	NR	NA
Baby Products	NR	NR	NR	NR	NR	NA	NR	NA
	Capryl Dimethicone				Caprylyl Methicone			
	2020[9]	1998[1]	2020[12]	1999[1]	2020[9]	1998[1]	2020[12]	1999[1]
Totals*	**NR**	**NR**	**1-5.5**	**NR**	**234**	**NA**	**0.0075-16**	**NA**
Duration of Use								
Leave-On	*NR*	*NR*	*1-5.5*	*NR*	*226*	*NA*	*0.0075-16*	*NA*
Rinse-Off	*NR*	*NR*	*1*	*NR*	*8*	*NA*	*0.22-12*	*NA*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NA*	*NR*	*NA*
Exposure Type								
Eye Area	NR	NR	1.5	NR	51	NA	0.22-16	NA
Incidental Ingestion	NR	NR	NR	NR	20	NA	2.8-7.5	NA
Incidental Inhalation-Spray	NR	NR	NR	NR	1; 63[a]; 38[b]	NA	0.8-6.2	NA
Incidental Inhalation-Powder	NR	NR	1[c]	NR	10; 38[b]	NA	0.014-6[c]; 0.0075-4	NA
Dermal Contact	NR	NR	1-5.5	NR	204	NA	0.0075-16	NA
Deodorant (underarm)	NR	NR	NR	NR	NR	NA	NR	NA
Hair - Non-Coloring	NR	NR	NR	NR	9	NA	0.5-6	NA
Hair-Coloring	NR	NR	NR	NR	NR	NA	NR	NA
Nail	NR	NR	NR	NR	1	NA	NR	NA
Mucous Membrane	NR	NR	NR	NR	20	NA	2.8-7.5	NA
Baby Products	NR	NR	1	NR	NR	NA	NR	NA

Table 2. Current and historical frequency and concentration of use according to duration and exposure

	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	Cetearyl Methicone				**Cetyl Dimethicone**			
	2020[9]	**1998[1]**	**2019[10]**	**1999[1]**	**2020[9]**	**1998[1]**	**2019[10]**	**1999[1]**
Totals*	**45**	**1**	**0.75-1.1**	**0.5-1**	**233**	**27**	**0.001-11.8**	**0.5-10**
Duration of Use								
Leave-On	*45*	*1*	*0.75-1.1*	*0.5-1*	*228*	*26*	*0.1-11.8*	*0.5-10*
Rinse-Off	*NR*	*NR*	*NR*	*NR*	*5*	*1*	*0.001-6*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	2	NR	NR	NR	64	5	1-6	0.5
Incidental Ingestion	NR	1	NR	0.6-1	14	NR	1.1-10	4-5
Incidental Inhalation-Spray	34[a];6[b]	NR	0.75[a]	0.5[b]	38[a]; 6[b]	4[a]; 2[b]	0.5-4[a]	2[a]; 2[b]
Incidental Inhalation-Powder	6[b]	NR	1.1[c]	0.5[b]	19; 6[b]	2; 2[b]	6; 0.1-11.8[c]	0.9-3; 2[b]
Dermal Contact	43	NR	0.9-1.1	0.5	210	24	0.001-11.8	0.9-10
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	2	NR	0.75	NR	7	1	0.5-6	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	1	NR	0.6-1	14	NR	0.001-10	4-5
Baby Products	NR	NR	NR	NR	NR	NR	5	NR
	Dimethicone				**Dimethoxysilyl Ethylenediaminopropyl Dimethicone**			
	2020[9]	**1998[1]**	**2019[10]**	**1999[1]**	**2020[9]**	**1998[1]**	**2019[10]**	**1999[1]**
Totals*	**14,050**	**1659**	**0.0000014-85**	**0.0001-80**	**NR**	**NR**	**0.043-2.1**	**NR**
Duration of Use								
Leave-On	*12,426*	*1333*	*0.002-85*	*0.0001-80*	*NR*	*NR*	*0.043*	*NR*
Rinse-Off	*1616*	*320*	*0.0000014-23.4*	*0.001-10*	*NR*	*NR*	*2.1*	*NR*
Diluted for (Bath) Use	*8*	*6*	*2.5-3*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	1976	111	0.25-37.8	0.3-13	NR	NR	NR	NR
Incidental Ingestion	347	12	0.4-71.3	0.001-20	NR	NR	NR	NR
Incidental Inhalation-Spray	119; 4763[a]; 2430[b]	56; 336[a]; 299[b]	1-85; 0.3-63.5[a]; 1-2.9[b]	0.2-16; 0.3-15[a]; 0.0001-10[b]	NR	NR	0.043[a]	NR
Incidental Inhalation-Powder	482; 2430[b]; 31[c]	87; 299[b]; 7[c]	0.33-53; 1-2.9[b]; 0.5-66.9[c]	0.3-30; 0.0001-10[b]; 2[c]	NR	NR	NR	NR
Dermal Contact	11,377	1313	0.0022-85	0.0001-30	NR	NR	NR	NR
Deodorant (underarm)	33[a]	9[a]	spray: 2-18.6; not spray: 5-40	0.5-23[a]	NR	NR	NR	NR
Hair - Non-Coloring	1522	249	0.0000014-63.5	0.08-80	NR	NR	0.043	NR
Hair-Coloring	291	29	0.00015-3.3	0.5	NR	NR	2.1	NR
Nail	397	36	0.002-75	0.001-3	NR	NR	NR	NR
Mucous Membrane	442	54	0.0022-71.3	0.001-20	NR	NR	NR	NR
Baby Products	34	8	0.21-10	2	NR	NR	NR	NR
	Hexyl Dimethicone				**Methicone**			
	2020[9]	**1998[1]**	**2020[12]**	**1999[1]**	**2020[9]**	**1998[1]**	**2019[10]**	**1999[1]**
Totals*	**NR**	**NA**	**0.17**	**NA**	**654**	**NR**	**0.00014-3.6**	**0.009-5**
Duration of Use								
Leave-On	*NR*	*NA*	*0.17*	*NA*	*635*	*NR*	*0.00014-3.6*	*0.009-5*
Rinse-Off	*NR*	*NA*	*NR*	*NA*	*18*	*NR*	*0.15-0.46*	*0.05-0.3*
Diluted for (Bath) Use	*NR*	*NA*	*NR*	*NA*	*1*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	NR	NA	0.17	NA	166	NR	0.1-3.6	0.02-0.9
Incidental Ingestion	NR	NA	NR	NA	91	NR	0.36	0.06
Incidental Inhalation-Spray	NR	NA	NR	NA	7[a]; 21[b]	NR	NR	0.3[b]
Incidental Inhalation-Powder	NR	NA	NR	NA	92; 21[b]	NR	0.064-1.5; 0.048-1.9[c]	0.08-5; 0.3[b]; 0.3[c]
Dermal Contact	NR	NA	0.17	NA	505	NR	0.00014-3.6	0.01-5
Deodorant (underarm)	NR	NA	NR	NA	NR	NR	spray: 0.25	NR
Hair - Non-Coloring	NR	NA	NR	NA	10	NR	0.46	NR
Hair-Coloring	NR	NA	NR	NA	5	NR	NR	0.3
Nail	NR	NA	NR	NA	24	NR	0.0035-2.5	0.009
Mucous Membrane	NR	NA	NR	NA	95	NR	0.36	0.06
Baby Products	NR	NA	NR	NA	NR	NR	0.46	0.3

Table 2. Current and historical frequency and concentration of use according to duration and exposure

	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	Stearoxy Dimethicone				**Stearyl Dimethicone**			
	2020[9]	**1998[1]**	**2019[10]**	**1999[1]**	**2020[9]**	**1998[1]**	**2019[10]**	**1999[1]**
Totals*	**44**	**21**	**0.8-1.5**	**0.1-3**	**183**	**7**	**0.2-8.3**	**0.8-6**
Duration of Use								
Leave-On	*43*	*20*	*0.8-1.5*	*0.1-3*	*176*	*6*	*0.2-8.3*	*0.8-6*
Rinse-Off	*1*	*1*	*NR*	*0.5*	*7*	*1*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	9	NR	NR	2-3	46	2	3.6-8.3	0.8-6
Incidental Ingestion	10	NR	0.8	3	25	2	0.38-2.6	4-6
Incidental Inhalation-Spray	7[a]; 8[b]	6[a]; 10[b]	NR	0.1; 0.2-3[a]; 2[b]	3; 28[a]; 35[b]	1[a]	0.38[a]	4[b]
Incidental Inhalation-Powder	8[b]	1; 10[b]	NR	2[b]	2; 35[b];	NR	0.2-2.3[c]	4[b]
Dermal Contact	32	21	1.5	0.5-3	149	3	0.2-8.3	1-6
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	not spray:1.2	NR
Hair - Non-Coloring	1	NR	NR	0.1-0.2	9	NR	0.3	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	10	NR	0.8	3	25	2	0.38-2.6	4-6
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR
	Stearyl Methicone				**Vinyl Dimethicone**			
	2020[9]	**1998[1]**	**2019[10]**	**1999[1]**	**2020[9]**	**1998[1]**	**2019[10]**	**1999[1]**
Totals*	**1**	**NR**	**NR**	**NR**	**1**	**NR**	**NR**	**NR**
Duration of Use								
Leave-On	*1*	*NR*	*NR*	*NR*	*1*	*NR*	*NR*	*NR*
Rinse-Off	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	1	NR	NR	NR
Incidental Inhalation-Spray	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Powder	NR	NR	NR	NR	NR	NR	NR	NR
Dermal Contact	1	NR	NR	NR	NR	NR	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	1	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

*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.

[a] It is possible these products are sprays, but it is not specified whether the reported uses are sprays.

[b] Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories.

[c] It is possible these products are powders, but it is not specified whether the reported uses are powders

NR – no reported use

NA – ingredient was not included in the original safety assessment.

Table 3. Methicone ingredients not reported to be in use[9-12]

Amodimethicone Hydroxystearate
C20-24 Alkyl Methicone
C24-28 Alkyl Dimethicone
C26-28 Alkyl Methicone
C32 Alkyl Dimethicone
Hexyl Methicone
Hydroxypropyldimethicone
Stearamidopropyl Dimethicone

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