Final Report on the Safety Assessment of Stearalkonium Hectorite[1]

Stearalkonium Hectorite is a reaction product of hectorite and Stearalkonium Chloride used in a wide variety of cosmetic formulations as a suspending agent—nonsurfactant. The Cosmetic Ingredient Review (CIR) previously evaluated the safety of Stearalkonium Chloride and an ingredient containing hectorite (Quaternium-18 Hectorite), and found both safe as currently used in cosmetic formulations. Hectorite clay is one of the minerals that make up bentonite clay. Stearalkonium Hectorite is formed by the cation exchange reaction of hectorite clay and Stearalkonium Chloride. The amount of free amines and amine hydrocarbons residual from this reaction is 0.45%; 0.5% sodium chloride is also present as an impurity. Stearalkonium Hectorite is used at concentrations up to 5% in cosmetics. In short-term dermal toxicity studies in rabbits at concentrations of 12.5% to 50%, no toxicity was observed. Stearalkonium Hectorite (50%) did not cause primary skin irritation in rabbits. Ocular toxicity test results in animals indicated only no or mild reactions. Stearalkonium Hectorite was not mutagenic in the Ames test or in a mouse lymphoma cell forward mutation assay. No data were available on the reproductive or developmental toxicity of this ingredient or of Stearalkonium Chloride; no birth defects were seen in a developmental toxicity study in rats using myristalkonium chloride. Stearalkonium Hectorite was not an ocular or skin irritant or a skin sensitizer in clinical tests. The potential that nitrosation of this ingredient or its impurities could occur to form nitrosamines was considered. Because any quaternary chlorides or amine hydrochlorides become strongly bonded to the hectorite clay, as does any residual Stearalkonium Chloride, they are not readily available for nitrosation. Based on the available data, it was concluded that Stearalkonium Hectorite is safe for use in cosmetics under the present practices of use.

INTRODUCTION

Stearalkonium Hectorite is a reaction product of hectorite and stearalkonium chloride that serves as a suspending agent—nonsurfactant in cosmetic formulations. The Cosmetic Ingredient Review (CIR) Expert Panel has previously evaluated the safety of related cosmetic ingredients, Stearalkonium Chloride and Quaternium-18 Hectorite, concluding that:

Stearalkonium Chloride is safe when incorporated in cosmetic products in concentrations similar to those presently marketed (Elder 1982a).

Quaternium-18 Hectorite is safe as a cosmetic ingredient in the present practices of use and concentration (Elder 1982b).

Information from these previous reports in summary form have been incorporated in this safety assessment.

CHEMISTRY

Definition and Structure

Stearalkonium Hectorite

Stearalkonium Hectorite is a creamy white, fine powder resulting from cation exchange reactions (Nikitakis and McEwen 1990) between the cationic quaternary ammonium salt, stearalkonium chloride (Figure 1) and hectorite (Figure 2). Stearalkonium Hectorite is often known by the trade name Bentone 27 (Wenninger, Canterbery, and McEwen 2000), and is classified as an aromatic amine modified Hectorite (Eichhorn and Mo 1983a).

Hectorite

Hectorite is one of the montmorillonite minerals that are the principal constituents of bentonite clay (Floyd 1981). Montmorillonites include all clay minerals with an expanding lattice (Floyd 1981; Spagnolo, Hatcher, and Faulset 1987). They generally have a high alumina end member with some slight replacement of the aluminium by magnesium and virtually no replacement of the silicone with magnesium (Floyd 1981). In Hectorite, the aluminum typically found in these clays has been replaced by magnesium or lithium, and all possible octahedral positions have been filled (Zlatkis and Jiao 1991). The lithium is tightly bound and generally unreactive, such that only severe chemical treatment can extract it (Eichhorn and Mo 1983a).

Hectorite is made up of a series of three-layer subunits. Each subunit consists of an octahedral layer that is sandwiched by two tetrahedral layers. The former layer contains magnesium (or lithium) and oxygen, and the latter layers contain silicon and oxygen (Figure 2). Oxygen molecules located along the faces of the octahedral layer are shared with the tetrahedral layers to give strong intralayer binding within a given subunit. Oxygen molecules also project from the free surfaces of the tetrahedral layer; Van der Waals forces provide a weak interlayer attraction

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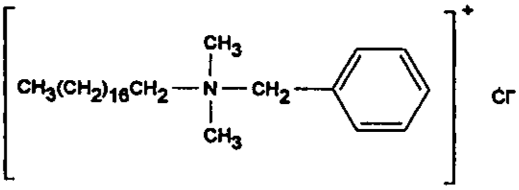

FIGURE 1
Chemical formula for stearalkonium chloride (Wenninger, Canterbery, and McEwen 2000).

between subunits, such that they are free to slide over one another, giving the clay a slick texture (Elder 1982b).

According to Mardis (1984), Hectorite is characterized by a negatively charged layer lattice structure that results from the replacement of normal lattice atoms with lower valency atoms of similar size (e.g., the replacement of magnesium by lithium). The negative charges are reflected to both faces of the clay platelet, where they are counterbalanced, in nature, by exchangeable inorganic cations. These cations, such as sodium, magnesium, and calcium are not part of the lattice structure itself. The clay edges are positively charged (Eichhorn and Mo 1983a).

The chemical composition of Hectorite is given by Eichhorn and Mo (1983a) and Zlatkis and Jiao (1991) as $(OH)_4Si_8(Mg_{5.34}Li_{0.66})O_{20}$. The composition of Hectorite varies according to its regional origin. Ranges taken from Elder (1982b) and Eichhorn and Mo (1983a) are: SiO_2 (53.95%–56.3%), MgO (25.89%–26%), F^-(3.47%), Na_2O (2.7%–3.04%), CaO (0.16%–2.5%), Li_2O (1.22%–1.51%), CO_2 (1.3%), Al_2O_3 (0.1%–0.14%), FeO (0%–0.05%), Fe_2O_3 (0.03%), K_2O (0.23%), H_2O (9.29%), and H_3O^+ (5.61%).

Chemical and Physical Properties

Stearalkonium Hectorite

The minimum gel strength, or viscosity at 77°C, of a 2.0% Stearalkonium Hectorite gel in toluene-methanol is 450 cP (dyne-second/cm^2). The amount of sulfated ash is 31.0% to 35.0% (Nikitakis and McEwen 1990).

In general, the polarity of the solvent in which an organoclay composition will be most compatible is inversely related to the number and length of the alkyl groups attached to the cation. In order for the reaction between the clay and the cation to proceed to completion, the cation must have at least one long chain, as is present in Stearalkonium Chloride. The other moieties attached to the cation center are divided into two classes—the filler and active groups. In the case of Stearalkonium Chloride, the filler groups are the methyl groups attached to the nitrogen. Active groups (e.g., benzyl groups) alter factors such as the solvent polarity range over which the compound is usable and the ease in which the organoclay can be dispersed (Mardis 1984).

Stearalkonium Hectorite renders other compounds more stable when added to them. Stearalkonium Hectorite is a hydrophobic agent that stabilizes emulsions by inhibiting oil-water phase separation. It has a gel-like consistency with thixotrophic properties; when it is disturbed, Stearalkonium Hectorite becomes more fluid-like. Stearalkonium Hectorite is expansible in water, methanol, ethanol, isopropanol, sorbitol, glycerine, and acetone (Elder 1982b; Rheox, Inc. 1996).

Hectorite

As described above, the subunit structure of Hectorite are only weakly bound by van der Waals forces at the edges of the tetrahedral layer (see Figure 2). The interlayer spacing between adjacent subunits is in dynamic equilibrium with the amount of available moisture. The weak interlayer forces allow water and other water-miscible compounds (such as methanol, ethanol, isopropanol, sorbitol, glycerine, and acetone) to permeate the interlayer spaces, causing the clay to swell (Elder 1982b).

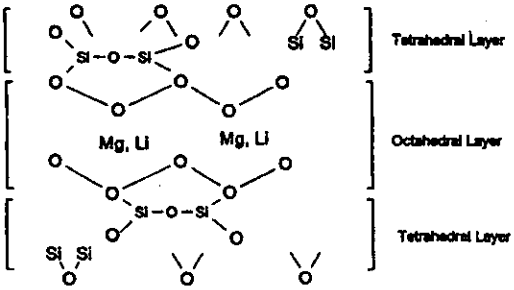

FIGURE 2
Hectorite subunit structure consisting of one octahedral layer between two tetrahedral layers. Oxygen molecules also project from the free surfaces of the tetrahedral layers (Elder 1982b).

Approximately 80% of the cation exchange sites of smectite clays are involved in reactions on the basal plane surface via substitution, and the remaining 20% of the cation exchange sites are on the edges of the small unit platelet (Eichhorn and Mo 1983a). The edges of the clay platelet are responsible for the rheological activities of the montmorillonite clays and their derivatives (Eichhorn and Mo 1983a; Mardis 1984). Although less well-defined than the oleophilic platelet faces, the edges are presumed to be electrically neutral and composed of inorganic hydroxyl moieties such as Al-OH, Mg-OH, and Si-OH (Mardis 1984). Face-to-face, face-to-edge, and edge-to-edge associations exist, causing the overlapping of individual platelets in a stack or bundle as well as overlapping between platelet stacks (Eichhorn and Mo 1983a). When displaced in a fluid, the clay platelets form three-dimensional networks through interplate hydrogen bonding. These hydrogen bonds are similar to their organic counterparts; they have low bond energies and are easily disrupted by shear. High-shear application processes break down the networks such that the coating viscosity is similar to that of a coating without a rheological additive. Under rest conditions, the hydrogen bonds rapidly reform and increase the viscosity of the applied coating (Mardis 1984).

Reactivity

Stearalkonium Hectorite is relatively inert. It is heat stable up to 500°C, and resists acid or base attacks within the pH range of 3 to 11 (Elder 1982b; Rheox, Inc. 1996).

Alkylbenzyldimethylammonium chlorides such as Stearalkonium Chloride are expected to produce traces of *N*-nitrosamines in the presence of nitrosating agents. Stearalkonium Chloride can also be solubilized by adding an excess of anionic or cationic compounds. Once solubilized, however, Stearalkonium Chloride's cationic portion loses its antimicrobial activity and the anionic portion loses its foaming characteristics (Elder 1982a).

In the cases of Quaternium 18-Hectorite and Quaternium 18-Bentonite, the clay-nitrogen bonds do not dissociate up to 500°C, and are not attacked by acid or base over the pH range 3 to 11 (Cosmetic, Toiletry, and Fragrance Association [CTFA] No date).

$$R^+Cl^- + Na^+\text{organoclay}^- \longrightarrow R^+\text{organoclay}^- + Na^+Cl^-$$

FIGURE 3

General reaction between Stearalkonium Chloride and Hectorite to form Stearalkonium Hectorite. $[R]^+$ is [trialkyl aryl ammonium]$^+$ (Nikitakis and McEwen 1990; Spagnolo, Hatcher, and Faulset 1987; Zlatkis and Jiao 1991).

Method of Manufacture

As shown in Figure 3, Stearalkonium Hectorite results from cation exchange reactions between Stearalkonium Chloride and Hectorite (Nikitakis and McEwen 1990) and the organic cation is [trialkyl aryl ammonium]$^+$ (Spagnolo, Hatcher, and Faulset 1987; Zlatkis and Jiao 1991).

The general procedure for preparing organic Hectorite derivatives is essentially the same as that for bentonite derivatives. Approximately 4.0 g of the clay is mixed in 200 ml water at 50 to 70°C until an aqueous suspension is formed. The organic salt (3–5 g) is added in an amount that exceeds the cation exchange capacity of the clay. The suspension is stirred for 3 to 4 hours, filtered, and washed with deionized water until free of anion. The resultant organoclay derivative is dried at ambient temperature overnight and then in an oven at 100°C for 1 to 2 hours (Zlatkis and Jiao 1991).

Excess cation is physicochemically adsorbed onto the faces of the clay if organic cation was present in an amount greater than the cation exchange capacity of the clay during production (Mardis 1984).

Impurities

Stearalkonium Hectorite contains 3 ppm and 20 ppm (maximums) elemental arsenic and elemental lead, respectively (Nikitakis and McEwen 1990). The only impurity reported in Stearalkonium Hectorite was sodium chloride, formed during the ionic exchange reaction of stearalkonium chloride and hectorite. Most of the sodium chloride formed during the reaction is washed out, leaving less than 0.5% sodium chloride. Any quaternary chlorides or amine hydrochlorides present in the starting materials undergo the ionic exchange reaction, no longer being amine chlorides, but instead amines strongly bonded to the clay. The only way to separate the amines from the clay was to destroy the clay through hydrofluoric acid digestion. "Any ionically bound quaternaries [did] not easily lend themselves to nitrosating agents," and any stearalkonium chloride in excess of the stoichiometric amount was adsorbed onto the clay (see Mardis 1984). Excess quaternary could be removed by methanol soxhlet extraction.

Typical concentrations of "adsorbed" cation were between 3.0% and 5.0% on Stearalkonium Hectorite. In more than 80 batches of stearalkonium chloride, the amount of amine hydrochloride was 0% to 0.23% (average = 0.01%), and free amine content was 0.01% to 1.5% (average = 0.97%). For an assumed combined total of 1.5% free amine and amine hydrochloride in the starting stearalkonium chloride, the amount in Stearalkonium Hectorite would be approximately 0.45%, as only 30% quaternium is used in the finished raw material (Rheox, Inc. 1996).

Stearalkonium Chloride contains 3.0% to 6.0% stearyl alcohol and 1.5% to 4.0% (combined) stearyl dimethylamine hydrochloride and stearyl dimethylamine. The latter impurities are easily nitrosated to from *N*-nitrosamines (Elder 1982a).

USE

Cosmetic

Stearalkonium Hectorite functions as a suspending agent—nonsurfactant in cosmetic product formulations (Wenninger, Canterbery, and McEwen 2000). Frequency of use data submitted to the Food and Drug Administration (FDA) in 1997 (Table 1) indicated that Stearalkonium Hectorite was used in 124 cosmetic formulations (FDA 1997). Although industry is no longer required to submit concentration of use data to the FDA (FDA 1992), data provided in 1984 stated that Stearalkonium Hectorite was used at concentrations mainly in the range of 0.1% to 10%, with one use at 10% to 25% (FDA 1984). Data submitted to CTFA in 1996 stated that Stearalkonium Hectorite was used in eyeliners at 2.0%, lipsticks at 1.0% (CTFA 1996a), and face masks at 1.4% (CTFA 1996a; Ivy Laboratories 1996). Toxicity studies were performed on an eyeliner that contained 0.198% Stearalkonium Hectorite (CTFA 1996b), a lipliner that contained 1.0% Stearalkonium Hectorite, and a face mask that consisted of 5.0% Stearalkonium Hectorite (National Testing Corp. 1989).

Noncosmetic

Stearalkonium Hectorite is commonly used as a rheological additive in the coatings industry (Eichhorn and Mo 1983a,

TABLE 1
Product formulation data on Stearalkonium Hectorite (FDA 1997)

Product category	Total no. of formulations in category	Total no. of formulations containing ingredient
Bath oils, tablets, and salts	117	1
Eyebrow pencil	89	6
Eyeliner	499	5
Eye shadow	501	1
Mascara	158	1
Other eye makeup preparations	116	2
Tonics, dressings, and other hair grooming aids	512	1
Foundations	283	1
Lipstick	758	25
Other makeup preparations	122	4
Basecoats and undercoats	46	15
Nail polish and enamel	78	44
Other manicuring preparations	59	10
Deodorants (underarm)	241	1
Other personal cleanliness products	262	1
Moisturizing	743	3
Suntan gels, creams, and liquids	134	1
1997 Total		**124**

1983b; Spagnolo, Hatcher, and Faulset 1987) to control flow behavior in solvent-based coatings (Zlatkis and Jiao 1991).

Stearalkonium Hectorite has been tested as a possible stationary phase in gas and column chromatography for the separation of aromatic isomers. Due to its short aryl group in the organic cation, however, Stearalkonium Hectorite has poor resolution and column efficiency and does not effectively separate xylene isomers, despite the structural similarity to other suitable bentones (Zlatkis and Jiao 1991).

GENERAL BIOLOGY

Antimicrobial Activity

Cationic quaternary ammonium compounds have antibacterial and antifungal activities that vary with the length of the alkyl chain, the greatest activity being associated with the C_{16} or C_{18} chain length (depending on the organism tested). This activity may increase with increased charge on the nitrogen atom, but may decrease if excessive atoms are clustered around it. Bactericidal activity tends to increase with critical micelle concentration, although no direct correlation has been reported between the surfactant activity and bactericidal action. A 1.0% solution of Stearalkonium Chloride inhibited bacterial growth in a germicidal activity study. When tested for bacteriostatic efficiency against *Salmonella typhosa*, *Staphylococcus aureus*, and *Bacillus anthracis*, Stearalkonium Chloride was an effective bacteriostat, particularly against *S. aureus* (Elder 1982a).

Adjuvant Activity

The adjuvant activity of 203 aliphatic nitrogenous bases was evaluated through the use of subcutaneous injections of diphtheria toxoid in guinea pigs. Adjuvant activity required a combination of basicity and a long aliphatic chain length (C_{12}). Active compounds were hemolytic and produced damage to monkey kidney or human epithelioid tissue culture monolayers. Stearalkonium Chloride was highly active by virtue of its long alkyl chain when administered as a single 0.1 ml dose (Elder 1982a).

Absorption, Metabolism, Distribution, and Excretion

A commercial mixture of alkylbenzyldimethylammonium chlorides (predominately C_{12-16}) was administered orally, rectally, or intramuscularly to rabbits, dogs, and cats at 10 times the lethal dose (not specified). All results indicated that the chlorides were poorly absorbed and distributed in the tissues (Elder 1982a).

ANIMAL TOXICOLOGY

Acute Oral Toxicity

The acute oral LD_{50} of Stearalkonium Chloride in rats (25% aqueous solution) was between 0.5 and 1.25 g/kg. The pure compound had an LD_{50} between 0.06 and 1.25 g/kg. A solution containing 20% stearalkonium chloride and 5% stearyl alcohol had an LD_{50} of 4.0 ± 0.1 ml/kg. In mice, undiluted stearalkonium chloride had an oral LD_{50} of 0.76 ± 0.11 g/kg (Elder 1982a).

Short-Term Dermal Toxicity

Stearalkonium Hectorite at concentrations of 12.5%, 25%, and 50% in water was applied to the skin of six rabbits per group. Six rabbits served as untreated control animals. The hair of each rabbit was clipped, and the skin of three rabbits per group was abraded. The experimental rabbits received three daily applications of Stearalkonium Hectorite 5 days a week for 3 weeks. For each application, 4 g/kg of the appropriate concentration of the test material was applied to the skin such that the test sites comprised at least 20% of the total body surface. The material was left in place for two hours and washed off; this was repeated twice each day. The rabbits were killed and examined at the end of the 3-week test period. The application of Stearalkonium Hectorite had no effect on general appearance or behavior, and no difference was observed in average weight gain between groups. Mild drying and scaling of the superficial layers persisted at the test sites for several days after initiation of the study. No differences in hematologic parameters or gross changes of the organs were observed. Microscopic lesions were detected in tissues of the heart, brain, kidneys, liver, and lungs, but were attributed to protozoan infection and not to Stearalkonium Hectorite toxicity (Food and Drug Research Laboratories [FDRL] 1971b).

Subchronic Dermal Toxicity

An aqueous solution of a product formulation containing 0.2% Stearalkonium Chloride and 0.05% stearyl alcohol was applied to the clipped skin (back and flanks) of six albino rabbits daily for 4 weeks as 2 ml doses. Mild and transient erythema, but no systemic effects, were apparent (Elder 1982a).

Chronic Oral Toxicity

An unidentified alkyldimethylbenzyl ammonium chloride surfactant (0.063%–0.5%) was given to 12 male rats per group in the diet for 2 years. Rats given 0.5% died early in the study. Rats of the lower dose groups that survived had reduced weight gains for the first year. The only gross or microscopic pathologic changes were "... produced by irritation of the gastrointestinal tract. To an extent which depended on the concentration of the surfactant agents in the diet, this irritation prevented proper nutrition. In severe cases of irritation, death resulted" (Elder 1982a).

Skin Irritation

Stearalkonium Hectorite was suspended in water containing 2.5% Polysorbate 80. The 50% (w/v) suspension was applied topically to the skin of six albino rabbits during a primary skin irritation study. The test material did not cause erythema or edema in any of the treated rabbits (FDRL 1971a).

Concentrations of 1.25%, 2.5%, and 25% Stearalkonium Chloride (0.5 ml doses) were applied to shaved, intact, and abraded skin of rabbits under occlusive patches to determine the compound's potential for dermal irritation. Primary irritation indices were 2.4, 1.0, and 6.0, respectively. The effect of 20% Stearalkonium Chloride on skin swelling was studied using the skin of guinea pigs. After being soaked in water for 1 hour, squares of stratum corneum were lifted out of the water and their dimensions determined. After immersion in the test solution for 16 hours, swelling of 1.6% was observed. The control, 13.5% sodium lauryl sulfate, produced swelling of 13.1% (Elder 1982a).

Ocular Irritation

Stearalkonium Hectorite (concentration not given) caused mild conjunctival irritation in four of six rabbits tested, and moderate conjunctival irritation in one of six rabbits tested. The observed irritation was reduced by removing the remaining test compound 24 hours after instillation (FDRL 1971c).

Undiluted Stearalkonium Hectorite did not produce ocular irritation in the three rabbits used in a Draize irritation study. The maximum irritation score (out of 110) was 0 for 3 days after instillation (CTFA 1996b).

When tested using the Eyetex in vitro ocular irritation test, an eyeliner containing 0.196% Stearalkonium Hectorite was classified as a minimal to mild irritant (Draize equivalent score 7.4–19.0). The Draize equivalent of a lipliner pencil that contained 1.0% Stearalkonium Hectorite was 9.4. A face mask that contained 5.0% Stearalkonium Hectorite was a mild to moderate irritant (Draize equivalent 19.9–36.5) (National Testing Corp. 1989).

A 25% solution of stearalkonium chloride was a severe ocular irritant in rabbits. Solutions of 1.25% or less were slightly and transiently irritating, with the effects limited to the conjunctivae; these effects disappeared after 3 to 4 days. The greatest concentration of an aqueous solution of 4:1 stearalkonium and stearyl alcohol that did not produce irritancy to rabbit ocular mucosa was 0.04% stearalkonium chloride and 0.1% stearyl alcohol (Elder 1982a).

MUTAGENICITY

Stearalkonium Hectorite was tested for mutagenic activity at 5, 15, 50, 150, 500, and 1500 μg/plate using *Salmonella typhimurium* strains TA1535, TA1537, TA1538, TA98, and TA100, with and without metabolic (S9) activation. The vehicle was 50 mg/ml dimethyl sulfoxide (DMSO). The positive controls were 2-aminoanthracene in DMSO; sodium azine in sterile, ultrapure water; 9-aminoacridine in DMSO; and 2-nitrofluorine in DMSO. Stearalkonium Hectorite at 1500 μg/plate precipitated during testing, the 500-and 1500-μg/plate amounts were toxic in the absence of S9, and 1500 μg/plate was toxic in the presence of S9. Stearalkonium Hectorite when tested in DMSO into the toxic range, was nonmutagenic in all strains tested, with and without S9 activation (Inveresk Research International 1995).

Stearalkonium Hectorite was tested for mutagenic potential using an in vitro mammalian cell assay (Huntingdon Life Sciences Ltd. 1997). The amounts tested ranged from 5 to 500 μg/ml Stearalkonium Hectorite for the preliminary toxicity assay, and 1 to 50 μg/ml for the mutation assays. Stearalkonium Hectorite was diluted with ethanol to give a final ethanol concentration of 1.0% (v/v). The test system used a subline of mouse lymphoma L5178Y cells, and relied upon the detection and quantitation of forward mutation from $TK^{+/-}$ (wild-type) to $TK^{-/-}$ (thymidine kinase deficient). The assay was performed in duplicate with and without S9 metabolic activation. Significant increases in mutation frequency were not observed in any of the tests. The investigators concluded that Stearalkonium Hectorite did not have mutagenic potential.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

No data on the reproductive and developmental toxicity of either Stearalkonium Hectorite or stearalkonium chloride were found.

A 50% solution of a related compound, myristalkonium chloride, did not adversely affect reproductive success or increase the incidence of terata in albino rats when given by gavage (10–50 mg/kg/day) on days 6 to 15 of gestation (Elder 1982a).

CLINICAL ASSESSMENT OF SAFETY

Skin Irritation And Sensitization

Stearalkonium Hectorite, supplied as a tan powder, was tested using 50 subjects in a repeat-insult patch test. The occlusive patch was 3 cm × 3 cm in size. No signs of toxicity or sensitization were observed (FDRL 1971d).

A facial mask containing 1.4% Stearalkonium Hectorite (25% aqueous solution) was tested for contact-sensitization potential using 27 adult volunteers (9 females and 18 males; 18–51 years old). Patches were applied to the upper outer arm, volar forearm, or the back of each subject, and the test consisted of an induction phase and challenge phase. During the induction phase, the skin sites were pretreated with 0.1 ml of 0.25% (SLS) for 24 hours, and an induction patch (0.1 ml of the test material) was applied to the same site and left in place for 48 hours (if placed over a weekend, the patch was left in place for 72 hours). A total of five pretreatments and induction exposures were performed. During the challenge phase, a skin site on the opposite arm, forearm, or side of the back was pretreated with 0.1 ml of 5.0% SLS for 1 hours, and the challenge patch was applied to the same site for 48 hours. The site was evaluated for sensitization 1 and 24 hours later. Two subjects were dropped from the study for reasons unrelated to the test material, and no adverse reactions or signs of contact allergenicity were observed in the remaining panelists (Ivy Laboratories 1996).

Fifty volunteers were treated with a 1% aqueous solution of Stearalkonium Chloride in a Shelanski repeated insult patch test. All subjects failed to react to the test solution. In a second study, a cotton patch saturated with an aqueous solution of 20% Stearalkonium Chloride and 5% stearyl alcohol was applied to the inner forearm of 50 subjects. The patch was covered with aluminum foil and fixed in place with adhesive tape for 48 hours. Definite erythema was observed in some panelists (number not reported). No evidence of sensitization was found upon challenge, 2 weeks later. As the test compound used was not highly purified, the observed primary irritation could have been due to the presence of impurities. Other researchers reported that a 0.8% concentration of Stearalkonium Chloride was nonirritating and nonsensitizing (Elder 1982a).

Ocular Irritation

Approximately 2 mg of Stearalkonium Hectorite (finely divided white powder) was instilled into the conjunctival sac of one eye of each of ten subjects. The contralateral eye served as the negative control. The subjects' eyes were examined at 1 minute, 1 hour and 24 hours after instillation, and the subjects rated their discomfort. All subjects reported the sensation of "sand or gravel" in the treated eye. None reported stinging or painful sensations. Twenty grams of Stearalkonium Hectorite were suspended in corn oil or physiological saline to result in a final volume of 100 ml. The two suspensions were instilled into the conjunctival sac as 0.1 ml test volumes. One eye of each volunteer was exposed to the corn oil suspension, and the other eye was exposed to the saline suspension. The subjects closed their eyes firmly for 1 minute, then rated any discomfort. The eyes were examined for visible signs of irritation at 1 and 24 hours after instillation. All subjects reported a "sand or gravel" sensation in the saline-treated eye. No ocular damage was observed in either eye after treatment with Stearalkonium Hectorite (FDRL 1971e).

SUMMARY

Stearalkonium Hectorite serves as a suspending agent in cosmetics. Stearalkonium Hectorite was used in 124 cosmetic formulations in 1997. Data from industry indicated that Stearalkonium Hectorite was used at concentrations up to 5% in cosmetics.

Stearalkonium Hectorite is formed by the cation exchange reaction of Hectorite clay and stearalkonium chloride. Excess cation is adsorbed onto the clay during the reaction; thus, the combined amount of free amines and amine hydrocarbons in Stearalkonium Hectorite is 0.45% (30% cation is used in the finished raw product). The only other major impurity reported was 0.5% sodium chloride.

Acute toxicity data of Stearalkonium Hectorite were not available, but data on stearalkonium chloride were found. The oral LD_{50} in rats of 25% aqueous solution of stearalkonium chloride was 0.5 to 1.25 g/kg. The pure compound had a LD_{50} of 0.06 to 1.25 g/kg. The LD_{50} of a 20% solution of stearalkonium chloride with 5% stearyl alcohol was 4.0 ml/kg. In mice, the oral LD_{50} of stearal konivm chloride was 0.76 g/kg.

During a 3-week dermal toxicity study using rabbits, 12.5% to 50% Stearalkonium Hectorite did not cause differences in hematologic parameters or gross and microscopic abnormalities. In a 4-week study, rabbits treated with an aqueous solution of a formulation containing 0.2% stearalkonium chloride and 0.05% stearyl alcohol had only mild and transient erythema at the treatment sites.

Rats fed 0.5% of an unidentified alkyldimethylbenzyl ammonium chloride died early in a 2-year chronic toxicity study. At lower doses, the rats had decreased weight gains during the first year of treatment, and had irritation of the gastrointestinal tract.

Stearalkonium Hectorite (50%) suspended in water with 2.5% polysorbate 80 did not cause primary skin irritation in rabbits. For stearalkonium chloride, the primary irritation indices in rabbits were 2.4, 1.0, and 6.0 for test concentrations of 1.25%, 2.5%, and 25%, respectively. Stearalkonium chloride at a concentration of 20% caused 1.6% swelling to the stratum corneum of guinea pigs. In contrast, 13.5% sodium lauryl sulfate (positive control) caused 13.1% swelling.

An unspecified concentration of Stearalkonium Hectorite caused mild conjunctival irritation in the eyes of 4/6 rabbits tested, and moderate irritation in the eyes of 1/6 rabbits. During a second ocular irritation study, undiluted Stearalkonium Hectorite was not an ocular irritant. Formulations containing up to 5.0% Stearalkonium Hectorite were classified as mild to moderate irritants in the Eyetex in vitro ocular irritation test. Stearalkonium chloride (25%) was a severe ocular irritant in rabbits, but solutions of $\leq$1.25% were only slightly and transiently irritating.

Stearalkonium Hectorite was not mutagenic in the Ames test (using five strains of *S. typhimurium* with and without metabolic activation) when tested in DMSO into the toxic range ($\geq$500 μg/plate). In a forward mutation assay using mouse lymphoma L5178Y cells, Stearalkonium Hectorite did not cause significant increases in mutation frequency.

No data on the reproductive and developmental toxicity of Stearalkonium Hectorite or stearalkonium chloride were available. A 50% solution of a related compound, myristalkonium chloride was not teratogenic when pregnant albino rats were treated with 10 to 50 mg/kg/day by gavage.

In clinical studies, Stearalkonium Hectorite powder did not cause dermal toxicity or sensitization in a repeated insult patch test using 50 subjects. A facial mask containing 1.4% Stearalkonium Hectorite (25% aqueous solution) did not cause contact sensitization when tested on 27 adults. Stearalkonium chloride caused erythema, but not sensitization. Concentrations of 0.8% to 1% produced no signs of irritation or sensitization. In ocular irritation assays, Stearalkonium Hectorite powder or a suspension in corn oil caused sensations of sand or gravel in the eyes of subjects.

DISCUSSION

The CIR Expert Panel evaluated data on the safety of Stearalkonium Hectorite, as well as data on its reactants, stearalkonium chloride and Hectorite clay. The Panel concluded that the available data were sufficient to support the safety in cosmetics of Stearalkonium Hectorite.

As the nitrogen of the starting material, stearalkonium chloride, is positively charged, it was considered unlikely that it would be available for nitrosation. Any quaternary chlorides or amine hydrochlorides present in the starting materials become strongly bound to the Hectorite clay, as does excess stearalkonium chloride, and are not readily available for nitrosation. The formation of *N*-nitrosamines was, therefore, considered not to be of concern.

CONCLUSION

Based upon the available data, the CIR Expert Panel concludes that Stearalkonium Hectorite is safe for use in cosmetics under the present practices of use.

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