Final Report

on the Safety Assessment of Synthetic Fluorphlogopite As Used in Cosmetics

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ABSTRACT

The Cosmetic Ingredient Review Expert Panel (the Panel) reviewed the safety of synthetic fluorphlogopite as used in cosmetics. Synthetic fluorphlogopite functions as a bulking agent and a viscosity increasing agent. The Panel reviewed available animal and human data related to this ingredient along with a previous safety assessment of other magnesium silicates. The Panel concluded that synthetic fluorphlogopite was safe in the practices of use and concentration as given in this safety assessment.

INTRODUCTION

This is a safety assessment of the cosmetic ingredient synthetic fluorphlogopite (sometimes spelled fluorophlogopite). Synthetic fluorphlogopite is a synthetic mimic of a natural mineral that functions in cosmetics as a bulking agent and a viscosity increasing agent – aqueous.

Synthetic fluorphlogopite is partially composed of magnesium aluminum silicate sheets. This composition makes it appropriate that data from similar silicate clays be included in this safety assessment. The silicate clay, magnesium aluminum silicate, as well as magnesium trisilicate, zeolite and other clays were previously reviewed by the Panel as part of a group of aluminum silicate clays and found to be safe as used in cosmetic products.[1] Summaries of the relevant data from that report are included in the appropriate sections below. The similar chemical structures and physicochemical properties as well as functions and concentrations in cosmetics of magnesium aluminum silicate and related clays enable referring to these ingredients and reading across the available toxicological data to support the safety assessment synthetic fluorphlogopite.

CHEMISTRY

Definition and Structure

Synthetic fluorphlogopite (CAS No. 12003-38-2) is a synthetic mimic of a mica-type, fluorine substituted mineral composed of magnesium aluminum silicate sheets, weakly bound together with potassium (Figure 1).[2]

Phlogopite, the non-flourine substituted mineral, like other micas, has a layered structure of magnesium aluminum silicate sheets weakly bonded together by layers of potassium ions.[3] These potassium ion layers produce the perfect cleavage. Single large plates or "books" of phlogopite can grow to considerable size.

Fluorphlogopite differs in that two of the hydroxyl groups, per aluminum atom, are replaced with fluorine atoms. Fluorine is present in the phyllosilicate mineral group in general and in the micas particularly as a substitute for OH. The presence of fluorine enhances the thermal stability of the trioctahedral mica structure.

Physical and Chemical Properties

Physical and chemical properties of synthetic fluorphlogopite are presented in Table 1.

In large pieces, fluorphlogopite is pale yellow and is transparent and non-fluorescent with vitreous to resinous luster; it shows yellowish-white color in thin section.[4] Mohs' hardness is 2–3.

A product description sheet describes synthetic fluorphlogopite as a white to grey free-flowing powder with an average particle size of 10 – 15 μm and a pH range of 5 – 8.[5] The particles have a low degree of surface reactivity (in contrast to natural phlogopites).

Another product data sheet reports that synthetic fluorphlogopite has a pH value of 7.0 - 11.0 (in a 10% Aqueous slurry), a bulk density of 0.240 - 0.300 g/cm^3, and a particle size distribution of 9.0 - 45 μm.[6] Another source reports particles sizes ranging from 20 – 150 μm.[7]

Possible impurities are listed in Table 2. Acid soluble substances are potentially leachable from synthetic fluorphlogopite, including fluorine ions.[8]

Synthetic fluorphlogopite is not soluble in water.[9] In a test of the solubility of the ions in distilled water, magnesium, aluminum, and potassium were present at $< 5 \times 10^{-6}$, $< 5 \times 10^{-5}$, and $< 5 \times 10^{-4}$ g/L, respectively, after stirring for up to 72 h at 30°C. The amount of potassium in the blank was similar to the amount in the test substance, suggesting that the detected potassium was in the water and not from the synthetic fluorphlogopite.

Synthetic fluorphlogopite, as opposed to natural fluorphlogopite, is virtually iron free.[4] However, synthetic fluorphlogopite may be intentionally manufactured with iron to more efficiently absorb UV-rays.[8]

Fluorphlogopite has some unique properties due to the replacement of most of the hydroxyl groups on aluminum (that are normally present in non-fluoro phlogopite) with fluoride. However, the aluminum-fluoride bond is only moderately thermodynamically stable. Over time and exposure, atmospheric oxygen and water can replace those fluorides ions, regenerating the more stable hydroxyl groups.

Synthetic fluorphlogopite is stable for 5 years in a sealed container at < 25°C and for at least 1 year once opened.[7] However, fluorine ions (F^-) are reported to leach out of synthetic fluorphlogopite particles and bricks.[10,11]

The Japanese Standard of Quasi-Drugs require that synthetic fluorplogopite have a pH between 5.5 and 7.5, a maximum of 2% acid soluble substance, ≤ 20 ppm lead, ≤ 5 ppm arsenic, and ≤20 ppm dissolution amount of fluoride.[12] Synthetic fluorphlogopite meeting these standards are reported to be > 99% pure.

Even though the previously reviewed magnesium aluminum silicate clays noted above are natural clays, and synthetic fluorphlogopite is not, they both are large, flat particles (0.8 x 0.8 x 0.1 μm) with a layered structure of magnesium

aluminum silicate sheets weakly bonded together. They both chemically inert and insoluble in water.

The previous safety assessment of magnesium aluminum silicate clays states that hectorite (magnesium/lithium silicate) clay contains fluorine,[1] which suggested a structural similarity to synthetic fluorphlogopite, however current information suggest that fluorine is not a significant component of hectorite.

Method of Manufacture

A reported manufacturing method of synthetic fluorphlogopite designed for industrial-scale batches (up to several tons) involved melting oxide (metal; i.e., aluminum and manganese)-fluoride mixtures at a given "soak" temperature (wherein the contents are liquid; up to 1450°C), and then cooling at a continuous rate of a few degrees per hour between 1400 and 1300°C.[13] This technique produced large fluorphlogopite monocrystals (several centimeters).

Another method synthesized fluorphlogopite single crystals, several millimeters in size, suited to laboratory uses. [14] A mixture of SiO_2, γ-Al_2O_2, MgO, and K_2SiF_6 was first melted at 1450°C for 3 h then cooled to 1385°C at a rate of 100°C/h and then quenched into cold water. The resulting charge was loaded back into the furnace, heated from ~1000°C to 1385°C at a rate of 500°C/h and finally cooled at a rate of 1°C/h down to 1300°C. This procedure led to the formation of large and detachable monocrystals of synthetic fluorphlogopite up to 1 cm in diameter.

The extent of fluorine substitution for OH groups depends on several factors.[4,15] The most important are (1) hydrofluoric acid activity in the fluid during the crystallization and post-crystallization phase; (2) temperature; and (3) cation population of the octahedral sheet. Crystal structure may be altered by adjusting the pressure during cooling.[3]

In order to minimize the number of fluoride ions available for leaching, the stoichiometric equivalent of fluorine is decreased to less than one (i.e., less K_2SiF_6 is added) and the melt temperature is decreased (between 900 and 1000ºC).[10] To remove any free fluoride, the resulting ingot is pulverized and the resulting powder is then heat treated at 600 to 1350ºC and then washed with an aqueous solution containing one or more acids or chelating agents.

USE

Cosmetic

Data on ingredients usage are provided to the Food and Drug Administration (FDA) Voluntary Cosmetic Registration Program (VCRP). The VCRP reports that synthetic fluorphlogopite is used in 666 leave-on products and 9 rinse-off products (Table 3).[16,17] The Personal Care Products Council reports maximum use concentrations of 0.00002% to 67%. It is used up to 67% in leave on products (face powders) and 30% in rinse off products (bath soaps and detergents). It is used up to 20% in lipsticks and 15% in eye makeup products.

Synthetic fluorphlogopite is used in perfumes with the maximum reported concentration of use of 0.05% and at 2% in indoor tanning preparations which may be propellant and pump spray products, and could possibly be inhaled. In practice, 95% - 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters >10 µm, with propellant sprays yielding a greater fraction of droplets/particles below 10 µm compared with pump sprays.[18,19] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal region and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.[20,21]

Non-Cosmetic

Flourphlogopite has been approved as a colorant in all types of food contact polymers at levels not to exceed 5.0% by weight of the finished polymer that comes in contact with all types of food.[22]

Natural phlogopites are used for their heat and electrical insulating properties.[4]

TOXICOKINETICS

Absorption, Distribution, Metabolism, and Excretion

SYNTHETIC FLUORPHLOGOPITE

There were no absorption, distribution, metabolism, or excretion studies of synthetic fluorphlogopite discovered.

MAGNESIUM ALUMINUM SILICATE AND RELATED CLAYS

There was no absorption of aluminum and elevated levels of silicon were observed in assayed plasma samples of dogs administered magnesium trisilicate (20 mg/kg) and zeolite (20 mg/kg) orally.[23]

The urinary excretion of silica was 5.2% in male subjects given 20 g of magnesium trisilicate.[24]

Heat treated montmorillonite (5, 15, and 45 mg) administered to rats by means of intratracheal instillation was restricted to alveoli within and adjacent to alveolar ducts.[25]

Cytotoxicity

MAGNESIUM ALUMINUM SILICATE AND RELATED CLAYS

A sample of aluminum silicate was toxic to pulmonary alveolar macrophages (PAM) measured by lactate dehydrogenase activity (LDH), β-galactosidase (β-GAL) activity, lactic acid production, cellular ATP activity, and the cellular DNA contents.[26] LDH activity and β-GAL release were increased at 33.3 µg/ml and 166.7 µg/ml aluminum silicate.

Aluminum silicate had relatively no effect on the hemolysis of rat red blood cells (RBC) up to 1000 μg/ml.

Many clays (attapulgite, bentonite, hectorite, kaolin, montmorillonite, pyrophyllite, and zeolite) demonstrated cytotoxicity to several macrophage type cell lines and have hemolyticactivity towards several species' RBCs (as low as 0.2 μg/ml attapulgite to bovine RBCs).[1,26-59] Toxicity was dependent on particle size, concentration, and mineral composition. Larger particle size cause more adverse effects. In most of the studies, a dose dependent effect on cytotoxicity or lysis was observed. Most mineral samples were not 100% pure and many samples already contained toxic dusts or minerals like quartz or cristobalite.

TOXICOLOGICAL STUDIES

Acute Toxicity

Dermal

MAGNESIUM ALUMINUM SILICATE AND RELATED CLAYS

The acute dermal LD_{50} was >3.5 g/kg for rabbits exposed to VEEGUM (magnesium aluminum silicate).[60]

Oral-Non-Human

SYNTHETIC FLUORPHLOGOPITE

The oral LD_{50} for female ICR (Crj: CD-1) mice and SD (Crj: CD) rats was > 9000 mg//kg synthetic fluorphlogopite.[61] There were no adverse clinical signs or physical findings at necropsy.

MAGNESIUM ALUMINUM SILICATE AND RELATED CLAYS

The following are a list of acute oral LD_{50} determinations: calcium silicate, 3400 mg/kg in rats; magnesium aluminum silicate, 50000 mg/kg in mice; zirconium silicate, > 200 mg/kg in mice; hectorite, >5 g/kg in rats; kaolin, 149 g/kg in rats (death due to bowel obstruction).[62-66]

Inhalation

SYNTHETIC FLUORPHLOGOPITE

In a 4-h acute inhalation study, synthetic fluorphlogopite (4.1 mg/L; median aerodynamic diameter of 2.44 μm with a geometric standard deviation of 2.18 and 2.20 μm) was administered to HanRcc:WIST(SPF) albino rats (n = 5/sex) in a nose-only system.[67] There were no clinical signs during exposure and during the 15-day observation period. There were no findings at necropsy. The LC_{50} was determined to be > 5.1 mg/L.

Repeated Dose Toxicity

Oral – Non-Human

MAGNESIUM ALUMINUM SILICATE AND RELATED CLAYS

In short-term oral toxicity studies, no adverse effects were seen in mice or rabbits dosed up to 5 g/kg magnesium aluminum silicate.[68]

Various zeolites (up to 3%) were added to the diets of pigs for 6 weeks.[69] No adverse effects were noted by the supplementation.

A feeding test with dogs and rats ingesting large amounts of VEEGUM (magnesium aluminum silicate; 10% of ration) for 90 days, showed that there were no adverse effects and VEEGUM was considered nontoxic.[70]

Guinea pigs had renal lesions after 4 months of drinking magnesium trisilicate (250 mg/L) in their tap water.[71] Rats fed 10% magnesium aluminum silicate had slightly elevated silicon levels of the spleen and dogs and rats fed 10% VEEGUM had no adverse effects in 90-day feeding studies.[70] No lesions were found in rats dosed up to 1000 mg/kg for 104 weeks.[72]

OCCUPATIONAL EXPOSURE

MAGNESIUM ALUMINUM SILICATE AND RELATED CLAYS

Occupational exposure to mineral dusts has been studied extensively. Fibrosis and pneumoconiosis has been documented in workers involved in the mining and processing of aluminum silicate, calcium silicate, zirconium silicate, Fuller's earth, kaolin, montmorillonite, pyrophyllite, and zeolite.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

SYNTHETIC FLUORPHLOGOPITE

There were no reproductive or developmental toxicity studies of synthetic fluorphlogopite discovered.

MAGNESIUM ALUMINUM SILICATE AND RELATED CLAYS

Calcium silicate (250 to 1600 mg/kg on days 6 – 18 of gestation) had no discernible effect on nidation or on maternal or fetal survival in rabbits.[73]

Magnesium aluminum silicate (6000 mg/kg on days 7 – 12 of gestation) had neither teratogenic nor adverse effects on the mouse fetus.[74]

Female rats receiving a 20% kaolin diet for up to 117 days prior to insemination through nidation exhibited maternal anemia but no significant decrease in birth weight of the pups was recorded.[75]

Type A Zeolite produced no adverse effects on the dam, embryo, or fetus in either rats (administered days 6 – 15) or rabbits (administered days 6 – 18) at any dose level (74 or 1600 mg/kg).[76]

Clinoptilolite (5%) administered in feed for 13 weeks had no effect on female rat reproductive performance.[77]

GENOTOXICITY

SYNTHETIC FLUORPHLOGOPITE

In a chromosomal aberration test of synthetic fluorphlogopite (0.02 – 0.16 mg/mL), there were no chromosomal structural abnormalities observed to Chinese hamster lung-derived fibroblast cells at 24 and 48 h.[61]

Synthetic fluophlogopite (0.500 – 5000 μg) was not mutagenic to *Salmonella typhimurium* (strains TA98, TA100, TA102, TA1535, TA1537) and *Escherichia coli* (strain WP2 uvrA) with and without metabolic activation.[78]

In a micronucleous test using V79 Chinese hamster cells, synthetic fluorphlogopite (5 – 100 μL) was not mutagenic with or without metabolic activation.[79] Controls had the expected results.

In an in vitro mammalian cell gene mutation test, synthetic fluorphlogopite (15.8 – 500 μg/mL) was not mutagenic with or without metabolic activation to V79 Chinese hamster cells.[80] Controls had the expected results.

MAGNESIUM ALUMINUM SILICATE AND RELATED CLAYS

No increase mutation frequencies were seen in the *Salmonella* TA-1530 or G-46 assay and no significant increase in recombinant activity was observed in the *Saccharomyces* D3 assay treated with calcium silicate.[64] Calcium silicate (150 mg/kg) orally administered to rats produced 3% breaks in bone marrow cells arrested in c-metaphase. In a metaphase spread of bone marrow cells, calcium silicate (up to 1500 mg/kg) produced no significant increase in the number of aberrations compared to controls. In a dominant lethal assay using rats, calcium silicate (up to 1500 mg/kg) did not induce any dominant lethal mutations.

In the *S. typhimurium* LT2 spot test (TA98, TA100, TA1535, TA1537, and TA1538) with or without metabolic activation, magnesium aluminum silicate and hectorite were found nonmutagenic.[81,82]

In primary hepatocyte cultures, the addition of attapulgite at 10 μg/cm^2 had no significant unscheduled DNA synthesis (UDS) response or modulated response to AAF (a positive control); attapulgite at 10 μg/cm^2 caused significant increases in UDS in rat pleural mesothelial cells.[29,83]

Zeolite particles (10 μm) produced an increase in the percentage of aberrant metaphases, mostly chromatid breaks.[84]

CARCINOGENICITY

SYNTHETIC FLUORPHLOGOPITE

There were no carcinogenicity studies of synthetic fluorphlogopite discovered.

Inhalation

MAGNESIUM ALUMINUM SILICATE AND RELATED CLAYS

Small primary neoplastic lesions were found in two of 48 rats exposed to a calcium silicate dust at a concentration of 10 mg/m^3 for 7 h/day, 5 days/week, for a total of 224 days over an elapsed period of 12 calendar months in an inhalation chamber.[85]

Moderate to extensive respiratory disease was noted in rats chronically exposed to Synthetic Zeolite A (20 mg/m^3; 5 h/d, 3/week) by inhalation methods.[72]

Other Exposures

MAGNESIUM ALUMINUM SILICATE AND RELATED CLAYS

Intratracheal injections of aluminum silicate (20 and 25 mg) in rats caused lesions in a dose-dependent manner and the intrapleural injections of four different aluminum silicate samples all resulted in lesions.[86] One aluminosilicate injection caused three malignant mesotheliomas, one pleural and two peritoneal.

No mesotheliomas developed in rats injected intraperitoneally with 25 mg of calcium silicate dust.[85]

Subcutaneous injection into the oral mucosa and into the back, periosteal injections into periosteal tissue, and intramuscular injections into the thigh of rats and guinea pigs with zirconium silicate resulted in mild inflammatory reactions.[66]

In a series of intrapleural injections of rats, Kaolin was used as a negative control.[87]

Minor inflammatory reactions, but no lesions, were found in rats given intratracheal injections of zeolite (clinoptilolite), and intraperitoneal injections of mordenite, Synthetic Zeolite 4A, and Synthetic Zeolite MS5A (one mesothelioma was seen in rats given MS4A).[72,88-93] An intrapleural injection of Nonfibrous Japanese Zeolite caused two mesotheliomas in rats.[93]

Subplantar injections of bentonite caused granulomas in rats.[94]

IRRITATION AND SENSITIZATION

Irritation

Dermal Non-Human

SYNTHETIC FLUORPHLOGOPITE

Synthetic fluorphlogopite (55% in distilled water; 0.3 g) was not irritating to the scratched skin of male Japanese White rabbits (n = 6) after 24 h under occlusion.[61]

Synthetic fluorphlogopite (55% in distilled water; 0.3 g; 5 d/week) was not dermally irritating to Hartley albino guinea pigs (n = 10) in a cumulative irritation test after 4 weeks.[61] There were no effects on body weights and necropsy did not reveal any changes in the organs.

Synthetic fluorphlogopite (0.5 g with a few drops of aqua da iniectabilia (injectable water); ~ 6 cm^2 semi-occlusion patch) was not a dermal irritant to female Crl:KBL(NZW) rabbits after 4 h.[95]

MAGNESIUM ALUMINUM SILICATE AND RELATED CLAYS

Magnesium aluminum silicate (4%) was a weak primary skin irritant in rabbits and had no cumulative skin irritation in guinea pigs. No gross effects were reported in any of these studies.[60]

Dermal - Human

SYNTHETIC FLUORPHLOGOPITE

In a dermal patch test (n = 42), a paste of synthetic fluorphlogopite (0.05 g in distilled water; 55%; 1.6 cm diameter patch) was not irritating after 48 h under oclusion.[61]

A powdery foundation containing synthetic fluorphlogopite (38.5%; diluted in distilled water to 21.2%) was tested in a 48 hour patch test. The test substance was not irritating.[61]

In an in vitro Human Skin Model Test, tissue treated with synthetic fluorphlogopite (1 mg) had a viability > 50%, therefore, was considered to lack irritant potential.[96] Controls had the expected results.

MAGNESIUM ALUMINUM SILICATE AND RELATED CLAYS

Applications of 2 g of VEEGUM made to the skin of two humans daily for 1 week caused no effects.[65]

Ocular Non-Human

SYNTHETIC FLUORPHLOGOPITE

In an chorioallantoic membrane (HET-CAM) eye irritation potential test, synthetic fluorphlogopite (100%) demonstrated no irritation potential.[97]

In a Bovine Corneal Opacity and Permeability Assay (BCOP), synthetic fluorphlogopite (20% in 0.9% sodium chloride solution) did not increase opacity or permeability of the treated corneas.[98] The author concluded that synthetic fluorphlogopite did not show ocular irritation or corrosive potential. Controls had the expected results.

In a primary eye irritation test using albino Crl:KBL(NZW) rabbits (n = 3), synthetic fluorphlogopite (0.1 g) was not an ocular irritant.[99] All animals had discharge and redness of conjunctiva 1 h after administration. One rabbit had chemosis at 1 h after administration.

MAGNESIUM ALUMINUM SILICATE AND RELATED CLAYS

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.[100]

Bentonite (1 – 5 mg/ml) caused severe iritis after injection into the anterior chamber of the eyes of rabbits.[101] When injected intralamellarly (0. – 0.25 mg/ml), widespread corneal infiltrates and retrocorneal membranes were recorded.

In a primary eye irritation study in rabbits, hectorite (100 mg) was moderately irritating without washing and practically non-irritating to the eye with a washout.[63]

Rats tolerated a single 10 g dose of Zeolite A without any adverse reaction in the eye.[72]

Sensitization

Non-Human

SYNTHETIC FLUORPHLOGOPITE

In a modified guinea pig maximization test (n = 10) with adjuvant exposure, synthetic fluorphlogopite (55% in distilled water; 0.1 g) was not sensitizing.[61]

In a local lymph node assay using mice (n = 5), synthetic fluorphogopite (5%, 10%, 25% w/v in acetone:olive oil 4:1) was not a dermal sensitizer.[102]

Human

SYNTHETIC FLUORPHLOGOPITE

A human repeated insult patch test (HRIPT; n = 107) was conducted of a pressed powder that contained synthetic fluorphlogopite (13.824%) under semi-occlusion.[103] The authors concluded that this product did not elicit dermal irritation or sensitization.

Photosensitization/Phototoxicity

SYNTHETIC FLUORPHLOGOPITE

Repeated administrations (days 1 - 4) of synthetic fluorphlogopite (55% in distilled water; 0.1g) in a adjuvant-strip assay was not dermally photosensitizing to female Hartley albino guinea pigs (n = 10) when exposed to UVA light (320 - 400 nm) at 10.2 joules/cm^2 and then challenged on day 21 (20 mg).[61]

Synthetic flurophlogopite (55% in distilled water) was not phototoxic to male Hartley albino guinea pigs (n = 5) when administered to shaved skin prior to a single exposure to UVA light (320 – 400 nm) at 14.0 joules/cm^2 for 30 min.[61] No skin reaction was observed at 24, 48 and 72 h after exposure.

SUMMARY

Synthetic fluorphlogopite is a synthetic mimic of a natural mica-type mineral that functions in cosmetics as a bulking agent and a viscosity increasing agent – aqueous. Synthetic fluorphlogopite is composed of magnesium aluminum silicate sheets, weakly bound together with potassium. Magnesium aluminum silicate clays were previously reviewed by the Panel with the conclusion that they are safe as used in cosmetic products.

The VCRP reports that synthetic fluorphlogopite is used in 560 leave-on products and 5 rinse-off products, at concentrations up to 67% in leave-on products (face powders) and up to 30% in rinse-off products (bath soaps and detergents).

There was no absorption of aluminum and elevated levels of silicon were observed in assayed plasma samples of dogs administered magnesium trisilicate and zeolite orally. Silica was excreted in the urine in human males orally administered magnesium trisilicate.

The acute dermal LD_{50} for magnesium aluminum silicate was >3.5 g/kg for rabbits.

The oral LD_{50} for mice and rats was > 9000 mg/kg synthetic fluorphlogopite.

The acute oral LD_{50} for calcium silicate was 3400 mg/kg in rats; 50000 mg/kg magnesium aluminum silicate in mice; > 200 g/kg zirconium silicate in mice; >5 g/kg hectorite in rats; 149 g/kg kaolin in rats.

The inhalation LC_{50} of synthetic fluorphlogopite for rats was > 5.1 mg/L.

In short-term oral toxicity studies, no adverse effects were seen in mice or rabbits dosed up to 5 g/kg magnesium aluminum silicate. Long-term feeding and drinking water studies revealed no adverse effects for magnesium aluminum silicate at 10% for dogs and rats and for magnesium trisilicate at 250 mg/L for guinea pigs.

Occupational exposure to aluminum silicate, calcium silicate, zirconium silicate, Fuller's earth, kaolin, montmorillonite, pyrophyllite, and zeolite has lead to fibrosis and pneumoconiosis.

There were no reproductive effects for calcium silicate at 1600 mg/kg for rabbits, type Z Zeolite at 74 or 1600 mg/kg for rats or rabbits. Magnesium aluminum silicate at 6000 mg/kg caused neither teratogenic nor adverse effects on the mouse fetus. Clinoptilolite had no effect on female rat reproductive performance.

Synthetic fluorphlogopite was not genotoxic in a chromosomal aberration test up to 0.16 mg/mL using Chinese hamster lung-derived fibroblast cells. It was not mutagenic to *Salmonella* and *E. coli* up to 5000 μg, to V79 Chinese hamster cells up to 100 μg/mL, or to mammal cells up to 500 μg/mL. Magnesium aluminum silicate and related clays were not mutgenic in multiple assays.

Mice exposed to calcium silicate dust at 10 mg/m^3 developed neoplastic lesions.

Synthetic fluorphlogopite was not dermally irritating to rabbits and guinea pigs at 55%. Magnesium aluminum silicate was a week primary skin irritant in rabbits at 4%. Synthetic fluorphlogopite was not dermally irritating to humans at 0.05 g in two 48-h assays. It was not predicted to be a dermal irritant in an in vitro Human Skin Model Test. VEEGUM was not dermally irritating at 2 g daily for 1 week.

In a HET-CAM and a BCOP assay, synthetic fluorphlogopite was not an ocular irritant to rabbits. Magnesium aluminum silicate, hectorite, and Zeolite A were not ocular irritants to rabbits or rats.

Synthetic fluophlogopite was not sensitizing to guinea pigs or mice. In an HRIPT, synthetic fluorphlogopite was not irritating or sensitizing in a product at 13.824%.

Synthetic fluorphlogopite was not photosensitizing or phototoxic to guinea pigs at 55%.

DISCUSSION

Synthetic fluophlogopite contains fluoride ions. The Panel concluded that these ions are unlikely to leach out of formulation due to the high heat used in the manufacturing process.

Because the particles are large and insoluble in water, synthetic fluorphlogopite is unlikely to penetrate the skin.

The Panel noted that there were negative results for bacterial and mammal mutagenicity data for synthetic fluorphlogopite. The combination of these negative results and the absence of mutagenicity in mammalian data for magnesium aluminum silicate supports assurance against mutagenicity.

Because this ingredient can be used in products that may be aerosolized, including perfumes and indoor tanning preparations (possible propellant and pump spray products), the Panel discussed the issue of incidental inhalation exposure. The acute inhalation data on the synthetic fluorphlogopite showed no adverse effects to rats. However, the chronic human industrial exposure data on the magnesium aluminum silicate related clays resulted in fibrosis and pneumoconiosis.

Although particles appear to have reached the lungs in these studies, the sizes of the particles used were either clearly within the respirable range (ie, ≤10 μm) or were not reported. This ingredient is reportedly used at maximum concentrations of 0.05% - 2% in cosmetic products that may be aerosolized and 0.6% - 67% in powders. The Panel noted that 95% - 99% of droplets/particles produced in cosmetic aerosols would not be respirable to any appreciable amount. The Panel determined that the sizes of a substantial majority of the particles of synthetic fluorphlogopite, as manufactured, and their function as a viscosity enhancer which leads to aggregation and agglomeration to form much larger particles in formulation, results in particles larger than those in the respirable range. Thus, the adverse effects reported using high doses of respirable particles in the inhalation studies would be of little concern for these ingredients used in cosmetics as they would be too large to be inhaled or respired. Coupled with the small actual exposure in the breathing zone and the concentration at which the ingredients are used, incidental inhalation would be a significant route of exposure that might lead to local respiratory or systemic toxic effects..

The Panel considered other data available to characterize the potential for synthetic fluorphlogopite to cause systemic toxicity, irritation, sensitization, or phototoxicity. They noted the lack of systemic toxicity in acute oral exposure and no irritation or sensitization. As stated above, the genotoxicity assays were negative for synthetic fluorphlogopite and the magnesium aluminum silicate clays in a chromosomal aberration assay and multiple bacterial assays. In addition, these large macromolecules are insoluble in water, and chemically inert under physiological conditions or conditions of use, which supports the view that they are unlikely to be absorbed.

CONCLUSION

The CIR Expert Panel concluded that synthetic fluorphlogopite is safe for use in cosmetics in the present practices of use and concentration described in this safety assessment.

TABLES AND FIGURES

Table 1. Chemical and physical properties of synthetic fluorphlogopite.

Property	Value	Reference
Physical Form	Platelet; crystalline; Fine grained powder	5,104,105
Color	White to grey	5
Density/Specific Gravity	2.8	104
Melting Point ^{o}C	1393-1403	14
Water Solubility	Insoluble	7,9

Table 2. Possible impurities in synthetic fluophlogopite.

Impurity	Amount	Reference
Acid soluble substances	0.7%	106
Lead	< 1.0 ppm	106
Arsenic	< 0.5 ppm	106
Dissolution amount of (leachable) fluorine	11 ppm	106
Iron	0.008 w/w%	8
Titanium	0.002%	8
Barium	0.001%	8
Sodium	0.025%	8
Manganese	0.001%	8
Chromium	0.002%	8
Vanadium	0.001%	8
Zinc	0.001%	8
Strontium	>0.001%	8
Copper	>0.001%	8

Table 3. Current frequency of use according to duration and type of exposure provided in 2012.[16,17]

	Synthetic fluorphlogopite	
	# of Uses	**Concentration (%)**
Total/Conc. range	675	0.00002-67
Duration of Use		
Leave-on	666	0.0000-67
Rinse-off	9	0.009-30
Diluted for (bath) use	NR	NR
Exposure Type		
Eye	210	0.001-48
Incidental ingestion	216	0.0008-20
Incidental inhalation-sprays	27	0.05-2
Incidental inhalation-powders	56	0.6-67
Dermal contact	410	0.00002-67
Deodorant (underarm)	NR	NR
Hair – non coloring	2	0.009-0.05
Hair - coloring	NR	NR
Nail	30	0.3-3
Mucous Membrane	223	0.0008-30
Baby products	NR	NR

NR = Not Reported; Totals = Rinse-off + Leave-on Product Uses.
Note: Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure type uses may not equal the sum total uses.

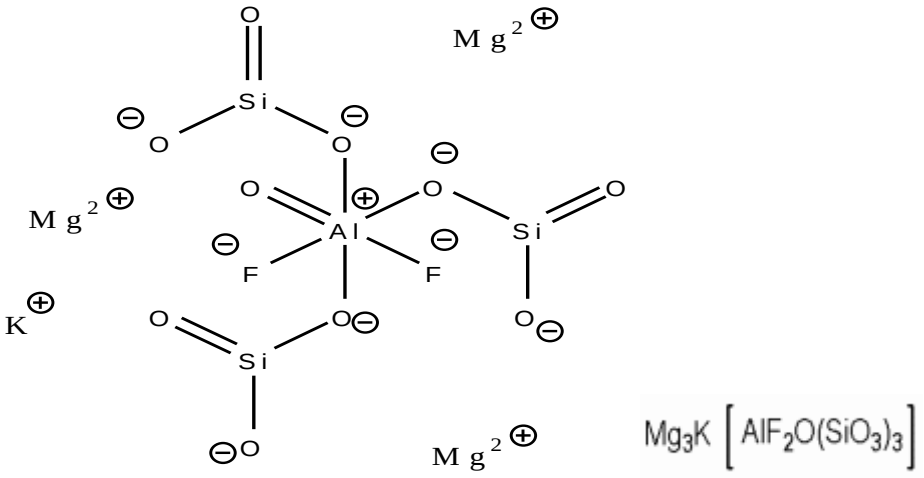

Figure 1. The structure and average formula of synthetic fluorphlogopite.[107]

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