Tentative Safety Assessment

Synthetic Fluorphlogopite

As Used in Cosmetics

March 16, 2012

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on this Tentative Safety Assessment and to identify additional published data that should be included or provide unpublished data which can be made public and included.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 All unpublished data submitted to CIR will be discussed in open meetings, will be available at the CIR office for review by any interested party, and may be cited in a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

The 2012 Cosmetic Ingredient Review Expert Panel members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Ronald A Hill, Ph.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; James G. Marks, Jr., M.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Director is F. Alan Andersen, Ph.D. This report was prepared by Lillian C. Becker, Scientific Analyst/Writer.

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TABLE OF CONTENTS

ABSTRACT

The Cosmetic Ingredient Review Expert 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 is safe as cosmetic ingredients in the present practices of use and concentration as given in this safety assessment.

INTRODUCTION

This report assesses the safety of synthetic fluorphlogopite (sometimes spelled fluorophlogopite) as used in cosmetics. Synthetic fluorphlogopite is a synthetic mimic of natural fluorphlogopite.

The silicate clay, magnesium aluminum silicate, as well as other clays were previously reviewed by the CIR Expert 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-fluorine 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 from phlogopite 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.

In the previous safety assessment of silicate clays noted above, hectorite (magnesium/lithium silicate) clay was given as containing fluorine,[1] which would have suggested a structural similarity to synthetic fluorphlogopite, but current information suggest that fluorine is not a significant component of hectorite.

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.

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.[9,10]

The Japanese Standard of Quasi-Drugs require that synthetic fluorphlogopite 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.[11] Synthetic fluorphlogopite meeting these standards are reported to be > 99% pure.

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.[12] This technique produced large fluorphlogopite monocrystals (several centimeters).

Another method synthesized fluorphlogopite single crystals, several millimeters in size, suited to laboratory uses. [13] 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.[4,14] 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).[9] 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

Synthetic fluorphlogopite functions in cosmetics as a bulking agent and a viscosity increasing agent-aqueous.[15]

Data on ingredients usage are provided by industry to the Food and Drug Administration (FDA) under the FDA's Voluntary Cosmetic Registration Program (VCRP). The VCRP reports that synthetic fluorphlogopite is used in 560 leave-on products and 5 rinse-off products (Table 3).[16,17] Based on an industry survey by the Personal Care Products Council, maximum use concentrations range from 0.00002% to 67%. This ingredient 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 also used in perfumes and indoor tanning preparations (possible propellant and pump spray products), and could possibly be inhaled. In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters >10 μm, with propellant sprays yielding a greater fraction of droplets/particles 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] However, the potential for inhalation toxicity is not limited to respirable droplets/particles deposited in the lungs. Inhaled droplets/particles deposited in the nasopharyngeal and thoracic regions of the respiratory tract may cause toxic effects depending on their chemical and other properties.

Non-Cosmetic

Fluorphlogopite has been approved as a food contact substance.[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 and zeolite orally.[23,24] The urinary excretion of silica was 5.2% in males 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 no effect on the hemolysis of rat red blood cells (RBC) up to 1000 μg/ml.

Attapulgite (0.05 – 0.5 mg/ml) samples and calcium silicate (5 and 10 mg/ml) caused increased hemolysis of human RBCs and calcium silicate caused increased LDH and β-GAL release.[27,28]

Many types of clay (attapulgite, bentonite, hectorite, kaolin, montmorillonite, pyrophyllite, and zeolite) demonstrated cytotoxicity to several macrophage type cell lines and have hemolyticactivity towards several species' RBCs.[1,26,27,29-60] Particle size, fibrogenicity, concentration, and mineral composition affected the outcome of exposure, with

larger particle sizes and longer and wider fibers causing more adverse effects. In most of the studies, a dose dependent effect on cytotoxicity or lysis was observed. Most mineral samples in these studies were not pure; many samples contained toxic dusts or minerals like quartz or cristobalite.

Miscellaneous Studies

MAGNESIUM ALUMINUM SILICATE AND RELATED CLAYS

In mice, intratracheal injections of bentonite and group C *Streptococcus* species caused an 85% mortality compared to a 5% control mortality; another intratracheal injection caused loose reticulin fibrils with no collagen.[41]

Kaolin injected with the *Streptococcus* species caused statistically significant but modest mortality in mice.[41]

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).[61]

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.[62] There were no adverse clinical signs or physical findings at necropsy.

MAGNESIUM ALUMINUM SILICATE AND RELATED CLAYS

Rats consuming bentonite (10%) in the diets overcame T-2 toxicosis completely.[63]

Various zeolites were added to the diets of pigs.[64] No adverse effects were noted by the supplementation.

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 g/kg in mice; hectorite, >5 g/kg in rats; kaolin, 149 g/kg in rats (death due to bowel obstruction).[65-69]

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.[70] 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.[71]

In feeding studies with dogs and rats ingesting VEEGUM (magnesium aluminum silicate; 10% of ration) for 90 days, there were no adverse effects and VEEGUM was considered nontoxic.[72]

Guinea pigs had renal lesions after 4 months of drinking magnesium trisilicate (250 mg/L) in their tap water.[73]

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.[72] No lesions were found in rats dosed up to 1000 mg/kg for 104 weeks.[74]

Inhalation – Human

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 available for synthetic fluorphlogopite.

MAGNESIUM ALUMINUM SILICATE AND RELATED CLAYS

Calcium silicate (250 to 1600 mg/kg) had no discernible effect on nidation or on maternal or fetal survival in rabbits.[75]

Magnesium aluminum silicate (6000 mg/kg) had neither a teratogenic nor adverse effects on the mouse fetus.[76]

Female rats receiving a 20% kaolin diet exhibited maternal anemia but no significant reduction in birth weight of the pups was recorded.[77]

Type A Zeolite produced no adverse effects on the dam, embryo, or fetus in either rats or rabbits at any dose level (74 or 1600 mg/kg).[78]

Clinoptilolite had no effect on female rat reproductive performance.[79]

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.[62]

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.[80]

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 in the *Saccharomyces* D3 assay treated with calcium silicate.[67] A subacute dose of 150 mg/kg of calcium silicate produced 3% breaks in bone marrow cells arrested in c-metaphase. In a metaphase spread of bone marrow cells, calcium silicate produced no significant increase in the number of aberrations compared to controls and in a dominant lethal assay 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.[31,83]

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 available for synthetic fluorphlogopite.

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]

Lebrija and Leichester Attapulgite samples caused one peritoneal mesothelioma, one adenocarcinoma, and three bronchoalveolar hyperplasia and two mesotheliomas, one peritoneal mesothelioma, one malignant alveolar tumor and eight bronchoalveolar hyperplasia (inhalation route) in rats (n = 20/sex).[86] Both samples contained long fibers.

Moderate to extensive respiratory disease, but no neoplasms, was noted in rats and hamsters chronically exposed to Synthetic Zeolite A by inhalation methods.[74]

Other Exposures

MAGNESIUM ALUMINUM SILICATE AND RELATED CLAYS

Intratracheal injections of aluminum silicate in rats caused lesions in a dose-dependent manner and the intrapleural injections of four different aluminum silicate samples all resulted in lesions.[87] 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.[88]

Attapulgite was injected intraperitoneally, intrapleurally, and intratracheally in various studies in rats.[43,86,89-93] Most studies reported that lesions and mesotheliomas were dependent on fiber length. Samples with a longer length caused greater numbers of mesotheliomas.

In a series of intrapleural injections of rats, Kaolin was used as a negative control.[86]

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).[74,94-99] An intrapleural injection of Nonfibrous Japanese Zeolite caused two mesotheliomas in rats.[99]

Subplantar injections of bentonite caused granulomas in rats.[100]

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.[62]

Synthetic fluorphlogopite (55% in distilled water) was not dermally sensitizing to Hartley albino guinea pigs (n = 10) in a cumulative irritation test after 4 weeks.[62] There were no signs of irritation.

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.[61]

Dermal - Human

SYNTHETIC FLUORPHLOGOPITE

In a dermal patch test (n = 42), a paste of synthetic fluorphlogopite (0.05 g in distilled water; 1.6 cm diameter patch) was not irritating after 48 h under oclusion.[62] This test was repeated with the same 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.[101]

Ocular Non-Human

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.[102,103]

Bentonite caused severe iritis after injection into the anterior chamber of the eyes of rabbits.[104] When injected intralamellarly, widespread corneal infiltrates and retrocorneal membranes were recorded.

In a primary eye irritation study in rabbits, hectorite was moderately irritating without washing and practically nonirritating to the eye with a washout.[105]

Rats tolerated a single 10 g dose of Zeolite A without any adverse reaction in the eye.[74]

Sensitization

Non-Human

SYNTHETIC FLUORPHLOGOPITE

In a guinea pig maximization test (n = 10), synthetic fluorphlogopite (55% in distilled water) was not sensitizing.[62]

In a local lymph node assay using mice (n = 5), synthetic fluorphlogopite (5%, 10%, 25% w/v in acetone:olive oil 4:1) was not a dermal sensitizer.[106]

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.[107] The authors concluded that this product did not elicit dermal irritation or sensitization.

Photosensitization/Phototoxicity

SYNTHETIC FLUORPHLOGOPITE

Repeated administrations (4 consecutive days) of synthetic fluorphlogopite (55% in distilled water) 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.[62]

Synthetic fluorphlogopite (55% in distilled water) was not phototoxic to female Hartley albino guinea pigs (n = 5) when administered to shaved skin prior to exposure to UVA light (320 – 400 nm) at 14.0 joules/cm^2 for 30 min.[62] 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 CIR with the conclusion that they are safe as used in cosmetic products as long as the products were formulated to be non-respirable.

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 and up to 30% in rinse-off products.

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 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 led to fibrosis and pneumoconiosis.

While there were no reproductive or developmental toxicity data for synthetic fluorphlogopite, 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 nor was mutagenic to *Salmonella* and *E. coli* up to 5000 µg. Magnesium aluminum silicate and related clays were not mutagenic to in multiple assays.

While there were no carcinogenicity data for synthetic fluorphlogopite, magnesium aluminum silicate and related clays were linked to inflammatory reactions, granulomas, and mesotheliomas in inhalation and tracheal injection studies.

Synthetic fluorphlogopite was not irritating to rabbits and guinea pigs. 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; neither was VEEGUM at 2 g daily for 1 week.

Magnesium aluminum silicate, hectorite, and Zeolite A were not ocular irritants to rabbits or rats.

Synthetic fluophlogopite was sensitizing to guinea pigs or mice. 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

Although there are data gaps, the similar chemical structures, physicochemical properties, and functions of the magnesium aluminum silicate clay ingredients allow for the interpolation of the available toxicological data to support the safety of synthetic fluorphlogopite.

Synthetic fluophlogopite contains fluoride ions. The Expert Panel concluded that these ions are secure in the compounds and unlikely to leach out if formulation due to the high heat in the manufacturing process.

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

The Expert Panel noted that there was only genotoxicity data available for synthetic fluorphlogopite were bacterial mutagenicity data. Mammalian genotoxicity data for magnesium aluminum silicate provided sufficient assurance that this similar ingredient would not be genotoxic.

Because these ingredients 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 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 (i.e., ≤10 µm) or were not reported. Additionally, related clays were linked to inflammatory reactions, granulomas, and mesotheliomas in animal inhalation and tracheal injection studies. The Expert Panel determined that the sizes of a substantial majority of the particles of synthetic fluorphlogopite, as manufactured, are larger than the respirable range and/or aggregate and agglomerate to form much larger particles in formulation. Thus, the adverse effects reported using high doses of respirable particles in industrial exposure and animal studies do not indicate risks posed by use in cosmetics.

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. 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 ingredients are large macromolecules, insoluble in water, and chemically inert under physiological conditions or conditions of use, which

supports the view that they are unlikely to be absorbed or cause local effects in the respiratory tract. Further, these ingredients are reportedly used at 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. Furthermore, several of these ingredients are used for viscosity increasing functions, indicating that they tend to swell and aggregate in water and other solvents and would, thus, be too large to be inhaled or respired. Coupled with the small actual exposure in the breathing zone and the concentrations at which the ingredients are used, this information indicates that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic toxic effects.

CONCLUSION

The CIR Expert Panel concluded that synthetic fluorphlogopite is safe 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	[108-110]
Color	White to grey	[5]
Density/Specific Gravity @ °C	2.8	[109]
Melting Point °C	1393-1403	[13]
Water Solubility g/L @ °C & pH	Insoluble	[7]

Table 2. Possible impurities in synthetic fluophlogopite.

Impurity	Amount	Reference
Acid soluble substances	0.7%	[111]
Lead	< 1.0 ppm	[111]
Arsenic	< 0.5 ppm	[111]
Dissolution amount of (leachable) fluorine	11 ppm	[111]
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 2011.[16,17]

	Synthetic fluorphlogopite	
	# of Uses	**Concentration (%)**
Total/Conc. range	565	0.00002-67
Duration of Use		
Leave-on	560	0.0000-67
Rinse-off	5	0.009-30
Diluted for (bath) use	NR	NR
Exposure Type		
Eye	169	0.001-48
Incidental ingestion	200	0.0008-20
Incidental inhalation-sprays	15	0.05-2
Incidental inhalation-powders	44	0.6-67
Dermal contact	336	0.00002-67
Deodorant (underarm)	NR	NR
Hair – non coloring	2	0.009-0.05
Hair - coloring	NR	NR
Nail	27	0.3-3
Mucous Membrane	203	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.

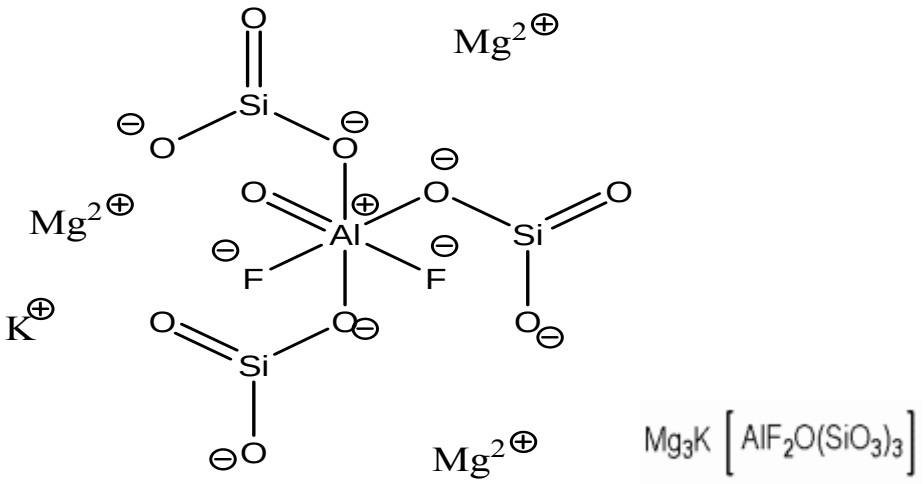

Figure 1. The structure and average formula of synthetic fluorphlogopite.[2]

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