Amended Safety Assessment of Silicates as Used in Cosmetics

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All interested persons are provided 60 days from the above release date (i.e., May 22, 2021) to comment on this safety assessment and to identify additional published data that should be included or provide unpublished data which can be made public and included.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 All unpublished data submitted to CIR will be discussed in open meetings, will be available at the CIR office for review by any interested party and may be cited in a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 24 silicate ingredients that are solid inorganic oxides, comprising, in part, silicon dioxide, that can be derived from naturally occurring minerals or can be produced synthetically. Reported functions in cosmetics include abrasives, absorbents, bulking agents, and deodorant agents. The Panel reviewed all relevant data, and concluded that the silicate ingredients are safe for use in cosmetics that are not expected to be incidentally inhaled with use when formulated to be non-irritating; that these ingredients are safe for use in products that may be incidentally inhaled when the presence of crystalline silica is < 0.1%, OR, the results of a repeated dose inhalation study demonstrate no adverse effects when crystalline silica is present at ≥ 0.1%; and that the data are insufficient to make a determination of safety for the utilization of these ingredients with airbrush use.

INTRODUCTION

The Expert Panel for Cosmetic Ingredient Safety (Panel) previously reviewed the safety of Aluminum Silicate, Calcium Silicate, and other silicates in a report that was published in 2003.[1] At that time, the Panel concluded that these ingredients are safe as used in cosmetic products. In accordance with its Procedures, the Panel evaluates the conclusions of previously-issued reports every 15 years, and it has been at least 15 years since this assessment has been issued. This report has been reopened to include additional ingredients, several of which were also previously reviewed in other safety assessments. Potassium Silicate, Sodium Metasilicate, and Sodium Silicate (report published in 2005) were found to be safe for use in cosmetic products in the practices of use and concentration described in the safety assessment when formulated to avoid irritation,[2] and Aluminum Calcium Sodium Silicate, Aluminum Iron Silicates, Magnesium Aluminometasilicate (previously known as Alumina Magnesium Metasilicate), and Sodium Potassium Aluminum Silicate (report finalized in 2009) were determined to be safe as cosmetic ingredients in the practices of use and concentrations as described in the safety assessment.[3]

In total, this report assesses the safety of 24 silicate ingredients (listed below; the 17 previously-reviewed ingredients are in red) as used in cosmetics. According to the web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI; *Dictionary*; see Table 1), the majority of these ingredients are reported to function as abrasives, absorbents, bulking agents, and/or deodorant agents in cosmetic products.[4]

Aluminum Calcium Sodium Silicate
Aluminum Iron Calcium Magnesium Germanium Silicates
Aluminum Iron Calcium Magnesium Zirconium Silicates
Aluminum Iron Silicates
Aluminum Silicate
Ammonium Silver Zinc Aluminum Silicate
Calcium Magnesium Silicate
Calcium Silicate
Lithium Magnesium Silicate
Lithium Magnesium Sodium Silicate
Magnesium Aluminometasilicate
Magnesium Aluminum Silicate
Magnesium Silicate
Magnesium Trisilicate
Potassium Silicate
Pyrophyllite
Sodium Magnesium Aluminum Silicate
Sodium Magnesium Silicate
Sodium Metasilicate
Sodium Potassium Aluminum Silicate
Sodium Silicate
Sodium Silver Aluminum Silicate
Zinc Silicate
Zirconium Silicate

The Panel has also reviewed other related ingredients. In a report that was finalized in 2019, the Panel concluded that synthetically-manufactured amorphous silica and hydrated silica are safe in the present practices of use and concentration when formulated to be non-irritating.[5] In 2013, the Panel published a report with the conclusion that silylates and surface-modified siloxysilicates (i.e., silica silylate, silica dimethyl silylate, trimethylsiloxysilicate, and trifluoropropyldimethyl/ trimethylsiloxysilicate) are safe as used in cosmetics when formulated and delivered in the final product not to be irritating or sensitizing to the respiratory tract.[6] The ingredients included in these reports are not part of this amended safety assessment.

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 Cosmetic Ingredient Review (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.

Some chemical and toxicological data on the silicate ingredients included in this safety assessment were obtained from robust summaries of data submitted to the European Chemical Agency (ECHA) by companies as part of the REACH chemical registration process.[7-13] Additionally, some data were obtained from assessments by the Organisation for Economic Co-Operation and Development Screening Information Data Sets (OECD SIDS).[14] These data summaries are available on the ECHA and OECD SIDS websites, respectively, and when deemed appropriate, information from the summaries has been included in this report.

Excerpts from the summaries of the 2003 and 2005 reports on silicates are disseminated throughout the text of this re-review document, as appropriate, and are identified by *italicized text*. (This information, except for chemical and physical properties, is not included in the tables or the summary section.) Select summary information from the 2019 silica report is also included. Data on the silicate ingredients from the report finalized in 2009 has been incorporated into this safety assessment due to reorganization. The original reports that were published or finalized in 2003, 2005, and 2009, and the reports on related ingredients, are available on the CIR website (https://www.cir-safety.org/ingredients).

CHEMISTRY

Definition

These silicate ingredients that are inorganic oxides, comprising in part, silicon dioxide, are solids that can be derived from naturally occurring minerals. However, the ingredients in this safety assessment can also be produced synthetically. The Panel considered the method of manufacture of these ingredients (whether synthetic or mined) to be of significant importance to safety, as synthetically-derived ingredients are expected to have controlled crystalline material formation. The definitions and functions of the silicate ingredients included in this safety assessment are provided in Table 1.

Chemical Properties

Chemical properties of silicate ingredients are provided in Table 2. These ingredients are inorganic salts of silica; as such, these ingredients are solids and can be either crystalline or amorphous. Most of these ingredients, generally, are not soluble in water, but a few, like Calcium Silicate and Sodium Metasilicate, have limited or full water solubility.[7,8,10,11,13]

Method of Manufacturing

While some of these ingredients are naturally occurring minerals, it is possible to manufacture these ingredients via partially synthetic means from other minerals, or via *de novo* synthesis. Aluminum Silicate is a naturally occurring mineral as well as artificially produced.[1] Synthetic Aluminum Silicate is formed by heating compositions of controlled proportions of silica, alumina, and alkalis under conditions to promote the specific structure. Sodium Silicate and Sodium Metasilicate are either made by high temperature fusion of silica and soda or by a hydrothermal process using silica and sodium hydroxide as starting materials.[2] Potassium Silicate can be also be produced by high temperature fusion of potassium carbonate and sand.

Method of manufacturing for Calcium Silicate, Magnesium Silicate, Magnesium Aluminum Silicate, Potassium Silicate, Sodium Magnesium Silicate, Sodium Metasilicate, Sodium Silicate, and Sodium Silver Aluminum, including particle size (prior to consumer product formulation) information where available, is provided in Table 3. These ingredients are produced from synthesized and mined materials.[15-19]

Composition/Impurities

Crystallinity and purity for Calcium Silicate, Magnesium Silicate, Magnesium Aluminum Silicate, Potassium Silicate, Sodium Magnesium Silicate, Sodium Metasilicate, and Sodium Silicate is provided in Table 3.[15,17,18] Crystallinity is reported to be < 0.2% for Calcium Silicate and Magnesium Silicate and <0.1% for Magnesium Aluminum Silicate, Potassium Silicate, Sodium Metasilicate, and Sodium Silicate. It was not detected by X-ray diffraction in Sodium Magnesium Silicate (limit of detection not reported),

Aluminum Calcium Sodium Silicate

A supplier reported that the Aluminum Calcium Sodium Silicate used in their trade name mixtures is amorphous and does not contain crystalline silica.[20] Another supplier reported that an X-ray powder diffraction analysis of an Aluminum Calcium Sodium Silicate product found it contained no crystalline silica and is amorphous Aluminum Silicate (no peaks were identified at 22º or 21/27º, which are the specific peaks for cristobalite and quartz, respectively).[21] The composition was 53.6% silicon dioxide, 29.45 aluminum oxide, 8.3% sodium oxide, and 8.3% calcium oxide.

Aluminum Silicate

Other minerals associated with natural Aluminum Silicates are anauxite, dickite, kaolinite, kochite, mullite, newtonite, pyrophyllite, takizolite, and terierite.[1]

Calcium Silicate

According to the *Food Chemicals Codex*, Calcium Silicate may not contain more than 10 mg/kg fluoride and not more than 5 mg/kg lead.[16] The Joint Food and Agriculture Organization of the United Nations (FAO)/World Health Organization (WHO) Expert Committee on Food Additives (JECFA) specified that Calcium Silicate contains not more than 50 mg/kg fluoride, not more than 5 mg/kg lead, and not more than 3 mg/kg arsenic.[22]

Magnesium Aluminum Silicate

A group of Magnesium Aluminum Silicate trade name mixtures contained 1% to 6% by volume weight crystalline Silica in the form of cristabalite.[1] The product may also contain quartz.

A supplier reported that their product consists of 100% Magnesium Aluminum Silicate.[17] In the testing of 4 lots of product, the presence of crystalline silica was non-detectable (limit of detection = 0.1%).

Magnesium Silicate

According to the *Food Chemicals Codex*, Magnesium Silicate may not contain more than 10 mg/kg fluoride and not more than 5 mg/kg lead.[16] JECFA specified that Magnesium Silicate contains not more than 1% free alkali (as sodium hydroxide), not more than 3% soluble salts, not more than 10 mg/kg fluoride, and not more than 5 mg/kg lead.[23]

Sodium Magnesium Aluminum Silicate

According to the *Food Chemicals Codex*, Sodium Magnesium Aluminum Silicate (listed as sodium magnesium aluminosilicate) may not contain more than 5 mg/kg lead.[16]

Sodium Magnesium Silicate

A supplier reported that their synthetic product is 100% pure Sodium Magnesium Silicate, with no crystalline silica.[18] The chemical composition is 59.0% silicon dioxide, 28.0% magnesium oxide, and 4.0% sodium oxide.

Sodium Metasilicate

The arsenic and lead maximum limits in Sodium Metasilicate are 3 ppm and 20 ppm, respectively.[2]

According to the *Food Chemicals Codex*, Sodium Metasilicate may not contain more than 5 mg/kg lead.[16]

Sodium Silicate

The arsenic and lead maximum limits in Sodium Silicate (40% solution) are 3 ppm and 20 ppm, respectively.[2]

Sodium Silver Aluminum Silicate

A supplier reported that in the production of Sodium Silver Aluminum Silicate, raw materials and the final product do not contain crystalline silica as an impurity.[24]

USE

Cosmetic

The safety of the cosmetic ingredients included 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 are 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 cosmetics industry in response to surveys, conducted by the Personal Care Products Council (Council), of maximum reported use concentrations by product category.

According to 2021 VCRP data, Magnesium Aluminum Silicate has the most reported uses in cosmetic products, with a total of 383; the majority of the uses are in leave-on eye makeup preparations and skin care preparations (Table 4).[25] Aluminum Calcium Sodium Silicate has the second most reported uses in cosmetic products, with a total of 103; the majority of the uses are in lipsticks. (The reported numbers of uses for the remaining ingredients in this report are much lower.) The frequencies of use for both of these ingredients have greatly changed since the original safety assessments were finalized; in 1998, Magnesium Aluminum Silicate was reported to have 632 uses, and in 2009, Aluminum Calcium Sodium Silicate was reported to have 7 uses.[1-3] The results of the concentration of use survey conducted in 2018 by the Council indicate Aluminum Calcium Sodium Silicate has the highest reported maximum concentration of use for leave-on products; it is used at up to 26.3% in eye shadows.[26] Magnesium Silicate is reported to have a maximum concentration of use for leave-on products of 21.6% in eye shadows.[27] According to the original safety assessment, the maximum use concentration in 2008 for Aluminum Calcium Sodium Silicate was 6% in foundations and lipsticks.[3] Additionally according to 1999 data, there were no reported uses for Magnesium Silicate.[1] Leave-on concentrations of use reported in the previous review of these silicate ingredients were lower than the current leave-on maximum concentration of use. The 10 silicate ingredients with no reported uses in the VCRP database or in the Council's concentration of use survey are listed in Table 5.

Many of the silicate ingredients described in this safety assessment may be used in products that can be incidentally ingested or come into contact with mucous membranes; for example, Magnesium Silicate is used in lipstick at 10% and Aluminum Calcium Sodium Silicate is used in lipstick at up to 5.5%.[26,27] Additionally, the silicate ingredients have been

reported to be used in products that may come into contact with the eyes, such as eye shadows, eye liners, and mascaras. Magnesium Silicate at up to 26.3% in eye shadows.[27]

Moreover, according to VCRP and Council survey data, these ingredients are reported to be used in spray products that could possibly be inhaled; for example, Calcium Silicate is used at up to 0.005% in hair color sprays and Lithium Magnesium Silicate is used at up to 0.4% in face and neck sprays. Concerning final consumer product formulations, the Panel has noted that in practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters > 10 μm, with propellant sprays yielding a greater fraction of droplets/particles below 10 μm compared with pump spray.[28-31] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and bronchial regions and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.[28,30] Ingredients in this report are also used in powders, and these products could possibly be inhaled. For example, Calcium Silicate and Magnesium Aluminum Silicate are reported to be used at up to 5% and 1% in face powders, respectively.[27] Conservative estimates of inhalation exposures to respirable particles during the use of loose powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace.[32-34]

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.[35] It has come to the attention of the Panel that some silicate ingredients are 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.

According to 21 CFR §73.2400, Pyrophyllite is an approved color additive for cosmetics in the US when applied externally in amounts consistent with good manufacturing practice.

In regulations on cosmetic products in the European Union, zirconium and its compounds (including Zirconium Silicate) are listed under Annex II-substances prohibited in cosmetic products. [36] Annex IV (colorants allowed in cosmetic products) lists natural hydrated Aluminum Silicate (containing calcium, magnesium or iron carbonates, ferric hydroxide, quartz-sand, mica, etc. as impurities); when used as a color in Europe, this ingredient must be labeled as CI 77004. The remaining silicate-related ingredients listed in this report are not restricted from use in any way under the rules governing cosmetic products in the European Union.

Non-Cosmetic

Aluminum Silicate is approved as an indirect food additive, according to the Code of Federal Regulations (CFR).[1] Pyrophyllite is listed as a naturally occurring color additive in the CFR. Calcium Silicate, Magnesium Aluminum Silicate, and Magnesium Trisilicate are used in over-the-counter drug products.

Potassium Silicate and Sodium Silicate were reported as being used in industrial cleaners and detergents.[2] Sodium Metasilicate is a generally recognized as safe (GRAS) food ingredient.

According to the Australian Industrial Chemicals Introduction Scheme (AICIS) the following ingredients are Tier I chemicals (not considered to pose an unreasonable risk to the health of workers and public health): Aluminum Silicate, Calcium Silicate, Magnesium Silicate, Magnesium Trisilicate, and Sodium Potassium Aluminum Silicate,).[37] Potassium Silicate, Sodium Silicate, and Sodium Metasilicate are Tier II chemicals (require risk management measures to be instituted for safe use for human health or the environment). The remaining silicates have no AICIS determination.

Aluminum Calcium Sodium Silicate

Aluminum Calcium Sodium Silicate (hydrated) is used for countering the effects of aflatoxin in animal feed.[38-49] This ingredient is also GRAS in the US in food for use as an anticaking agent at a level not exceeding 2% in accordance with good manufacturing practices (21 CFR §182.2729).

Calcium Silicate

Calcium Silicate is used in endodontics in root canal sealer preparations and dental cements.[50-52]

Pyrophyllite

According to 21 CFR §73.1400, Pyrophyllite is an approved color additive for drugs in the US when applied externally in amounts consistent with good manufacturing practice. As described in the regulation, this ingredient is a naturally occurring mineral substance consisting predominantly of a hydrous aluminum silicate intimately mixed with lesser amounts of finely divided silica. Small amounts (< 3%) of other silicates, like potassium aluminum silicate, may be present. Specifications indicate that Pyrophyllite should not have more than 20 ppm lead and not more than 3 ppm arsenic

Sodium Magnesium Aluminum Silicate

Sodium Magnesium Aluminum Silicate is reported to be used in print enhancement (imparting high brightness and opacity), paper filler, and carbonless copy intensifier.[53]

Zinc Silicate

Zinc Silicate is reported to be used as phosphors (in television screens), in spray ingredients (spray type not stated), and to remove traces of copper from gasoline.[53,54]

TOXICOKINETICS

Absorption, Distribution, Metabolism, Excretion (ADME)

In a study of dogs to determine the bioavailability of silicon and aluminum from several mineral compounds, no statistically significant absorption of aluminum was recorded in assayed plasma samples of dogs given Magnesium Trisilicate orally.[1] This study did note elevated levels of silicon. The urinary silica excretion following orally dosing five human males with 20 g of Magnesium Trisilicate was 5.2%.

Sodium Silicate administered orally in rats acts as a mild alkali and was readily absorbed from the alimentary canal and excreted in the urine.[2] Urinary silicon excretion following orally dosing rats with Sodium Silicate at 40 and 1000 mg/kg was 18.9% and 2.8%, respectively.

Animal

Oral

Sodium Metasilicate

In a dietary ADME study, 5 guinea pigs received silica (0.8 mg/g feed) as three separate forms (Sodium Metasilicate, hydrated silica, and silica solution (30%)) in single doses or in four repeated doses every 48 h.[55,56] Urine and feces were collected in 48-h increments after each dose of each form and analyzed for silica content. For the Sodium Metasilicate doses, the urinary output of silica peaked within 48 h and gradually returned to normal after 8 d. When administered four times, 48 h apart, the peak was maintained, but did not increase. Within 48 h after the last dose, the concentration of silica in the urine began to return to normal. With the silica solution and hydrated silica, the urinary output of silica also peaked within 48 h and gradually returned to normal after 8 d, but the peaks were much lower than those observed with Sodium Metasilicate. When administered four times, 48 h apart, the silica concentrations behaved similarly to the Sodium Metasilicate form, except with a lower peak. In this study, approximately 63% of the silica was recovered. The authors of the study suggested that the silica in the urine was in the soluble or molybdate reactive form, and that the silica particles underwent depolymerization prior to excretion.

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

Synthetically-Manufactured Amorphous Silica and Hydrated Silica

In acute inhalation studies that ranged in duration from 1 to 6 h, the LC_{50}s for Hydrated Silica (30% SiO_2) and Silica (concentration not reported) in rats were > 3300 mg/m^3 and > 191,300 mg/m^3, respectively.

Silicates

The acute dermal LD_{50} was > 3500 g/kg for rabbits exposed to Magnesium Aluminum Silicate.[1] The following are acute oral LD_{50} determinations: Calcium Silicate, 3400 mg/kg in rats; Magnesium Aluminum Silicate, 50,000 mg/kg in mice; and Zirconium Silicate, > 200,000 mg/kg in mice

The toxicity of Potassium Silicate, Sodium Metasilicate, and Sodium Silicate has been related to the molar ratio of SiO_2/Na_2O and the concentration.[2] The acute oral LD_{50} of Sodium Metasilicate ranged from 847 mg/kg in male rats to 1349.3 mg/kg in female rats, and from 770 mg/kg in female mice to 820 mg/kg in male mice. Gross lesions of variable severity were found in the oral cavity, pharynx, esophagus, stomach, larynx, lungs, and kidneys of dogs receiving 250 mg/kg or more of a commercial detergent containing Sodium Metasilicate. Similar lesions were seen in pigs given the same detergent and dose as in the previous study. Male Sprague-Dawley rats orally administered 464 mg/kg of a 20% solution containing either 2.0 or 2.4 ratio of Sodium Silicate to 1.0 ratio of sodium oxide showed no signs of toxicity, whereas doses of 1000 and 2150 mg/kg produced gasping, dyspnea, and acute depression. Acute intraperitoneal injections of a neutralized 2% solution of Sodium Metasilicate in white rats resulted in a decrease in spleen weight and relative enlargement of the kidneys.

Acute dermal, oral, and inhalation data are summarized in Table 6. Potassium Silicate (30% solution in water) had a dermal LD_{50} > 5000 mg/kg in rats.[9] In oral rat studies, the LD_{50}s were > 2000 mg/kg for Aluminum Silicate (concentration not reported), Sodium Magnesium Aluminum Silicate (concentration not reported), and Sodium Silicate.[8,11,12] Calcium Silicate (20%) and Potassium Silicate (concentration not reported) had LD_{50}s of > 10,000 mg/kg and > 5000 mg/kg in rats, respectively.[9,13,14] An oral LD_{50} for Sodium Silicate in male mice was 6600 mg/kg.[11] Orally administered Aluminum Calcium Sodium Silicate had no adverse effects when tested up to 800 mg/kg in mice.[57,58] In an inhalation study, the LC_{50} for Potassium Silicate (30%) was > 2060 mg/m^3 following 4.4 h.[9]

Short-Term, Subchronic, and Chronic Toxicity Studies

Synthetically-Manufactured Amorphous Silica and Hydrated Silica

In short-term inhalation studies with Hydrated Silica, inflammatory and pulmonary lesions were observed in rats at 30 mg/m^3. Inflammatory responses were also observed in rats exposed to Silica in studies that lasted between 5 to 14 d. No significant lung histopathological findings or adverse changes in inflammatory markers were observed in rats that were exposed to nanoparticle Silica (particle size 50 - 79 nm; concentrations 0.4 - 5.4 mg/m^3) for 4 wk. In subchronic inhalation studies, inflammatory responses were noted in the lungs and lymph nodes along with pulmonary lesions after exposure to Hydrated Silica at 35 mg/m^3 (particle and agglomerate/aggregate size 1 to ~120 µm). In a 13-wk inhalation study of Silica in rats, the NOEL was 1.3 mg/m^3. Inflammation and pulmonary lesions, including fibrosis, were noted in this study and another 13-wk rat study (fibrosis subsided during recovery). In inhalation studies of 9- to 12-mo duration, Hydrated Silica caused pulmonary inflammation and emphysema in rats exposed to 25 to 85 mg/m^3. The LOAEC in rabbits exposed for 9 mo to Hydrated Silica was 28 mg/m^3. No silicotic processes were noted in studies of rabbits, rats, and guinea pigs exposed to an average of 126 mg/m^3 Hydrated Silica for 12, 15, and 24 mo, respectively. No neoplasia was observed. In a 12-mo study with Hydrated Silica and Silica in rats, the LOAEC was 6.9 mg/m^3 due to interstitial fibrosis (which was comparable between test and control groups). The same test materials also were associated with nodular fibrosis in an 18-mo study with monkeys, although the animals may have been exposed to quartz or asbestos fibers. The LOAEC in a 6-mo rat inhalation study with Silica was 53 mg/m^3. Emphysema and fibrosis were noted around 4 mo of exposure. Inflammatory responses and pulmonary lesions were noted in rat, guinea pigs, rabbits, and monkeys in studies up to 24 mo in duration. More than half of the studies summarized in this report included recovery periods of various durations that showed that observed lung effects began to resolve or did not worsen after exposure ceased.

Silicates

In short-term oral toxicity studies, no adverse effects were seen in mice or rabbits dosed up to 5 g/kg Magnesium Aluminum Silicate; beagle dogs and rats fed 1.3 g/kg/d Aluminum Silicate had no renal lesions.[1] Dogs and rats fed 1.8 g/kg/d Magnesium Trisilicate for 4 wk had polydipsia and polyuria, and all dogs had renal cortical lesions. Guinea pigs had renal lesions after 4 mo of drinking Magnesium Trisilicate (250 mg/L) in tap water. Rats fed 10% Magnesium Aluminum Silicate had slightly elevated silicon levels of the spleen and dogs and rats fed 10% Magnesium Aluminum Silicate had no adverse effects in 90-d feeding studies. Beagle dogs fed 2.4 g/kg/d of Sodium Silicate for 4 wk had gross renal lesions but no impairment of renal function.[2]

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY STUDIES

Calcium Silicate (250 to 1600 mg/kg on gestation days 6 through 18) had no discernible effect on nidation or on maternal or fetal survival in rabbits.[1] Magnesium Aluminum Silicate (600 to 6000 mg/kg on gestation days 7 through 12) had no adverse effects on the mouse fetus.

Rats given Sodium Silicate (600 and 1200 ppm of added silica) in the drinking water in reproductive studies had a reduced number of offspring; 67% of controls at 600 ppm and 80% of controls at 1200 ppm.[2] Three adult rats injected intratesticularly and subcutaneously with 0.8 mM/kg of Sodium Silicate showed no morphological changes in the testes and no effect on the residual spermatozoa in the ductus deferens.

GENOTOXICITY STUDIES

No increase in mutation frequencies was seen in the Salmonella TA-1530 or G-46 assay and no significant increase in recombinant activity was observed in the Saccharomyces D3 assay with Calcium Silicate.[1] In the S. typhimurium LT2 spot test (TA98, TA100, TA1535, TA1537, and TA1538) with or without metabolic activation, Magnesium Aluminum Silicate was found to be non-mutagenic. A subacute dose of 150 mg/kg of Calcium Silicate in rats produced 3% breaks in bone marrow cells arrested in c-metaphase. In a metaphase spread of rat bone marrow cells, Calcium Silicate produced no significant increase in

the number of aberrations compared to controls, and in a rat dominant lethal assay, it did not induce any dominant lethal mutations. Routes of administration were not reported for these rat studies.

Sodium Metasilicate was non-mutagenic in a DNA damage and repair assay without metabolic activation using Bacillus subtilis.[2] Sodium Silicate was non-mutagenic in studies using Escherichia coli strains B/Sd-4/1,3,4,5 and B/Sd-4/3,4.

Genotoxicity data are summarized in Table 7. Aluminum Silicate and Sodium Metasilicate were not genotoxic in Ames tests or a hypoxanthine-guanine phosphoribosyl transferase (HGPRT) gene mutation assays, Sodium Silicate was not genotoxic in a HGPRT gene mutation assay or a chromosome aberration test, and Zinc Silicate was not genotoxic in an Ames test.[7,10-12]

Mutagenic Inhibition

Aluminum Calcium Sodium Silicate

In a study of mutagenic inhibition, aflatoxin (2.5 mg/kg) was incorporated into rat feed with Aluminum Calcium Sodium Silicate (hydrated; 0.5%).[47] The feed was given to groups of 10 Sprague-Dawley rats for 15 d, after which the animals were killed and bone marrow samples were collected for chromosomal analysis. In the marrow of the rats given aflatoxin alone, structural and numerical aberrations of chromosomes, mainly chromatid breaks and chromatid gaps, were observed. In the rats that received Aluminum Calcium Sodium Silicate, these effects were decreased for every category of aberration except polyploidy.

CARCINOGENICITY STUDIES

No carcinogenicity studies were discovered in the published literature, and no unpublished data were submitted.

OTHER RELEVANT STUDIES

Cytotoxicity

A sample of Aluminum Silicate in an in vitro assay was toxic to pulmonary alveolar macrophages, and lactate dehydrogenase activity (LDH) and β-galactosidase (β-GAL) release were increased.[1]

DERMAL IRRITATION AND SENSITIZATION STUDIES

Magnesium Aluminum Silicate (4%) was a weak primary skin irritant in rabbits and had no cumulative skin irritation in guinea pigs.[1] No gross effects were reported in any of the studies. Sodium Magnesium Silicate (4%) had no primary skin irritation in rabbits and had no cumulative skin irritation in guinea pigs.[1] Dermal irritation of Potassium Silicate, Sodium Metasilicate, and Sodium Silicate ranged from negligible to severe, depending on the species tested and the molar ratio and concentration tested.[2] Sodium Metasilicate was negative in the local lymph node assay (LLNA) at up to 6%, but a delayed-type hypersensitivity response was observed to the test material in mice sensitized at 4% and challenged at 6%.

Applications of 2 g of Magnesium Aluminum Silicate made to the skin of two humans daily for 1 wk caused no effects.[1] Sodium Metasilicate/carbonate detergent (37% Sodium Metasilicate) mixed 50/50 with water was considered a severe skin irritant when tested on intact and abraded human skin.[2] Detergents containing 7%, 13%, and 6% Sodium Silicate mixed 50/50 with water, however, were negligible skin irritants to intact and abraded human skin. Sodium Silicate (10% of a 40% aqueous solution) was negative in a human repeat-insult patch test (HRIPT). The same aqueous solution of Sodium Silicate was considered mild under normal use conditions in a study of cumulative irritant properties. Sodium Metasilicate and Sodium Silicate were studied in modified soap chamber tests. No burning or itching was observed and low erythema + edema scores were noted. Sodium Metasilicate and Sodium Silicate, tested in elbow crease studies and semi-occluded patch tests, produced low grade and transient irritation.

Dermal irritation and sensitization data summarized here are detailed in Table 8. Aluminum Silicate and Zinc Silicate were predicted to be not irritating in EpiDerm™ skin assays.[7,12] In rabbit studies, the irritation potential of Potassium Silicate (up to 36%) and Sodium Metasilicate (up to 97%) were dependent on concentration, with irritation observed starting at 33% for Potassium Silicate and slight irritation starting at 10% for Sodium Metasilicate.[9,10,14] Aluminum Silicate (up to 25%) and Zinc Silicate (up to 50%) were not sensitizing in LLNA studies.[7,12] Potassium Silicate (30%) was not sensitizing in guinea pig sensitization test.[9]

OCULAR IRRITATION STUDIES

A 4% solution of Magnesium Aluminum Silicate and a 4% solution of Sodium Magnesium Silicate caused minimal eye irritation in a Draize eye irritation test.[1]

Potassium Silicate was nonirritating in two acute eye irritation studies in rabbits.[2] Sodium Metasilicate (42.4% water) was corrosive to the rabbit eye. Sodium Silicate was a severe eye irritant in acute eye irritation studies. A skin freshener (10% of a 40% aqueous solution) containing Sodium Silicate was nonirritating. Sodium Silicate in another three Draize eye irritation studies was highly irritating (at molar ratios of 2 and 2.9 and concentrations of 44% and 43%), irritating (at molar ratios of 1 and 2 and concentrations of 10% and 8%), and nonirritating (at molar ratio of 3.2 and concentration of 36%), respectively.

In vitro and animal ocular irritation data are summarized in Table 9. Aluminum Silicate (tested pure) was predicted to be not irritating using the hen's egg test chorioallantoic membrane (HET-CAM) method.[12] Sodium Metasilicate (undiluted) was predicted to be corrosive in the isolated rabbit eye study,[10] and Zinc Silicate (20%) was predicted to be irritating in a bovine corneal opacity and permeability (BCOP) test.[7] Potassium Silicate was not irritating, at concentrations up to 29%, to slightly irritating, at 30% and 35%, in rabbit eyes.[9,14]

CLINICAL STUDIES

Case Reports

Colloidal Sodium Metasilicate (0.5 l) was fatal to one man and neutralized Sodium Silicate (more than 1 g/kg) produced vomiting, diarrhea, and gastrointestinal bleeding in another man in separate case reports of oral ingestion.[2]

Sodium Metasilicate

Acute kidney injury was reported in a 52-yr-old man who had ingested approximately 150 ml of a plate developer solution containing Sodium Metasilicate.[59] The patient also developed severe upper airway obstruction due to laryngeal edema, severe inflammation of the upper gastrointestinal tract with narrowing of the esophagus and pyloric region. The patient succumbed to his injuries a few months after ingestion.

Reactive airway dysfunction syndrome was reported in a 43-yr-old man who had inhaled dishwasher detergent powder containing Sodium Metasilicate.[60] The patient was employed as an apprentice cook and accidentally inhaled the detergent while preparing to use an institutional dishwasher.

OCCUPATIONAL AND ENVIRONMENTAL EXPOSURE

While no occupational exposure data to the specific silicate ingredients were discovered, general data on amorphous and crystalline silica exist in the published literature. Occupational data on amorphous silica has been summarized in the synthetically-manufactured amorphous silica and hydrated silica safety assessment.[5] Available regulatory information data on silica is provided below.

According to the Agency for Toxic Substances and Disease Registry (ATSDR), data from occupational exposure studies are insufficient to determine whether or not amorphous silica is associated with adverse effects in humans because exposure in most studies included a mixture of crystalline and amorphous silica.[61] The ATSDR noted that results of animal studies on synthetic amorphous silica polymorphs indicate that inhalation exposure is associated with pulmonary toxicity: however, progressive fibrosis was not observed and most effects were reversible. Because NOAEL and LOAEL values could not be certainly identified, an inhalation minimal risk level (MRL) for amorphous silica could not be developed for any exposure duration. For crystalline silica, the ATSDR noted that while this substance is associated with silicosis and other pulmonary disease, an inhalation MRL could not be developed due to the inability to determine a no-effect level.

The ATSDR also reported that both amorphous and crystalline silica can be found in ambient air through release by natural and human processes.[61] Ambient amorphous silica levels have been found to range from <0.2 $\mu g/m^3$ to 135 $\mu g/m^3$, and ambient urban crystalline silica levels have been found to range from 0.25 $\mu g/m^3$ to 2.87 $\mu g/m^3$.

The Occupational Safety and Health Administration (OSHA) action level for crystalline silica is 25 $\mu g/m^3$ averaged over an 8-h day.[62] The permissible exposure limit (PEL) for crystalline silica is 50 $\mu g/m^3$. For amorphous silica, the PEL is 80 mg/m^3 or 20 million particles per cubic foot air averaged over an 8-h work shift.[63]

The National Institute for Occupational Safety and Health (NIOSH) recommended exposure limit (REL) is 0.05 mg/m^3 for crystalline silica and 6 mg/m^3 for amorphous silica.[64]

The California Office of Environmental Health Hazard Assessment (OEHHA) has set a chronic inhalation reference exposure level) of 3 $\mu g/m^3$ for crystalline silica (silicon dioxide, quartz, tridymite, cristobalite) based on occupational exposure studies of crystalline silica and the development of silicosis in miners and other related occupations.[65]

SUMMARY

This report assesses the safety of 24 silicate ingredients as used in cosmetics. The majority of these ingredients function as abrasives, absorbents, bulking agents, and/or deodorant agents in cosmetic products. The Panel previously reviewed the safety of Aluminum Silicate, Calcium Silicate, Magnesium Silicate, Magnesium Trisilicate, Sodium Magnesium Silicate, Zirconium Silicate, Lithium Magnesium Silicate, and Lithium Magnesium Sodium Silicate in a report that was published in 2003; the Panel concluded that these ingredients are safe as used in cosmetic products. In accordance with its procedures, the Panel evaluates the conclusions of previously-issued reports every 15 years, and it has been at least 15 years since this assessment has been issued. This report has been reopened to add additional ingredients, including several that were also previously reviewed. A report on Potassium Silicate, Sodium Metasilicate, and Sodium Silicate was published in 2005 with the conclusion that these ingredients are safe for use in cosmetic products in the practices of use and concentration described in the safety assessment when formulated to avoid irritation. A report on Alumina Magnesium Metasilicate (now called Magnesium Aluminometasilicate), Aluminum Iron Silicates, and Sodium Potassium Aluminum Silicate was finalized by the Panel in 2009, with the conclusion that these ingredients are safe as cosmetic ingredients in the practices of use and concentrations as described in the safety assessment.

These silicate ingredients that are inorganic oxides, comprising in part, silicon dioxide, are solids that can be derived from naturally occurring minerals. However, the ingredients in this safety assessment can be produced synthetically. The Panel considered the method of manufacture of these ingredients (whether synthetic or mined) to be of significant importance to safety, as synthetically derived ingredients are expected to have controlled material formation (i.e. exclusion of crystalline formation).

According to 2021 VCRP data, Magnesium Aluminum Silicate has the most reported uses in cosmetic products, with a total of 383; the majority of the uses are in leave-on eye makeup preparations and skin care preparations. Aluminum Calcium Sodium Silicate has the second most reported uses in cosmetic products, with a total of 103; the majority of the uses are in lipsticks. (The reported numbers of uses for the remaining ingredients in this report are much lower.) The frequencies of use for both of these ingredients have greatly changed since the original safety assessments were finalized; in 1998, Magnesium Aluminum Silicate was reported to have 632 uses, and in 2009, Aluminum Calcium Sodium Silicate was reported to have 7 uses. The results of the concentration of use survey conducted in 2018 by the Council indicate Aluminum Calcium Sodium Silicate has the highest reported maximum concentration of use for leave-on products; it is used at up to 26.3% in eye shadows. Magnesium Silicate is reported to have a maximum concentration of use for leave-on products of 21.6% in eye shadows. According to the original safety assessment, the maximum use concentration in 2008 for Aluminum Calcium Sodium Silicate was 6% in foundations and lipsticks. Additionally, according to 1999 data, there were no reported uses for Magnesium Silicate.

Potassium Silicate (30% solution in water) had a dermal LD_{50} > 5 g/kg in rats. In oral rat studies, the LD_{50}s were > 2 g/kg for Aluminum Silicate (concentration not reported), Sodium Magnesium Aluminum Silicate (concentration not reported), and Sodium Silicate. Calcium Silicate (20%) and Potassium Silicate (concentration not reported) had LD_{50}s of > 10 g/kg and > 5 g/kg in rats, respectively. An oral LD_{50} for Sodium Silicate in mice was 6.60 g/kg. Orally administered Aluminum Calcium Sodium Silicate had no adverse effects when tested up to 0.8 g/kg in mice. In an inhalation study, the LC_{50} for Potassium Silicate (30%) was > 2060 mg/m^3 following 4.4 h.

Aluminum Silicate, Sodium Metasilicate, Sodium Silicate, and Zinc Silicate were not genotoxic in Ames tests, HGPRT gene mutation assays, or chromosome aberration tests. Aluminum Calcium Sodium Silicate (hydrate; 0.5%) inhibited chromosomal aberrations (except polyploidy) in rats that received the test material and aflatoxin in feed. No carcinogenicity studies on the silicate ingredients were discovered in the published literature, and no unpublished data were submitted.

Aluminum Silicate and Zinc Silicate were predicted to be not irritating in EpiDerm™ skin assays. In rabbit studies, the irritation potential of Potassium Silicate (up to 36%) and Sodium Metasilicate (up to 97%) were dependent on concentration, with irritation observed starting at 33% for Potassium Silicate and slight irritation starting at 10% for Sodium Metasilicate. Aluminum Silicate (up to 25%) and Zinc Silicate (up to 50%) were not sensitizing in LLNA studies. Potassium Silicate (30%) was not sensitizing in guinea pig sensitization tests.

Aluminum Silicate (tested pure) was predicted to be not irritating using the hen's egg test chorioallantoic membrane (HET-CAM) method. Sodium Metasilicate (undiluted) was predicted to be corrosive in the isolated rabbit eye study, and Zinc Silicate (20%) was predicted to be irritating in a bovine corneal opacity and permeability (BCOP) test. Potassium Silicate was not irritating, at concentrations up to 29%, to slightly irritating, at 30% and 35%, in rabbit eyes.

Case reports of severe injury were reported from ingestion and inhalation of Sodium Metasilicate.

Occupational exposure limits for amorphous and crystalline silica have been set by OSHA and NIOSH. The California OEHHA has determined a limit to address continuous exposure for up to a lifetime. Silica exists in ambient air at ranges of <0.2 µg/m3 to 135 µg/m3 for amorphous silica and 0.25 µg/m^3 to 2.87 µg/m^3 for crystalline silica (urban air).

DISCUSSION FROM 2019 SYNTHETICALLY-MANUFACTURED AMORPHOUS SILICA AND HYDRATED SILICA REPORT

The Panel assessed the safety of synthetically-manufactured amorphous Silica and Hydrated Silica, and considered the method of manufacture of these ingredients (synthetic and not mined) to be of significant importance when reviewing safety.[5] The Panel emphasized that this report reviews only the safety of synthetically-manufactured amorphous Silica and Hydrated Silica. Crystalline silica, and synthetic and mined silicates are not toxicologically similar to synthetically-manufactured amorphous Silica and Hydrated Silica, and thus require separate reviews.

Data were sufficient to assess the safety of synthetically-manufactured amorphous Silica and Hydrated Silica, and the Panel determined that these two ingredients do not pose an incidental inhalation safety risk, under conditions of cosmetic use. The exposures that were tested in inhalation studies were at much higher concentrations than those possible with cosmetic use, and had very few adverse effects. Aggregation and agglomeration of Silica and Hydrated Silica particles in cosmetic formulations reduces potential inhalation exposure. While the Panel noted the effects on trachea-bronchial lymph nodes in mice, the carcinogenicity study used such high concentrations of Hydrated Silica that the effects were due to the overload of the animal system; therefore, concern over incidental inhalation of Silica in cosmetics was mitigated.

The Panel was concerned, however, that the potential exists for dermal and ocular irritation with the use of products formulated using Silica and Hydrated Silica. Therefore, the Panel specified that products containing these ingredients must be formulated to be non-irritating.

DISCUSSION

The Panel assessed the safety of 24 silicate ingredients. These inorganic oxides, comprising, in part, silicon dioxide, are solids that can be derived from naturally occurring minerals or can be produced synthetically. The Panel considered the method of manufacture of these ingredients (i.e., whether synthetic or mined) to be of significant importance to safety, as synthetically-derived ingredients are expected to have controlled crystalline material formation.

The Panel expressed concern that the potential exists for dermal irritation with the use of products formulated using silicate ingredients. Therefore, the Panel specified that products containing these ingredients must be formulated to be non-irritating.

Crystalline silica may be present in silicate ingredients, especially in ingredients that are naturally-sourced. Respirable crystalline silica may lead to an increased risk of lung diseases such as silicosis, chronic obstructive pulmonary disease, and lung cancer. Therefore, the Panel expressed concern about potential exposure to crystalline silica in formulations containing silicate ingredients which may be incidentally inhaled. No repeated dose inhalation studies of silicate ingredients were available. Consequently, the Panel determined that in the absence of these studies, the presence of crystalline silica in these ingredients should be below 0.1%, which is the level of detection for crystalline silica in the current state-of-the-art methodology X-ray diffraction. The Panel emphasized that this qualification is not an endorsement of safety at this level.

The Panel has become aware, through alternative sources, of the emergence of the use of airbrush technologies with silicate ingredients. The Panel considered information suggesting that a fraction of airborne particles resulting from airbrush delivery are respirable (i.e., aerodynamic equivalent diameter < 10 µm). 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).

CONCLUSION

The Panel concluded that the following 24 silicate ingredients are safe in the present practices of use and concentration in cosmetics that are not expected to be incidentally inhaled when formulated to be non-irritating. Additionally, the Panel concluded that these ingredients are safe for use in products that may be incidentally inhaled when the presence of crystalline silica is < 0.1%, OR, the results of a repeated dose inhalation study demonstrate no adverse effects when crystalline silica is present at ≥ 0.1%. However, the Panel also concluded that the available data are insufficient to make a determination of safety for the utilization of these ingredients with airbrush use.

Aluminum Calcium Sodium Silicate
Aluminum Iron Calcium Magnesium Germanium Silicates*
Aluminum Iron Calcium Magnesium Zirconium Silicates*
Aluminum Iron Silicates*
Aluminum Silicate
Ammonium Silver Zinc Aluminum Silicate
Calcium Magnesium Silicate*
Calcium Silicate
Lithium Magnesium Silicate
Lithium Magnesium Sodium Silicate
Magnesium Aluminometasilicate
Magnesium Aluminum Silicate
Magnesium Silicate
Magnesium Trisilicate*
Potassium Silicate
Pyrophyllite*
Sodium Magnesium Aluminum Silicate*
Sodium Magnesium Silicate
Sodium Metasilicate
Sodium Potassium Aluminum Silicate
Sodium Silicate
Sodium Silver Aluminum Silicate*
Zinc Silicate*
Zirconium Silicate*

**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 and reported functions of the ingredients in this safety assessment.[4]

Ingredient & CAS No.	Definition	Function(s)
Aluminum Calcium Sodium Silicate 1344-01-0	Aluminum Calcium Sodium Silicate is a complex silicate refined from naturally occurring minerals.	Bulking Agents
Aluminum Iron Calcium Magnesium Germanium Silicates	Aluminum Iron Calcium Magnesium Germanium Silicates is a ceramic powder consisting mainly of silicon dioxide, aluminum oxide, ferric oxide, calcium oxide, magnesium oxide and germanium oxide.	Anticaries Agents; Antifungal Agents; Antimicrobial Agents; Antioxidants
Aluminum Iron Calcium Magnesium Zirconium Silicates	Aluminum Iron Calcium Magnesium Zirconium Silicates is a ceramic powder consisting mainly of silicon dioxide, aluminum oxide, ferric oxide, calcium oxide, magnesium oxide and zirconium oxide.	Bulking Agents
Aluminum Iron Silicates	Aluminum Iron Silicates is a ceramic powder consisting mainly of silicon dioxide, aluminum oxide, and ferric oxide.	Abrasives; Bulking Agents
Aluminum Silicate 1327-36-2	Aluminum Silicate is a complex inorganic salt that has a composition consisting generally of 1 mole of alumina and 1 to 3 moles of silica.	Abrasives; Absorbents; Anticaking Agents; Bulking Agents: Opacifying Agents; Slip Modifiers
Ammonium Silver Zinc Aluminum Silicate	Ammonium Silver Zinc Aluminum Silicate is a complex silicate formed from the reaction of zinc nitrate, Ammonium Nitrate, and Silver Nitrate with zeolite.	Absorbents; Deodorant Agents; Preservatives
Calcium Magnesium Silicate 12765-06-9	Calcium Magnesium Silicate is a synthetic silicate clay consisting chiefly of calcium and magnesium silicates	Absorbents; Deodorant Agents
Calcium Silicate 1344-95-2	Calcium Silicate is a hydrous or anhydrous silicate with varying proportions of calcium oxide and silica.	Absorbents; Bulking Agents; Opacifying Agents
Lithium Magnesium Silicate 37220-90-9	Lithium Magnesium Silicate is a synthetic silicate clay consisting mainly of lithium and magnesium silicates.	Binders; Bulking Agents; Viscosity Increasing Agents - Aqueous
Lithium Magnesium Sodium Silicate 53320-86-8	Lithium Magnesium Sodium Silicate is a synthetic silicate clay consisting mainly of lithium, magnesium and sodium silicates.	Bulking Agents; Viscosity Increasing Agents - Aqueous
Magnesium Aluminometasilicate 12408-47-8	Magnesium Aluminometasilicate is the inorganic compound consisting of varying amounts of magnesium oxide, aluminum oxide and silica.	Absorbents; Anticaking Agents; Bulking Agents; Opacifying Agents; Slip Modifiers; Viscosity Increasing Agents – Aqueous; Viscosity Increasing Agents – Nonaqueous
Magnesium Aluminum Silicate 12199-37-0 12511-31-8	Magnesium Aluminum Silicate is a complex silicate refined from naturally occurring minerals.	Absorbents; Anticaking Agents; Bulking Agents; Opacifying Agents; Slip Modifiers; Viscosity Increasing Agents - Aqueous
Magnesium Silicate 1343-88-0	Magnesium Silicate is an inorganic salt of variable composition which consists mainly of $MgO \cdot SiO_2 \cdot xH_2O$.	Absorbents; Anticaking Agents; Bulking Agents; Opacifying Agents; Slip Modifiers; Viscosity Increasing Agents - Aqueous
Magnesium Trisilicate 14987-04-3	Magnesium Trisilicate is the inorganic compound that conforms generally to the formula $2MgO \cdot 3SiO_2 \cdot xH_2O$.	Abrasives; Absorbents; Anticaking Agents; Bulking Agents; Opacifying Agents; Slip Modifiers; Viscosity Increasing Agents - Aqueous
Potassium Silicate 1312-76-1	Potassium Silicate is a potassium salt of silicic acid.	Corrosion Inhibitors
Pyrophyllite 113349-10-3; 113349-11-4; 113349-12-5; 12269-78-2; 141040-73-5; 141040-74-6	Pyrophyllite is a naturally occurring mineral substance consisting predominantly of a hydrous aluminum silicate represented as $Al_2O_3 \cdot 4SiO_2 \cdot H_2O$.	Absorbents; Colorants; Opacifying Agents
Sodium Magnesium Silicate	Sodium Magnesium Silicate is a synthetic silicate clay with a composition mainly of magnesium and sodium silicate.	Binders; Bulking Agents
Sodium Magnesium Aluminum Silicate 12040-43-6	Sodium Magnesium Aluminum Silicate is the complex silicate obtained by the reaction of Sodium Silicate and Sodium Aluminate in an aqueous solution of Magnesium Nitrate.	Absorbents
Sodium Metasilicate 6834-92-0	Sodium Metasilicate is the inorganic salt that conforms to the formula Na_2SiO_3.	Chelating Agents; Corrosion Inhibitors
Sodium Potassium Aluminum Silicate 12736-96-8; 66402-68-4	Sodium Potassium Aluminum Silicate is a complex silicate refined from naturally occurring minerals, or derived synthetically.	Bulking Agents
Sodium Silicate 1344-09-8	Sodium Silicate is a sodium salt of silicic acid.	Buffering Agents; Corrosion Inhibitors; pH Adjusters
Sodium Silver Aluminum Silicate	Sodium Silver Aluminum Silicate is the complex silicate obtained by the reaction of sodium silicate with sodium aluminate in an aqueous solution of sodium nitrate, sodium hydroxide and silver nitrate.	Absorbents; Deodorant Agents
Zinc Silicate 13597-65-4	Zinc Silicate is an inorganic salt consisting of variable amounts of zinc oxide and silica.	Deodorant Agents
Zirconium Silicate 10101-52-7 1344-21-4	Zirconium Silicate is the inorganic compound that conforms to the formula $ZrSiO_4$.	Abrasives; Opacifying Agents

Table 2. Chemical properties

Property	Value	Reference
	Aluminum Silicate	
Physical Form	Light brown to brown, odorless beads	[12]
Formula Weight (Da)	162.05 - 426.05	[1]
Density (g/ml @ 20ºC)	3.156; 3.247	[1]
	Calcium Silicate	
Physical Form	White or slightly cream-colored free-flowing powder	[1]
Formula Weight (Da)	116.16	[1]
Density (g/ml @ 25ºC)	0.227	[13]
Melting Point (ºC)	1710	[13]
Water Solubility (mg/l @ 20ºC)	260	[13]
pH	8.4-12.5 (5% slurry)	[22]
	Magnesium Aluminum Silicate	
Physical Form	Off-white to creamy white small flakes or micronized powder	[1]
Formula Weight (Da)	262.4	[1]
pH	9.0-10.0 (5% aqueous solution)	[1]
	Magnesium Silicate	
Physical Form	Fine, white, odorless, tasteless powder, free from grittiness	[1]
pH	7.0-11.0 (1 in 10 slurry)	[23]
	Magnesium Trisilicate	
Physical Form	Fine, white, odorless, tasteless powder, free from grittiness	[1]
	Potassium Silicate	
Physical Form	Yellowish to colorless, translucent to transparent, hygroscopic	[2]
Density (g/ml @ 20ºC)	1.26-1.60	[9]
Vapor Pressure (mmHg @ 1175ºC)	0.00772	[9]
Melting Point (ºC)	905	[9]
	Sodium Magnesium Silicate	
pH	8.5-10.5 (2% aqueous dispersion)	[1]
	Sodium Magnesium Aluminum Silicate	
Physical Form	White powder	[8]
Density (g/ml @ 20ºC)	2.11	[8]
Melting Point (ºC)	> 400	[8]
Water Solubility (mg/l @ 20ºC)	2.24	[8]
	Sodium Metasilicate	
Physical Form	Nonahydrate, efflorescent platelets	[2]
Formula Weight (Da)	122.08	[2]
Density (g/ml)	2.614	[2]
Vapor Pressure (mmHg @ 1175ºC)	0.00772	[10]
Melting Point (ºC)	1089	[2]
Water Solubility (g/l @ 20 ºC)	210	[10]
pH	12 (0.1% solution)	[2]
	Sodium Silicate	
Physical Form	Colorless to white or grayish-white, crystal-like clumps or aqueous solutions	[2]
Density (g/ml)	1.26 - 1.71	[11]
Vapor Pressure (mmHg)	0.00120	[11]
Melting Point (ºC)	730 - 870	[11]
Water Solubility (mg/l @ 20 ºC)	115	[11]
Acidity/Alkalinity	Strongly alkaline	[2]
	Zinc Silicate	
Physical Form	White crystals or white powder	[53,54]
Formula Weight (Da)	222.90	[54]
Density (g/ml)	4.103	[53]
Melting Point (ºC)	1509	[53]
Water Solubility (µg/l @ 20 ºC)	162.01	[7]
	Zirconium Silicate	
Physical Form	Bipyramidal crystals, colorless unless has impurities and radioactive bombardment; red or various colored crystals	[1]
Formula Weight (Da)	183.31	[1]
Density (g/ml)	4.56	[1]
pH	6-7.5 (10% aqueous slurry)	[1]

Table 3. Method of manufacturing and product specifications for silicate ingredients.[15]

Ingredient	Form	Typical Particle Size	Crystallinity	Method of Manufacturing	Purity	Reference
Calcium Silicate	Powder solid	2-30 µm	< 0.2%	Reaction of Sodium Silicate and a calcium source in solution. The suspension received from the reaction is filtered and the Calcium Silicate is further washed and dried.	Purity typically in accordance with JECFA specification; not specifically marketed for cosmetics use.	15
Calcium Silicate (generic)	NR	NR	NR	Manufactured from diatomaceous earth or precipitated silica; diatomaceous earth-based products are produced through hydrothermal reaction processes, which combine natural, or flux-calcined diatomaceous earth with hydrated lime to produce synthetic mineral forms of gyrolite and tobermorite; in precipitated or other silica-based products, Calcium Silicate is produced by reacting Sodium Silicate and calcium oxide.	NR	16
Magnesium Silicate	Powder solid	3-20 µm, some grades larger	< 0.2%	Reaction of Sodium Silicate and a magnesium source in solution. The suspension received from the reaction is filtered and the Magnesium Silicate is further washed and dried	Purity typically in accordance with JECFA specification; not specifically marketed for cosmetics use.	15
Magnesium Aluminum Silicate	NR	NR	< 0.1%	Obtained by mining; material undergoes several processing steps after being extracted from the Earth, including washing, drying, and milling in order to obtain a product with uniform characteristics.	100%	17
Potassium Silicate	Liquid	NA – Liquid	< 0.1%	Reaction of sand and potassium carbonate, reaction is dissolved, filtered, and sold as a liquid.	Impurities originate in the raw materials. Typical total impurity levels are less than 500 ppm.	15
Sodium Magnesium Silicate	NR	NR	ND by X-ray diffraction	Hydrothermal synthesis from silicon, sodium, and magnesium sources	100%	18
Sodium Metasilicate	Powder	212-859 µm	< 0.1%	Sodium Metasilicate is made by adding caustic soda to liquid Sodium Silicate to obtain an equal molar ratio of sodium oxide to sodium dioxide. The resulting metasilicate liquor is then cooled to crystallize the pentahydrate product or passed through a dryer to remove water and yield the anhydrous product.	Impurities originate in the raw materials. Typical total impurity levels are less than 500 ppm.	15
Sodium Silicate (hydrous)	Powder or granules	80-700 µm	< 0.1%	Reaction of sand and sodium carbonate at high temperature, reaction is dissolved, filtered, and spray dried to make powder	Impurities originate in the raw materials. Typical total impurity levels are less than 500 ppm.	15
Sodium Silicate	Liquid	NA – Liquid	< 0.1%	Reaction of sand and sodium carbonate at high temperatures, reaction is dissolved, filtered, and sold as a liquid.	Impurities originate in the raw materials. Typical impurity levels are less than 500 ppm.	15
Sodium Silver Aluminum	NR	NR	NR	Obtain by reaction of nitric acid, sodium hydroxide, and sodium aluminate with Sodium Silicate (water glass) in ion exchange water at 100º C; resulting solution is then reacted with silver nitrate and dried at 150º C.	NR	19

JECFA = Joint Food and Agriculture Organization of the United Nations (FAO)/World Health Organization (WHO) Expert Committee on Food Additives
NA = Not applicable NR = Not reported ND = not detected

Table 4. Current and historical frequency and concentration according to duration and type of exposure for previously reviewed silicates.[1-3,25-27]

	Aluminum Silicate				Aluminum Calcium Sodium Silicate			
	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	2021	**1998**	**2018**	**1999**	**2021**	**2009**	**2018**	**2008**
Totals*	**5**	**10**	**2.8-4.6**	**0.5-37**	**103**	**7**	**0.0001-26.3**	**0.4-6**
Leave-On	4	6	NR	0.5-3	101	7	0.0001-26.3	0.4-6
Rinse-Off	1	4	2.8-4.6	2-37	2	NR	NR	NR
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR	NR	NR
Eye Area	NR	2	NR	0.5	10	NR	0.006-26.3	0.5
Incidental Ingestion	NR	NR	NR	37	59	NR	3.5-5.5	6
Incidental Inhalation-Spray	1; 2[a]	1[a]	NR	NR	1; 9[a]; 1[b]	1[a]	NR	NR
Incidental Inhalation-Powder	NR	NR	NR	NR	1[b]	1	NR	NR
Dermal Contact	2	8	2.8-4.6	2-3	33	3	0.006-26.3	0.4-6
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	1	NR	NR	NR	3	NR	NR	NR
Hair-Coloring	2	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	8	4	0.0001-0.25	0.5
Mucous Membrane	NR	NR	4.6	37	59	NR	3.5-5.5	6
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

	Ammonium Silver Zinc Aluminum Silicate				Calcium Silicate			
	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	2021	**NA**	**2018**	**NA**	**2021**	**1998**	**2018**	**1999**
Totals*	**27**	**NA**	**0.001**	**NA**	**28**	**132**	**0.00013-20**	**0.3-10**
Leave-On	27	NA	NR	NA	27	115	0.00013-5	0.3-10
Rinse-Off	NR	NA	0.001	NA	1	1	1.5-20	8
Diluted for (Bath) Use	NR	NA	NR	NA	NR	16	0.86-1.3	NR
Eye Area	19	NA	NR	NA	2	11	1	1-8
Incidental Ingestion	NR	NA	NR	NA	NR	3	0.00013	0.5
Incidental Inhalation-Spray	NR	NA	NR	NA	1[a]; 1[b]	NR	0.005	NR
Incidental Inhalation-Powder	2	NA	NR	NA	16; 1[b]	75	0.25-5; 4.7-5[c]	0.3-10
Dermal Contact	27	NA	0.001	NA	28	128	0.25-20	0.3-10
Deodorant (underarm)	NR	NA	NR	NA	NR	NR	NR	NR
Hair - Non-Coloring	NR	NA	NR	NA	NR	NR	1.5	NR
Hair-Coloring	NR	NA	NR	NA	NR	NR	0.005	NR
Nail	NR	NA	NR	NA	1	1	NR	NR
Mucous Membrane	NR	NA	NR	NA	9	19	0.00013-1.3	0.5
Baby Products	NR	NA	NR	NA	NR	NR	NR	NR

Table 4. Current and historical frequency and concentration according to duration and type of exposure for previously reviewed silicates.[1-3,25-27]

	Lithium Magnesium Silicate				Lithium Magnesium Sodium Silicate			
	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	2021	**1998**	**2018**	**1999**	**2021**	**1998**	**2018**	**1999**
Totals*	**1**	**NR**	**0.3-5**	**NR**	**97**	**NR**	**0.0005-6**	**NR**
Leave-On	1	NR	0.3-5	NR	95	NR	0.0005-6	NR
Rinse-Off	NR	NR	NR	NR	2	NR	0.4	NR
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR	NR	NR
Eye Area	NR	NR	NR	NR	13	NR	0.0005-4	NR
Incidental Ingestion	NR	NR	NR	NR	46	NR	NR	NR
Incidental Inhalation-Spray	1[b]	NR	0.4; 0.3[a]	NR	1[a]	NR	6[a]	NR
Incidental Inhalation-Powder	1[b]	NR	5[c]	NR	1	NR	3[c]	NR
Dermal Contact	1	NR	0.4-5	NR	48	NR	0.0005-4	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	0.5	NR
Hair - Non-Coloring	NR	NR	0.3	NR	NR	NR	6	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	2	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	46	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

	Magnesium Aluminometasilicate				Magnesium Aluminum Silicate			
	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	2021	**2009**	**2018**	**2008**	**2021**	**1998**	**2018**	**1999**
Totals*	**22**	**NR**	**NR**	**0.002-0.01**	**383**	**632**	**0.0004-11**	**0.1-5**
Leave-On	21	NR	NR	0.002-0.01	303	509	0.0008-11	0.1-5
Rinse-Off	1	NR	NR	NR	80	122	0.0004-10	0.1-5
Diluted for (Bath) Use	NR	NR	NR	NR	NR	1	NR	NR
Eye Area	2	NR	NR	NR	72	76	0.0025-4.5	0.2-5
Incidental Ingestion	NR	NR	NR	NR	1	3	0.93	0.7
Incidental Inhalation-Spray	1[a,b]	NR	NR	0.002-0.01[b]	67[a]; 82[b]	2; 106[a]; 75[b]	0.5-0.8[a]	0.3-5[a,b]
Incidental Inhalation-Powder	1[b]	NR	NR	0.002-0.01[b]	7; 82[b]; 4[c]	75[b]	1; 0.3-11[c]	0.3-5[b]
Dermal Contact	21	NR	NR	0.002-0.01	360	583	0.0004-11	0.1-5
Deodorant (underarm)	NR	NR	NR	NR	2[a]	5[a]	0.5-0.7	0.5-1[a]
Hair - Non-Coloring	NR	NR	NR	NR	9	10	0.19-0.8	1-2
Hair-Coloring	NR	NR	NR	NR	1	1	NR	2
Nail	NR	NR	NR	NR	NR	2	NR	NR
Mucous Membrane	NR	NR	NR	NR	9	19	0.93	0.5-2
Baby Products	NR	NR	NR	NR	4	NR	NR	NR

Table 4. Current and historical frequency and concentration according to duration and type of exposure for previously reviewed silicates.[1-3,25-27]

	Magnesium Silicate				Potassium Silicate			
	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	2021	**1998**	**2018**	**1999**	**2021**	**2001**	**2018**	**1999/2000**
Totals*	**42**	**NR**	**0.001-21.6**	**NR**	**1**	**2**	**NR**	**NR**
Leave-On	40	NR	0.001-21.6	NR	NR	1	NR	NR
Rinse-Off	2	NR	NR	NR	1	1	NR	NR
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR	NR	NR
Eye Area	14	NR	3-21.6	NR	NR	NR	NR	NR
Incidental Ingestion	5	NR	10	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	1[a]; 2[b]	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Powder	5; 2[b]	NR	1[c]	NR	NR	NR	NR	NR
Dermal Contact	35	NR	0.001-21.6	NR	1	1	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	NR	1	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	1	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	5	NR	10	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

	Sodium Magnesium Silicate				Sodium Metasilicate			
	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	2021	**1998**	**2018**	**1999**	**2021**	**2001**	**2018**	**1999/2000**
Totals*	**63**	**34**	**0.13-0.2**	**0.08-5**	**63**	**191**	**0.001-15**	**13-18**
Leave-On	55	33	0.13	0.08-5	4	NR	0.001	NR
Rinse-Off	7	1	0.2	0.3-5	59	191	1.2-15	13-18
Diluted for (Bath) Use	1	NR	NR	NR	NR	NR	0.1	NR
Eye Area	13	13	NR	0.08-0.4	NR	NR	NR	NR
Incidental Ingestion	18	1	NR	0.3-3	NR	NR	NR	NR
Incidental Inhalation-Spray	1[a]; 4[b]	2[a]; 5[b]	NR	1-5[a]; 0.1-5[b]	1[a,b]	NR	NR	NR
Incidental Inhalation-Powder	7; 4[b]	4; 5[b]	NR	0.4; 0.1-5[b]	1[b]	NR	NR	NR
Dermal Contact	43	31	0.13-0.2	0.08-5	1	2	0.001-1.2	NR
Deodorant (underarm)	NR	NR	NR	0.5[a]	NR	NR	NR	NR
Hair - Non-Coloring	NR	1	NR	NR	3	1	NR	NR
Hair-Coloring	NR	NR	NR	NR	59	188	5-15	13-18[e]
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	20	1	NR	0.3	NR	NR	0.1	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

Table 4. Current and historical frequency and concentration according to duration and type of exposure for previously reviewed silicates.[1-3,25-27]

	Sodium Potassium Aluminum Silicate				Sodium Silicate			
	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	2021	**2009**	**2018**	**2008**	**2021**	**2001**	**2018**	**1999/2000**
Totals*	**31**	**1**	**0.36-1.1**	**0.001-4**	**55**	**22**	**0.017-35**	**0.06-55**
Leave-On	31	NR	0.36-1.1	0.001-4	14	2	NR	0.6-1
Rinse-Off	NR	1	NR	NR	41	20	0.017-35	0.06-55
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR	NR	NR
Eye Area	1	NR	1.1	NR	7	1	NR	NR
Incidental Ingestion	9	NR	NR	NR	2	NR	0.44	0.6
Incidental Inhalation-Spray	9[a]	NR	NR	NR	1[a]; 2[b]	1[b]	NR	NR
Incidental Inhalation-Powder	1	NR	0.36[c]	NR	2[b]	1[b]	NR	NR
Dermal Contact	22	1	0.36-1.1	NR	27	14	0.017-1.5	0.06-10
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	2	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	24	8	15-35	1-55[f]
Nail	NR	NR	NR	0.001-4	NR	NR	NR	NR
Mucous Membrane	9	NR	NR	NR	3	2	0.44-1.4	0.06-7
Baby Products	NR	NR	NR	NR	NR	NR	NR	0.6

NR = Not reported. NA = Not applicable.

† 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 may be sprays, but it is not specified whether the reported uses are sprays.

[b.] Not specified whether a powder or a spray, so this information is captured for both categories of incidental inhalation.

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

[d.] Concentration of use in aerosol deodorants reported to be 0.0001% - 0.084%.

[e.] Hair bleaches were diluted from 13% -18% to 7% -14% before use.

[f.] Hair bleaches were diluted from 16%-55% to 1%-20% before use.

Table 5. Ingredients not reported to be in use.[25-27]

Aluminum Iron Calcium Magnesium Germanium Silicates
Aluminum Iron Calcium Magnesium Zirconium Silicates
Aluminum Iron Silicates*
Calcium Magnesium Silicate
Magnesium Trisilicate*
Pyrophyllite*
Sodium Magnesium Aluminum Silicate
Sodium Silver Aluminum Silicate
Zinc Silicate
Zirconium Silicate*

*Previously reviewed ingredients in red. Additionally, no uses were reported in original safety assessment.

Table 6. Acute toxicity studies

Ingredient/Concentration/Vehicle	Dose/Study Protocol	Results	LD_{50} or LC_{50}	Reference
Dermal				
30% Potassium Silicate solution in water; molar ratio = 2.47	5000 mg/kg bw applied for 24 h to 5 male and 5 female Sprague-Dawley rats; test sites were occluded	Erythema and alopecia noted at application site of 4 females and 1 male between days 1 and 8; no other adverse effects during observation period or necropsy	> 5000 mg/kg	[9]
Oral				
Aluminum Calcium Sodium Silicate (hydrated)	400, 600, or 800 mg/kg; 6 female Balb/c mice; no further details	No adverse effects reported	> 800 mg/kg bw	[57,58]
Aluminum Silicate in water; concentration not reported	2000 mg/kg bw; 3 female Sprague-Dawley rats via gavage	No mortality occurred from dosing; no clinical signs of toxicity; no treatment-related effects at necropsy	> 2000 mg/kg bw	[12]
20% Calcium Silicate in feed	10,000 mg/kg bw; 10 male and 10 female Wistar rats via diet	No mortality occurred from dosing; no significant clinical findings; no treatment-related effects at necropsy	> 10,000 mg/kg bw	[13]
Potassium Silicate; undiluted; no further details reported	5000 mg/kg bw in 3 female Sprague-Dawley rats via gavage	No deaths occurred following treatment; no clinical or gross macroscopic signs of toxicity observed	> 5000 mg/kg bw	[9]
Potassium Silicate; concentration and vehicle not reported	3300, 3960, 4750, 5700, or 6860 mg/kg bw; 5 male and 5 female Cpb; Wu Wistar rats per dose; method of delivery not reported	Deaths per dose = 1/10 at 2.50 ml/kg, 2/10 at 3.00 ml/kg, 2/10 at 3.60 ml/kg, 3/10 at 4.32 ml/kg, and 10/10 at 5.20 ml/kg; sedation, signs of abdominal discomfort, sluggishness and unconsciousness were all reversible; no treatment-related effects at necropsy	5700 mg/kg bw	[14]
Sodium Magnesium Aluminum Silicate in water; no further details reported	2000 mg/kg bw in 6 female Sprague-Dawley rats via gavage	No deaths occurred following treatment; no clinical or gross macroscopic signs of toxicity observed	> 2000 mg/kg bw	[8]
Sodium Silicate; molar ratio = 3.35; no additional details provided	Male mice; no additional details provided	No details provided	6600 mg/kg bw	[11]
Sodium Silicate; molar ratio 3.27; concentration and vehicle not reported	3430, 4110, 4930, 5890, 7120, or 8490 mg/kg bw; 5 male and female Cpb:Wu Wistar rats per dose via gavage	Deaths per dose = 0/10 at 3430 mg/kg, 2/10 at 4110 mg/kg, 9/10 at 4930, 5890, and 7120 mg/kg, and 10/10 at 8490 mg/kg; sedation, signs of abdominal discomfort, sluggishness and unconsciousness; no treatment-related effects at necropsy	5150 mg/kg bw	[11]
Sodium Silicate; molar ratio = 3.3; no additional details provided	Rats; no additional details provided	No details provided	> 2000 mg/kg bw	[11]
Sodium Silicate in water; molar ratio = 3.38	Male Wistar rats; no additional details provided	Breathing difficulties, staggering gait, reduced motility; additional effects not reported	8650 mg/kg bw	[11]
Inhalation				
30% Potassium Silicate solution in water; molar ratio 2.47; particle size distribution = 4% at 9 µm, 8.3% at 5.8 µm, 11.1% at 4.7 µm, 12% at 3.3 µm, 32% at 2.1 µm, 2.6% at 1.1 µm, 7.4% at 0.7 µm, and 2.6% at 0.4 µm)	2060 mg/m^3; whole body exposure for 4.4 h to 5 male and 5 female Sprague-Dawley rats	Animals had hunched posture and hypoactivity during exposure that reversed; no deaths or adverse effects during observation period or necropsy	> 2060 mg/m^3	[9]

Table 7. Genotoxicity studies

Ingredient/Concentration/Dose	Species/Strain/Cell	Method	Results	Reference
		In Vitro		
Aluminum Silicate in water, up to 5017 µg/plate, with or without metabolic activation	*Salmonella typhimurium* strains TA97a, TA98, TA100, TA102, and TA1535	Ames test	Not genotoxic	[12]
Aluminum Silicate in DMSO; up to 250 µg/ml without metabolic activation; up to 500 µg/ml with metabolic activation	Chinese hamster ovary	HGPRT gene mutation assay	Not genotoxic	[12]
Sodium Metasilicate; up to 5000 µg/plate, with or without metabolic activation	*S. typhimurium* strains TA98, TA100, TA 1535, TA 1537 and *Escherichia coli* WP2	Ames test	Not genotoxic	[10]
Sodium Metasilicate; up to 675 µg/ml without metabolic activation and up to 1800 µg/ml with metabolic activation	Chinese hamster V79 cells	HGPRT gene mutation assay	Not genotoxic	[10]
36% Sodium Silicate; molar ratio = 3.3; up to 156.3 µg/ml with and without metabolic activation	Chinese hamster V79 cells	Chromosome aberration test	Not genotoxic	[11]
36% Sodium Silicate; molar ratio = 3.35; up to 675 µg/ml without metabolic activation and up to 1800 µg/ml with metabolic activation	Chinese hamster V79 cells	HGPRT gene mutation assay	Not genotoxic	[11]
Zinc Silicate; 100, 316, 1000, 3160 or 5000 µg/plate with or without metabolic activation	*S. typhimurium* strains TA98, TA100, TA102, TA1535, and TA1537	Ames test	Not genotoxic	[7]

Table 8. Dermal irritation and sensitization

Ingredient/Concentration/ Dose/Vehicle	Test System	Method	Results	Reference
		Irritation – In Vitro		
Aluminum Silicate; 25 mg in Dulbecco's phosphate buffered saline	EpiDerm™ tissue	EpiDerm™ human skin model; material applied for 30 min	Not irritating	[12]
Zinc Silicate; undiluted; 25 mg	EpiDerm™ tissue	EpiDerm™ reconstructed human epidermis model in accordance with OECD Test Guideline 439; test material applied to 0.63 cm^2 test tissue for 60 min	Not irritating	[7]
		Irritation – Animal		
25% dilution of 29% (weight) Potassium Silicate; molar ratio = 3.9; 0.5 ml in deionized water	5 New Zealand White rabbits; sex not reported	Dermal irritation study in accordance with OECD Test Guideline 404; test material applied to shaved test site and occluded for 4 h before being rinsed; test site examined for up to 7 d	Not irritating; PDII = 0	[9,14]
25% dilution of 35% (weight) Potassium Silicate; molar ratio = 3.4; 0.5 ml in deionized water	3 New Zealand White rabbits; sex not reported	Dermal irritation study in accordance with OECD Test Guideline 404; test material applied to shaved test site and occluded for 4 h before being rinsed; test site examined for up to 7 d	Not irritating; very slight erythema 24 and 48 h after treatment; PDII = 0	[9,14]
29% (weight) Potassium Silicate; molar ratio = 3.9; 0.5 ml in deionized water	5 New Zealand White rabbits; sex not reported	Dermal irritation study in accordance with OECD Test Guideline 404; test material applied to shaved test site and occluded for 4 h before being rinsed; test site examined for up to 7 d	Not irritating; slight erythema cleared by 24 h ;PDII = 0.25	[9,14]
33% (weight) Potassium Silicate; molar ratio = 3.0; 0.5ml in water	1 male New Zealand White rabbit	Dermal irritation study in accordance with OECD Test Guideline 404; test material applied to shaved test site and semi-occluded for 4 h before being rinsed off with water; test site examined for up to 5 d	Moderately irritating; well-defined erythema and very slight edema persisted for at least 5 d; PDII =3	[9,14]
35% (weight) Potassium Silicate; molar ratio = 3.4; 0.5ml in deionized water	3 New Zealand White rabbits; sex not reported	Dermal irritation study in accordance with OECD Test Guideline 404; test material applied to shaved test site and occluded for 4 h before being rinsed; test site examined for up to 7 d	Not irritating; slight erythema after 1 h that cleared after 48 h; PDII = 0.17	[9,14]

Table 8. Dermal irritation and sensitization

Ingredient/Concentration/ Dose/Vehicle	Test System	Method	Results	Reference
36% (weight) Potassium Silicate; molar ratio = 2.0; 0.5ml in water	1 female New Zealand White rabbit	Dermal irritation study in accordance with OECD Test Guideline 404; test material applied to shaved test site and semi-occluded for 4 h before being rinsed off with water; test site examined for up to 5 d	Slightly irritating; transient erythema observed cleared by day 5; primary dermal irritation index (PDII) = 1	[9,14]
10% aq. Sodium Metasilicate; 0.5 ml in water	3 rabbits; strain and sex not reported	Dermal irritation study in accordance with OECD Test Guideline 404; test material applied to shaved test site and semi-occluded for 4 h before being rinsed; test site examined for up to 72 h	Slightly irritating; severity of erythema reduced but persisted through day 2; edema in 1 animal reversed by day 2; PDII = 1.22	[10]
50% aq. Sodium Metasilicate; 0.5 ml in water	3 rabbits; strain and sex not reported	Dermal irritation study in accordance with OECD Test Guideline 404; test material applied to shaved test site and semi-occluded for 4 h before being rinsed; test site examined for up to 72 h	Irritating; PDII = 3.67	[10]
57.5% (weight) Sodium Metasilicate (pentahydrate); 0.5 g	3 white landrace rabbits; sex not reported	Dermal irritation study in accordance with OECD Test Guideline 404; test material applied to shaved test site and semi-occluded for 4 h before being rinsed; test site examined for up to 14 d	Corrosive; 2/3 animals had acute skin necrosis and the 3rd had pigmented necrosis; wounds persisted for more than 14 d; PDII = 7.8	[10]
83% (w/w) Sodium Metasilicate as aqueous paste; pH 12.4; 0.5 g/0.10 purified water; 0.3 ml applied	3 male New Zealand hybrid rabbits	Dermal irritation study in accordance with OECD Test Guideline 404; test material applied to shaved test site and semi-occluded for 4 h before being rinsed; test site examined for up to 14 d	Corrosive; erythema persisted for at least 14 d; edema observed 1 h post-treatment but cleared by 72 h; necrosis persisted 7-14+ d; PDII = 4.67	[10]
97% (weight) Sodium Metasilicate (anhydrous); 0.5 g	3 white landrace rabbits; sex not reported	Dermal irritation study in accordance with OECD Test Guideline 404; test material applied to shaved test site and semi-occluded for 4 h before being rinsed; test site examined for up to 14 d	Corrosive; 2/3 animals had acute skin necrosis with well-defined edema; wounds persisted for more than 14 d; third animal had wounds that were observed at up to 72 h but had healed by day 14;PDII = 5.1	[10]
Sodium Metasilicate (anhydrous); 0.5 g in water	1 male New Zealand White rabbits	Dermal irritation study in accordance with OECD Test Guideline 404; test material applied to shaved test site and semi-occluded for 4 h before being rinsed; test site examined for up to 5 d	Corrosive; necrosis observed; PDII = 8; no erythema or edema observed when applied as dry powder	[10]
Sodium Metasilicate (pentahydrate); 0.5 g in water	1 female New Zealand White rabbits	Dermal irritation study in accordance with OECD Test Guideline 404; test material applied to shaved test site and semi-occluded for 4 h before being rinsed; test site examined for up to 5 d	Corrosive; necrosis observed; PDII = 8; no erythema or edema observed when applied as dry powder	[10]
Sodium Metasilicate; concentration not reported; fine powder with pH of 12.4 tested undiluted; 0.5 g	3 New Zealand White rabbits; sex not reported	Dermal irritation study in accordance with OECD Test Guideline 404; test material applied to shaved test site and semi-occluded for 4 h before being rinsed; test site examined for up to 14 d	Not irritating; 1/3 animals had erythema and edema 1 h post-treatment that cleared by 72 h; PDII = 0.17	[10]
Sensitization – Animal				
0%, 5%, 10%, or 25% (w/v) Aluminum Silicate in dimethyl sulfoxide; application volume = 25 µl	4 female CBA/CaOlaHsd mice/dose group	Local lymph node assay (LLNA)	Not sensitizing; stimulation indices (SI) below 3	[12]
30% Potassium Silicate solution; molar ratio = 2.47	20 male Hartley guinea pigs received test material; 10 animals served as control	Buehler sensitization test; animals were induced with undiluted test material and challenged at 75%	Not sensitizing	[9]
0%, 10%, 25%, or 50% Zinc Silicate in acetone/olive oil (4:1; v/v)	6 female NMRI mice/dose group	LLNA	Not sensitizing; SI below 1.4; irritant response noted	[7]

Table 9. Ocular irritation

Ingredient/Concentration/ Dose/Vehicle	Test System	Method	Results	Reference
		In Vitro		
Aluminum Silicate tested pure; no vehicle; 164.3 mg	Lohmann Leghorn chicken eggs	HET-CAM method; treatment duration = 5 min	Not irritating	[12]
Sodium Metasilicate; undiluted; 50 mg	New Zealand White rabbit eyes	Isolated rabbit eye study; treatment duration = 0.17 min; eyes studied for opacity for up to 4 h post-treatment	Corrosive	[10]
Zinc Silicate; 20% suspension in 750 µl of physiological saline solution (0.9% NaCl)	Bovine corneas	Bovine corneal opacity and permeability test (BCOP); exposure was 4 h	Irritating; mean opacity score of 3 corneas was 6.31; mean fluorescein retention/leakage score was < 0.01	[7]
		Animal		
25% dilution of 29% (weight) Potassium Silicate; molar ratio = 3.9; 0.1 ml in deionized water	6 New Zealand White rabbits; sex not reported	Ocular irritation study in accordance with OECD Test Guideline 405; eyes not rinsed; observed for up to 7 d post-treatment	Not irritating	[9,14]
25% dilution of 35% (weight) Potassium Silicate; molar ratio = 3.4; 0.1 ml in water	3 New Zealand White rabbits; sex not reported	Ocular irritation study in accordance with OECD Test Guideline 405; eyes not rinsed; observed for up to 7 d post-treatment	Not irritating	[9,14]
29% (weight) Potassium Silicate; molar ratio = 3.9; 0.1 ml in water	6 New Zealand White rabbits; sex not reported	Ocular irritation study in accordance with OECD Test Guideline 405; eyes not rinsed; observed for up to 7 d post-treatment	Not irritating	[9,14]
~30% Potassium Silicate in water; molar ratio = 2.47; 0.1 ml	3 New Zealand White rabbits; sex not reported	Ocular irritation study; eyes not rinsed; observed for up to 7 d post-treatment	Slightly irritating	[9]
35% (weight) Potassium Silicate; molar ratio = 3.4; 0.1 ml in water	3 New Zealand White rabbits; sex not reported	Ocular irritation study in accordance with OECD Test Guideline 405; eyes not rinsed; observed for up to 7 d post-treatment	Slightly irritating; redness and chemosis of the conjunctivae (scores 1.0-1.3 and 1.3-1.5, respectively) observed up to 7 d post-treatment	[9,14]

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