Safety Assessment of Alkonium Clays as Used in Cosmetics

Status:	Draft Report for Panel Review
Release Date:	May 22, 2015
Panel Meeting Date:	June 15-16, 2015

The 2015 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 Lillian J. Gill, D.P.A. This report was prepared by Lillian C. Becker, Scientific Analyst/Writer.

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MEMORANDUM

To: CIR Expert Panel and Liaisons

From: Lillian C. Becker, M.S.
Scientific Analyst and Writer

Date: May 22, 2015

Subject: Safety Assessment of Alkonium Clays As Used In Cosmetics

Attached is the draft report of Alkonium Clays as used in cosmetics.[*alkcly_062015_Rep*] The SLR was posted in March, 2015. The SLR included a request for the following types of data:

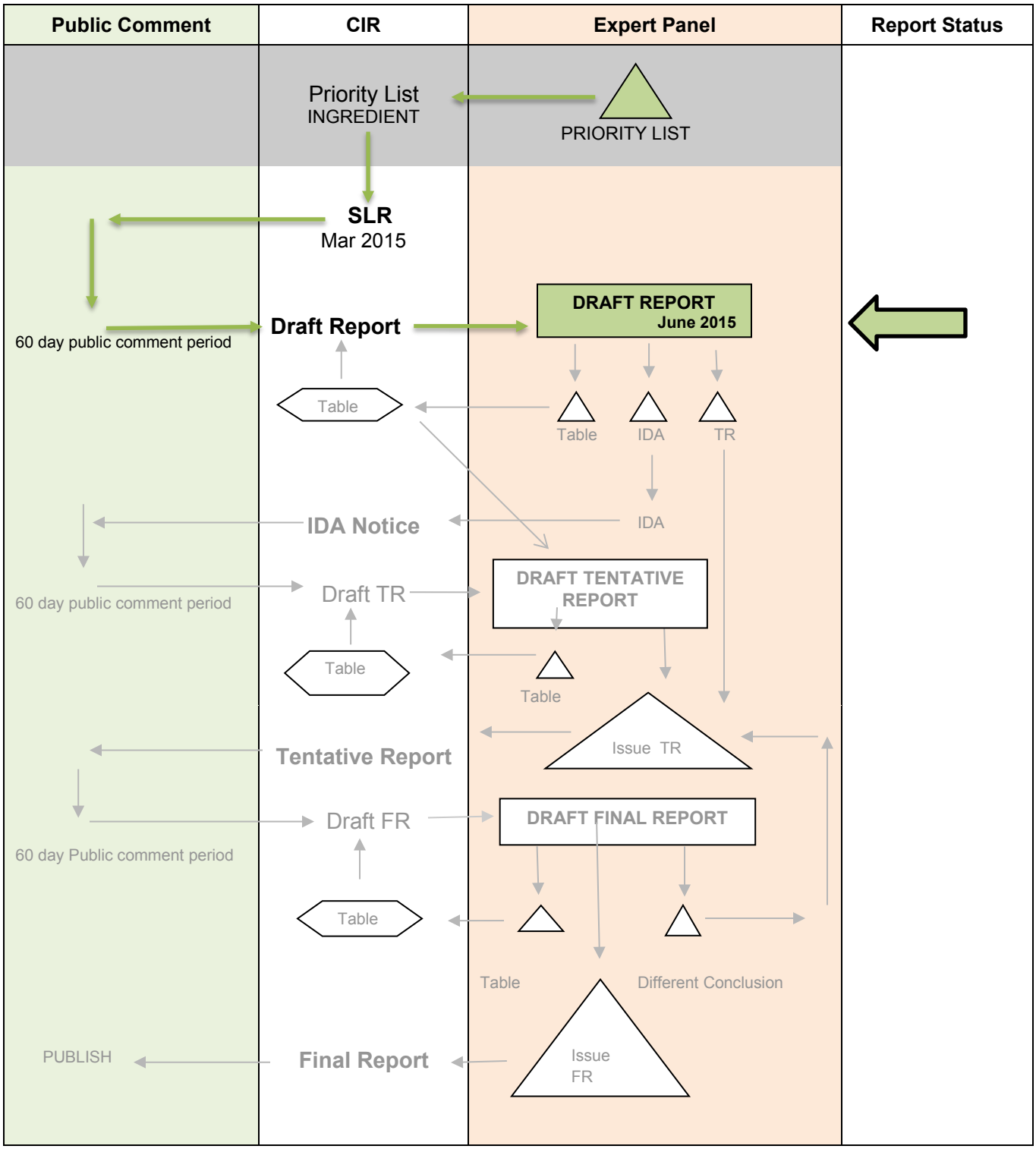
- Chemical and physical properties;
- Impurities data;
- Toxicokinetic data, specifically on the dermal absorption of these ingredients; if these ingredients were to have appreciable dermal absorption or if toxicokinetic assays are not possible, oral toxicity data, including reproductive/developmental toxicity and carcinogenicity data, and genotoxicity data are needed. These data may be less critical if there is no appreciable dermal penetration, however, the data would improve the resulting safety assessment;
- Oral, inhalation, and/or dermal toxicity data;
- Dermal, ocular, and/or other mucous membrane irritation and sensitization data; and
- Any other relevant safety information that may be available.

Concentration of use data were submitted by the Council and incorporated into the report. [*alkcly_062015_Data1; alkcly_062015_Data2*] All of the published data were on stearalkonium bentonite, and no published data were available for the remaining ingredients. Two HRIPTs on products containing stearalkonium bentonite and quaternium-90 montmorillonite/quaternium-90 sepiolite were submitted by industry and have been incorporated into the report. [*alkcly_062015_Data3; alkcly_062015_Data4*] Some data on a related ingredient (benzyl-dimethyl-hydrogenated tallow ammonium montmorillonite) was located on the ECHA database and has been incorporated for read across purposes.

Since the data from the ammonium hectorite report is relevant to the this safety assessment, it is included in the packet.[*alkcly_062015_prev*]

Council comments were address.[*alkcly_062015_PCPC*] No further comments were submitted.

The Panel is to examine the data in the report and decide if the data are sufficient to issue a conclusion of safety. If a conclusion can be reached, the Panel is to develop the basis for the Discussion. If the Panel determines that the data are not sufficient to reach a conclusion of safety, an Insufficient Data Announcement should be issued, which includes a list of data needs.


Public Comment
CIR
Expert Panel
Report Status
Priority List
INGREDIENT
PRIORITY LIST
SLR
Mar 2015
60 day public comment period
Draft Report
DRAFT REPORT
June 2015
Table
Table
IDA
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IDA Notice
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60 day public comment period
Draft TR
DRAFT TENTATIVE REPORT
Table
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Issue TR
Tentative Report
Draft FR
DRAFT FINAL REPORT
60 day Public comment period
Table
Table
Different Conclusion
Issue FR
PUBLISH
Final Report

Alkonium Clays Data Profile for June, 2015. Writer - Lillian Becker																		
	ADME			Acute toxicity			Repeated dose toxicity			Irritation			Sensitization					
	Dermal Penetration	Log K_{ow}	Use	Oral	Dermal	Inhale	Oral	Dermal	Inhale	Ocular Irritation	Dermal Irr. Animal	Dermal Irr Human	Sensitization Animal	Sensitization Human	Repro/Devel toxicity	Genotoxicity	Carcinogenicity	Phototoxicity
Benzalkonium montmorillonite																		
Benzalkonium sepiolite																		
Hydrogenated tallowalkonium bentonite																		
Quaternium-18/ benzalkonium bentonite																		
Quaternium-90 bentonite			X															
Quaternium-90 montmorillonite			X											X				
Quaternium-90 sepiolite			X											X				
Stearalkonium bentonite		est	X	X	X		X			X	X		X	X		X		
Read across																		
Benzyl-dimethyl-hydrogenated tallow ammonium montmorillonite clay				X		X												
Quatemium-18 hectorite								X										
Stearalkonium hectorite								X										
Dihydrogenated tallow benzylmonium hectorite															X			

est=estimated

Search Strategy – Alkonium Clays

SciFinder – Substance search. 109 hits. None useful.

INCI names and CAS nos. 109 hits. Removed patents – 22 hits. None useful.

"Alkonium clays" – 2 hits. None useful.

"Bentonite toxicity" – 4 hits. 1 ordered

"Montmorillonite toxicity" – 282 hits. Removed patents – 206 hits. English – 176 hits. 16 ordered.

"Sepiolite toxicity" – 73 hits. Removed patents – 48 hits. English – 33 hits. Ordered 3.

HPVIS – INCI names and CAS nos. No hits.

Google - INCI names and CAS nos. A few MSDS sheets; NICNAS 2013 on Stearalkonium Bentonite.

ECHA – CAS Nos and INCI names. 1 hit. Searched downloaded database for montmorillonite (2 hits), sepiolite (no hits), and bentonite (1 hit). Only the montmorillonite was useful for read across. Most of the data had sparse details and not useful. Used what was relevant.

NTP – INCI names and CAS Nos. No hits.

Report History – Alkonium Clays

June, 2014 – This group of ingredients was added to the priority list.

March, 2015 – SLR was posted on the CIR website with a request for more data.

- Chemical and physical properties;
- Impurities data;
- Toxicokinetic data, specifically dermal absorption of these ingredients; if these ingredients were to have appreciable dermal absorption or if toxicokinetic assays are not possible, oral toxicity data, including reproductive/developmental toxicity and carcinogenicity data, are needed, as are genotoxicity data; these data may not be crucial if these ingredients have no appreciable dermal penetration, however, if they were available, they would improve the resulting safety assessment;
- Oral, inhalation, and/or dermal toxicity data;
- Dermal, ocular, and/or other mucous membrane irritation and sensitization data; and
- Any other relevant safety information that may be available.

June, 2015 – The Panel examines the draft report.

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INTRODUCTION

This is a review of the available scientific literature and unpublished data provided by industry relevant to assessing the safety of the alkonium clays as used in cosmetics. Alkonium clays are the products of the reactions of an ammonium salt with a smectite clay. These 8 ingredients are:

- benzalkonium montmorillonite
- benzalkonium sepiolite
- hydrogenated tallowalkonium bentonite
- quaternium-18/benzalkonium bentonite
- quaternium-90 bentonite
- quaternium-90 montmorillonite
- quaternium-90 sepiolite
- stearalkonium bentonite

In cosmetics, these ingredients are reported to function as dispersing agents-nonsurfactant, emulsion stabilizers, and viscosity increasing agents-nonaqueous (Table 1).[1]

Alkonium clays are derived from a group of phyllosilicate, layered, clay-based minerals (known as smectites), the most prominent of which are montmorillonite, beidellite, nontronite, saponite, and hectorite. The alkonium clays are grouped together because of their similarities in chemical structure, chemical composition, exchangeable ion type, and the small crystal size of these minerals.

Ingredients similar to the alkonium clays have been reviewed by the Cosmetic Ingredient Review (CIR) Expert Panel (Panel) and may be useful for read across (Table 2). Ammonium hectorites (disteardimonium hectorite, dihydrogenated tallow benzylmonium hectorite, stearalkonium hectorite, and quatemium-18 hectorite), hectorite, and quaternium-18 hectorite, quaternium-18 bentonite, hectorite, bentonite, montmorillonite and other clays and earths were found to be safe as used.[2-6]

Components of the alkonium clays in this safety assessment have been reviewed by the Panel and may be useful in the determination of safety (Table 2). Quaternium-18 and stearalkonium chloride were determined to be safe as used, and benzalkonium chloride is safe up to 0.1%.[7-9] Quaternium-90 has not been reviewed by the Panel. However, quaternium-90 and quaternium-18 are structurally similar (both are dialkyl dimonium chlorides, which vary only in fatty alkyl chain lengths; from palm oil and tallow, respectively). Thus, information on quaternium-18 is relevant for the determination of the safety of ingredients containing quaternium-90.

Data for benzyl-dimethyl-hydrogenated tallow ammonium montmorillonite clay were discovered on the European Chemicals Agency (ECHA) website.[10] While this is not benzalkonium montmorillonite, the data for this clay is included because the similarity in chemical structures may justify read across.

CHEMISTRY

Definition and Structure

Alkonium clays are the products of the reactions of an ammonium salt with smectite clay. Definitions of these ingredients are presented in Table 1.

Alkonium clays are derived from a group of phyllosilicate, layered, clay-based minerals, the general term for which is smectites, and the most prominent of which are montmorillonite, beidellite, nontronite, saponite, and hectorite.[5] These clays are differentiated by variations in chemical composition involving substitutions of aluminum for silicon in tetrahedral cation sites and for aluminum, iron, magnesium, and lithium in octahedral cation sites (Figure 1).

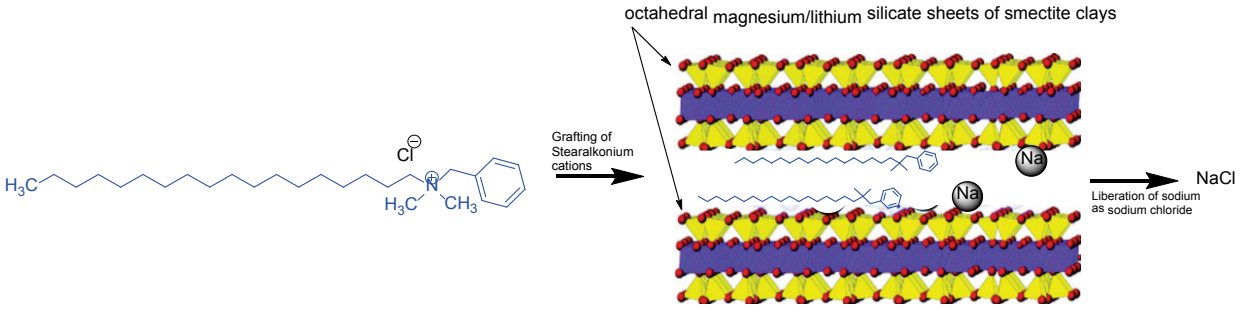

Figure 1. Synthesis of alkonium clays.

Smectite minerals are a subset of clays that include alkonium clays, and have a variable net negative charge that is balanced by sodium, calcium, or magnesium ions adsorbed externally on interlamellar surfaces.[5] The structure, chemical composition, exchangeable ion type, and small crystal size of smectite minerals are responsible for several unique properties, including a large chemically active surface area, a high cation exchange capacity, interlamellar surfaces having unusual hydration characteristics, and the ability to strongly modify the flow behavior of liquids. Because of isomorphous substitution of cations in the octahedral sheet during hectorite formation, the surfaces of these minerals have a delocalized net negative charge in the lattice. Cations located between 2 consecutive layers (octahedral sheets) contribute to compensate for the structural charge and to keep the layers bound. Thus, cations like sodium are attracted to the mineral surface to counterbalance the interlayer charge. These cations can easily be exchanged, because they are retained in the mineral structure by electrostatic attractions.

The structure of alkonium clays depend on the charges of the layers and the lengths of the alkyl chains. Short-chain alkylammonium ions are monolayered. Long-chain alkylammonium ions are bilayered.[11,12] Smectites are highly charged and are composed of 3 kinked alkyl chains.[13] The basal spacing of alkylammonium smectites increases, in steps, with the alkyl-chain length.[14]

NATURAL SMECTITE CLAYS (BENTONITE, MONTMORILLONITE, AND SEPIOLITE)

Smectites (aka organoclays) are closely related and the names have been used interchangeably to describe structurally similar clay minerals in the literature.[15] Natural deposits in which one of these clay minerals predominate are more commonly referred to by the predominant clay mineral's name. Thus, considering the similarity in the clay minerals of this category, the defining differentiation between the groups is the cation that is reacted with the clay.

Bentonite is a widely distributed natural material consisting predominantly of the clay mineral montmorillonite, a smectite mineral.[15,16] Bentonite is formed of highly colloidal and plastic clays, and is produced by in situ devitrification of volcanic ash.[17]

Montmorillonite occurs abundantly as dust at and near surface deposits of bentonite and is dispersed widely by air and moving water.[17] Montmorillonite is thus ubiquitous in low concentrations worldwide in soil, in the sediment load of natural waters, and in airborne dust. In geology, the term "montmorillonite" is ambiguous, and is used to refer to both a group of related clay minerals (where smectite is a more appropriate term) and to a specific member (montmorillonite) of that group.[18]

In structure, sepiolite can be considered transitional because it is found between the chain-structured and layer-structured silicates.[19,20] Sepiolite is essentially hydrated magnesium silicates with minor amounts of substituting elements.[21] Intracrystalline adsorption is limited in sepiolite due to the sizes of the channels in the crystal structure and the non-expanding nature of the clays. Therefore, only small and highly polar molecules interact with the "inner" surfaces, and nonpolar organic molecules absorbs to external surfaces. Polar organic molecules can penetrate into the channels, but preliminary outgassing of the material is usually necessary to remove "zeolitic" water. For example, short-chain alcohols can penetrate into the channels after outgassing.

Sepiolite is found in sedimentary strata in arid and semi-arid climates around the world.[21] Deposits of sepiolite have been reported in China, France, Japan, Madagascar, the Republic of Korea, Spain, Turkey, the United Republic of Tanzania, and the United States.[19,22,23]

Physical and Chemical Properties

Chemical and physical properties of stearalkonium bentonite are presented in Table 3. Stearalkonium bentonite particle sizes were reported to be: <100 μm, approximately 90%; < 10 μm, 30%; and < 0.5 μm, 0.02%.[24] A description of the chemical and physical properties of the other ingredients in this safety assessment were neither discovered in the literature nor submitted for review.

MONTMORILLONITE, BENTONITE, AND SEPIOLITE

Alkonium clays have a high capacity for expansion and swelling and can be easily hydrated and dehydrated.[25]

Intracrystalline adsorption is limited in sepiolite due to the sizes of the channels in the crystal structure and the non-expanding nature of the clays.[26] Therefore, only small and highly polar molecules interact with the "inner" surfaces, and nonpolar organic molecules absorb to external surfaces. Polar organic molecules can penetrate into the channels, but preliminary outgassing of the material is usually necessary to remove "zeolitic" water. For example, short-chain alcohols can penetrate into the channels after outgassing.

Bentonite has the ability to form thixotrophic gels with water, absorb large quantities of water, and a high cation exchange capacity.[16] The absorption of water causes an accompanying increase in volume of as much as 12-15 times its dry bulk, and a high cation exchange capacity. Freshly exposed bentonite is white to pale green or blue and, darkens in time to yellow, red, or brown.[17]

Montmorillonite clay is composed of minute particles that, under electron microscopy, appear as aggregates of irregular or hexagonal flakes or, less commonly, thin laths.[27] Differences in substitution affect, and in some cases control, morphology.

Method of Manufacture

Clay minerals, such as the alkonium clays, are synthesized by grafting cationic surfactants to clay (ie, exchanging the interlayer sodium cations with a cationic surfactant). These cationic surfactants are quaternary ammonium compounds with the template formula $[(CH_3)_3NR]^+$, $[(CH_3)_2NRR']^+$, and $[CH_3NRR'R'']^+$, where R, R', and R'' are alkyl or aromatic hydrocarbons. For instance, in stearalkonium bentonite some of the inorganic cations of bentonite have been replaced by $[(CH_3)_2NRR']^+$, where R and R' are an octadecyl alkyl chain (ie, stearyl group) and a benzyl group, respectively. The exchange is typically performed by the addition of the appropriate ammonium chloride (eg, stearalkonium chloride) to an alcohol/water slurry of the clay.[28] The major by-products are inorganic chlorides (eg, sodium chloride), which are removed during processing. This cation exchange shifts the nature of these minerals from hydrophilic to lipophilic.[28]

Montmorillonite salts may be made either by neutralizing the acid clay with the appropriate organic base or by treating the clay with a large excess of the organic salt in water solution.[29] The solution is heated to boiling and then shaken for 30 min. The compound is separated by centrifuging and washing with water and alcohol to remove any excess amine, if an excess had been used.

Impurities

As noted above, these ingredients have a high cation exchange capacity. Depending on the composition of a given cosmetic formulation, the degree to which these alkonium salts may be exchanged out of these ingredients will vary. Accordingly, there may be some resultant free alkonium salts.

Stearalkonium bentonite may contain up to 5% quartz and up to 0.005% benzenemethanol.[24]

NATURAL SMECTITE CLAYS BACKGROUND (MONTMORILLONITE, BENTONITE, AND SEPIOLITE)

Clays contain trace elements (ie, antimony, arsenic, cadmium, cobalt, copper, lead, mercury, nickel, selenium, tellurium, thallium, zinc) in concentrations that are widely variable, depending on their geological origin.[30] These trace elements may be in the clay mineral structure or adsorbed on clay particles, which plays the most important role in controlling the distribution and abundance of these elements within these clays. Chemical elements in crystalline positions are usually locked in the clay, whereas those adsorbed may be mobilized and transferred to leaching solutions.

Natural bentonite may contain feldspar, cristobalite, and crystalline quartz.[31]

In an analysis of natural sepiolite samples from Japan, Spain, China, and Turkey, only the sample from China had small amounts of talc and calcite.[32]

USE

Cosmetic

The Panel assesses the safety of cosmetic ingredients based on the expected use of these ingredients in cosmetics. The Panel reviews data received from the Food and Drug Administration (FDA) and the cosmetics industry to determine the expected cosmetic use. The data received from the FDA are collected from manufacturers on the use of individual ingredients in cosmetics, by cosmetic product category, through the FDA Voluntary Cosmetic Registration Program (VCRP), and the data from the cosmetic industry are submitted in response to a survey of the maximum reported use concentrations, by category, conducted by the Personal Care Products Council (Council).

According to the 2015 VCRP survey data, stearalkonium bentonite had the most reported uses at 423, including 420 leave-on uses and 3 rinse-off uses (Table 4).[33] Most of these uses were in nail products (272 uses in nail polish and enamel), but this ingredient was also used in lipstick (64 uses) and in products used around the eye (7 uses). Quaternium-90 bentonite was reported to be used in 64 leave-on products, including 31 products used around the eye and 16 lipsticks.

In the survey conducted by the Council of the maximum use concentrations of ingredients in this group, stearalkonium bentonite was reported to be used at concentrations up to 6.5% in nail polish and enamel, 2.4% in lipstick, and 2.5% in eye shadow.[34] Quaternium-90 bentonite was reported to be used up to 6.1% in mascara, 2.2% in face powder, and 6.1% in lipstick.

For 2 ingredients, no uses were reported to the VCRP, but a use concentration was provided in the industry survey. The VCRP did not report any uses for quaternium-90 montmorillonite, but the industry survey indicated that it is used in 2 types of leave-on formulations (foundations and aerosol suntan products) at concentrations up to 0.8%. No uses were reported by the VCRP for quaternium-90 sepiolite. However, the Council reported that it was used in 2 types of leave-on products (foundations and aerosol suntan products) at concentrations up to 3.2%. It should be presumed that both of these ingredients are used in at least 2 cosmetic formulations.

There were no reported uses for:

- hydrogenated tallowalkonium bentonite
- quaternium-18/benzalkonium bentonite
- benzalkonium montmorillonite
- benzalkonium sepiolite

Quaternium-90 montmorillonite is used in aerosol suntan products at concentrations up to 0.8% and quaternium-90 sepiolite is used in aerosol suntan products up to 3.2%. In practice, 95% to 99% of the droplets/particles released from

cosmetic sprays have aerodynamic equivalent diameters >10 μm.[35-38] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and bronchial regions and would not be respirable (ie, they would not enter the lungs) to any appreciable amount.[35,38]

None of the alkonium clays named in this report are restricted from use in any way under the rules governing cosmetic products in the European Union.[39]

The National Industrial Chemicals Notification and Assessment Scheme (NICNAS) of Australia concluded that stearalkonium bentonite did not pose an unreasonable risk to public health when used in cosmetic products at concentrations up to 5% concentration.[24]

Non-Cosmetic

Large volumes of smectite clay minerals are used as a binder in foundry sand; a filter/clarifier/decolorizer; pet waste/odor absorbent; oil/grease absorbent; and pesticide carrier.[40] Smaller volumes are used in medical and pharmaceutical applications, building products, radioactive waste disposal, lubricants, detergents, seed coating, and water purification.

TOXICOKINETICS

Absorption, Distribution, Metabolism, and Excretion

Data on toxicokinetics of the alkonium clays in this safety assessment were not found in the published literature, nor were unpublished data submitted. However, due to the confounding chemical nature of these alkonium clays, toxicokinetic assays were not expected to be found.

TOXICOLOGICAL STUDIES

Single Dose (Acute) Toxicity

Dermal – Non-Human

STEARALKONIUM BENTONITE

The dermal LD_{50} of stearalkonium bentonite was >2000 mg/kg (in deionized water) in Sprague-Dawley rats (n=5/sex).[24] The test was conducted according to the Organization for Economic Cooperation and Development (OECD) Test Guideline (TG) 402.

Oral – Non-Human

STEARALKONIUM BENTONITE

The oral LD_{50} of stearalkonium bentonite was >5000 mg/kg (in corn oil) in albino Wistar rats (n=5/sex).[24] Clinical signs included matted fur and unkempt appearance on days 1 and 2 of observation. One male animal showed slight depression on day 4 prior to its death on day 5. At necropsy, a slightly reddened gastric mucosa was noted in a single rat. The test was conducted in a manner similar to the OECD TG 401.

BENZYL-DIMETHYL-HYDROGENATED TALLOW AMMONIUM MONTMORILLONITE CLAY

The reported oral LD_{50} for benzyl-dimethyl-hydrogenated tallow ammonium montmorillonite clay was >5000 mg/kg in Sprague-Dawley rats (n not specified).[10]

Inhalation – Non-Human

Data on the acute inhalation toxicity of the alkonium clays in this safety assessment were not found in the published literature, nor were unpublished data submitted.

BENZYL-DIMETHYL-HYDROGENATED TALLOW AMMONIUM MONTMORILLONITE CLAY

The reported inhalation LC_{50} for benzyl-dimethyl-hydrogenated tallow ammonium montmorillonite clay was >206 mg/L air when Sprague-Dawley rats (n not specified) were exposed for 1 h.[10]

Repeated Dose Toxicity

Dermal

Data on the repeated dose dermal toxicity of the alkonium clays in this safety assessment were not found in the published literature, nor were unpublished data submitted.

Oral – Non-Human

STEARALKONIUM BENTONITE

In a 28-day oral toxicity test of stearalkonium bentonite (100, 316, and 1000 mg/kg in 0.1% aqueous solution of Na-carboxymethylcellulose) in Fischer CDF(F344)/CRLBR, SPF rats (n=5/sex), the no-observed-effect-level (NOEL) was 1000 mg/kg/d when administered by gavage, based on the absence of test substance-related toxicological effects at any of the doses administered.[24] The test was conducted according to OECD TG 407. Clinical signs were similar in the treatment and control groups. Chromodakryorrhoea was observed occasionally in both the control and treatment groups. There were no

differences in feed consumption or body weight gain in males. Decreased body weights were recorded for females in the high dose recovery group (duration of recovery period not specified), but were considered by the study authors to be of no toxicological relevance. No differences were observed in hematology or clinical biochemistry parameters, appearance of spontaneous lesions, or organ weight changes in the males, and no dose-related trends observed at necropsy or by histopathology examination. Decreases in organ weights in the females (heart and brain) at the end of recovery period were considered to be of no toxicological relevance, because there were no corresponding differences observed at the end of the exposure period.

Inhalation – Non-Human

Data on the repeated dose inhalation toxicity of the alkonium clays in this safety assessment were not found in the published literature nor were unpublished data provided.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

Data on reproductive and developmental toxicity of the alkonium clays in this safety assessment were not found in the published literature, nor were unpublished data provided.

GENOTOXICITY

In Vitro

STEARALKONIUM BENTONITE

Stearalkonium bentonite (3.16, 10, 31.6, 100, and 316 µg/plate, with and without metabolic activation, in dimethyl sulfoxide) was not genotoxic to *Salmonella typhimurium* (strains TA1535, TA1537, TA98, TA100, and TA102).[24] The positive control yielded the expected results. Pronounced cytotoxicity was noted in all test strains at 316 µg/plate, with and without metabolic activation. In the assays without metabolic activation, cytotoxicity was also noted in several strains at 31.6 and/or 100 µg/plate. The test was performed according to the OECD Test Guideline 471.

In Vivo

STEARALKONIUM BENTONITE

In a micronucleus assay, conducted according to the OECD TG 474, stearalkonium bentonite (1000, 1500, and 2000 mg/kg in 0.1% aqueous solution of Na-carboxymethylcellulose) was not clastogenic in Crl:NMRI BR mice (n=5/sex) when administered by gavage.[24] There were no mortalities prior to scheduled killing. The ratios between the polychromatic and normochromatic erythrocytes in the female mice at all doses were similar to that of the control data. However, the ratios were greater in males at all doses at 24 h. Because the values were within the historical negative control data ranges, the differences were not considered to be attributable to the test substance. The number of micronucleated polychromatic erythrocytes in the high dose groups (both sexes) was higher than that of the corresponding negative control group 48 h after administration. However, all counts were within the range of historical negative control data, thus the study authors considered the effect to be unrelated to the treatment. The concurrent negative and positive controls produced the expected results.

CARCINOGENICITY

Data on carcinogenicity of the alkonium clays in this safety assessment were not found in the published literature, nor were unpublished data submitted.

IRRITATION AND SENSITIZATION

Irritation

Dermal – Non-Human

STEARALKONIUM BENTONITE

Stearalkonium bentonite (100%) was not irritating to the intact or abraded skin of New Zealand White rabbits (n=6) when applied under occlusion for 24 h.[24] The test was conducted in a manner consistent with the OECD TG 404 guidelines and the test sites were examined at 24 and 72 h after patch removal. The mean erythema/eschar and edema scores for the intact sites were 0 out of 4; the mean erythema/eschar score for the abraded sites was 0.3, and the edema score was 0.25.

The maximum non-irritating concentration for stearalkonium bentonite injected intradermally was 1.25% in distilled water when tested in albino Hartley guinea pigs (n not specified).[24] The maximum non-irritating concentration when administered topically to the skin was 60% in distilled water. No further details were provided.

Ocular

STEARALKONIUM BENTONITE

Stearalkonium bentonite (100%; 0.1 g) was severely irritating when instilled into the eyes of New Zealand White rabbits (n=7).[24] The test was conducted in a manner similar to the OECD TG 405 guidelines and the rabbits were observed for 7 days after exposure. If the test substance was still present in the eye at 24 h after exposure, the eye was rinsed with

distilled water. The most severe outcome observed for conjunctiva/redness was grade 3 (diffuse beefy red) in all rabbits 24 h after instilling the test substance. One rabbit still exhibited a grade 2 response (more diffuse, crimson red, individual vessels not easily discernible) on day 7. The most severe observation for conjunctiva/chemosis was grade 4 (swelling with lids about half-closed to completely closed) in 5 of 6 rabbits examined 24 h post exposure. One rabbit still exhibited a grade 2 response (obvious swelling with partial eversion of the lids) on day 7. The highest score for conjunctiva/discharge was grade 3 (discharge with moistening of the lids and hairs and of a considerable area around eye) in 2 of 6 rabbits at 24 h post exposure. This was resolved by day 7. The most severe observation for corneal opacity was grade 2 (easily discernible translucent areas, details of iris slightly obscured) in 2 of 6 rabbits at 24 h post exposure. The highest score was grade 3 (opalescent areas, no details of iris visible, size of pupil barely discernible) was observed in 1 of 6 animals at 48 h post exposure. One rabbit still exhibited the highest grade 4 for opaqueness; the iris was invisible on day 7. Five of 6 rabbits exhibited a grade 1 iridial inflammation response (sluggish reaction) with the effect persisting in 1 rabbit through day 7.

Stearalkonium bentonite (31-36 mg in 0.1 mL; vehicle not specified) was slightly irritating to the conjunctiva of female New Zealand White rabbits (n =3).[24] Neither cornea nor irises were affected. Slight conjunctival redness was observed in 2 rabbits from 1 through 48 h after exposure. Slight-to-moderate chemosis of the conjunctiva was observed in 2 rabbits at 1 through 48 h after exposure. Ocular discharge was noted in 2 rabbits from 1 to 24 h after administration. The test was conducted according to the OECD TG 405.

Sensitization

Dermal – Non-Human

STEARALKONIUM BENTONITE

Stearalkonium bentonite was not sensitizing to albino Hartley guinea pigs (n=20) when topically applied at 60% (in distilled water) during the induction phase and topically at 30% and 60% during the challenge phase.[24] There were no signs of sensitization at 24 and 48 h after the challenges. The test was conducted according to the OECD TG 406. The test sites were treated with 10% lauryl sodium sulfate in petroleum jelly prior to the induction phase.

Dermal - Human

STEARALKONIUM BENTONITE

In a human repeated insult patch test (HRIPT; n=100) of a product containing stearalkonium bentonite (1.452%; 0.2 g), there were no signs of irritation or sensitization.[41] The test substance was applied to a patch pad and remained in the open air for 15-20 min before administration to the infrascapular area of the back or the upper arm for 24 h. There were 9 administrations in the induction phase.

QUATERNIUM-90 SEPIOLITE AND QUATERNIUM-90 MONTMORILLONITE

In an HRIPT (n=56) of a leave-on product containing quaternium-90 sepiolite (3.2%) and quaternium-90 montmorillonite (0.8%), there were no signs of irritation or sensitization.[42] The test substance (0.2 mL) was administered to the upper back on 0.75" x 0.75" occlusive patches and left for 24 or 48 h for 9 administrations.

SUMMARY

This is a review of the available scientific literature and unpublished data submitted by industry assessing the safety of alkonium clays as used in cosmetics. Alkonium clays are derived from a group of phyllosilicate, layered, clay-based minerals, including montmorillonite, saponite, and hectorite. These ingredients are grouped together because of the similar chemical structures, chemical composition, exchangeable ion type, and small crystal size of these minerals.

In cosmetics, these ingredients are reported to function as dispersing agents-nonsurfactant; emulsion stabilizers; viscosity increasing agents-nonaqueous.

Stearalkonium bentonite had the most reported uses at 423 including 420 leave-on uses and 3 rinse-off uses; it was reported to be used up to 6.5% in nail polish and enamel, 2.4% in lipstick, and 2.5% in eye shadow. Quaternium-90 bentonite was reported to be used in 64 leave-on products; it was reported to be used up to 6.1% in mascara, up to 2.2% in face powder, and up to 6.1% in lipstick.

The dermal LD_{50} of stearalkonium bentonite was >2000 mg/kg in rats. The oral LD_{50} of stearalkonium bentonite was >5000 mg/kg in rats. In a 28-day oral toxicity test of stearalkonium bentonite, the NOEL was 1000 mg/kg/d in rats.

Stearalkonium bentonite was not genotoxic to *S. typhimurium* (strains TA1535, TA1537, TA98, TA100, and TA102). It was cytotoxic at 316 µg/plate, without and with metabolic activation. In the tests without metabolic activation, cytotoxicity was also noted in several strains at concentrations of 31.6 and/or 100 µg/plate. In a micronucleus assay, stearalkonium bentonite was not clastogenic in mice when tested at doses of up to 2000 mg/kg.

Stearalkonium bentonite was not irritating to intact or abraded skin of rabbits at 100%. Stearalkonium bentonite was not irritating when injected intradermally at 1.25% and was not irritating when topically applied to the skin at a concentration of 60% in guinea pigs.

In one study, stearalkonium bentonite was a severe ocular irritant when instilled into the eyes of rabbits at 100%. In another study, stearalkonium bentonite (31-36 mg/ 0.1 mL) was slightly irritating to rabbit eyes. Neither cornea nor irises were affected.

Stearalkonium bentonite was not sensitizing to guinea pigs when topically induced with a 60% solution and challenged topically with 30% and 60% solutions.

In an HRIPT of a product containing stearalkonium bentonite at 1.452%, and in another of a leave-on product containing quaternium-90 sepiolite at 3.2% and quaternium-90 montmorillonite at 0.8%, there were no signs of irritation or sensitization.

DISCUSSION

The Discussion is scheduled to be developed at the June, 2015 Panel meeting.

CONCLUSION

The Conclusion may be developed at the June, 2015 Panel meeting.

TABLES

Table 1. Definitions and functions of the ingredients in this safety assessment.[1]

Ingredient CAS No.	Definition	Function
Hydrogenated tallowalkonium bentonite	Hydrogenated tallowalkonium bentonite is the product of the reaction of hydrogenated tallowalkonium chloride and bentonite.	Viscosity increasing agent-aqueous
Quaternium-18/ benzalkonium bentonite	Quaternium-18/benzalkonium bentonite is a reaction product of bentonite and quaternium-18 and benzalkonium chloride.	Dispersing agent-nonsurfactant
Quaternium-90 bentonite 226226-22-8	Quaternium-90 bentonite is a reaction product of bentonite and quaternium-90.	Dispersing agent-nonsurfactant
Stearalkonium bentonite 130501-87-0	Stearalkonium bentonite is a reaction product of bentonite and stearalkonium chloride.	Dispersing agent-nonsurfactant
Benzalkonium montmorillonite	Benzalkonium montmorillonite is the reaction product of benzalkonium chloride and montmorillonite.	Dispersing agent-nonsurfactant; emulsion stabilizer; viscosity increasing agent-nonaqueous
Benzalkonium sepiolite	Benzalkonium sepiolite is the product obtained by the reaction of benzalkonium chloride and sepiolite.	Dispersing agent-nonsurfactant; emulsion stabilizer; viscosity increasing agent-nonaqueous
Quaternium-90 montmorillonite	Quaternium-90 montmorillonite is the product obtained by the reaction of quaternium-90 and montmorillonite.	Dispersing agent-nonsurfactant; emulsion stabilizer; viscosity increasing agent-nonaqueous
Quaternium-90 sepiolite	Quaternium-90 sepiolite is the product obtained by the reaction of quaternium-90 and sepiolite.	Dispersing agent-nonsurfactant; emulsion stabilizer; viscosity increasing agent-nonaqueous

Table 2. Data on related ingredients to the alkonium clays in this safety assessment.

Related ingredient	Summary data	Reference
Ammonium hectorites - disteardimonium hectorite, dihydrogenated tallow benzylmonium hectorite, stearalkonium hectorite, and quatemium-18 hectorite	Safe as used; highest concentration of use: 28%. Single dose (acute) toxicity-oral :LD_{50} dihydrogenated tallow benzylmonium hectorite, 5.0 g/kg for rats; quaternium-18, >10 g/kg. Single dose (acute) toxicity-inhalation: LC_{50} dihydrogenated tallow benzylmonium hectorite, >5.2 mg/L for rats after 4 hours; aerosolized quaternium-18 hectorite was not toxic to rats at 202 mg/L after 1 h. Repeated dose toxicity: Stearalkonium hectorite was not dermally toxic to rabbits at concentrations of 12.5% to 50% over 3 weeks. Quaternium-18 hectorite administered to the skin of rabbits for 3 weeks was not toxic up to 50%. Genotoxicity: Stearalkonium hectorite was not mutagenic to *S. typhimurium* up to 1500 µL/plate or mouse lymphoma cells up to 500 µL/plate. Dermal irritation and sensitization: Stearalkonium hectorite did not cause erythema or edema to albino rabbits at 50% w/v. Quaternium-18 hectorite at 50% was not irritating to rabbits. Dihydrogenated tallow benzylmonium hectorite at 0.5 g in 0.5 mL saline was not irritating when administered to the intact and abraded skin of rabbits. Disteardimonium hectorite was not irritating to humans in 2 patch tests at 15%. Stearalkonium hectorite was not irritating or sensitizing to humans at 100%. Dihydrogenated tallow benzylmonium hectorite (concentration not provided) did not cause delayed contact hypersensitivity in albino guinea pigs. Quaternium-18 hectorite was not irritating or sensitizing up to 100% in HRIPTs. Ocular irritation: Stearalkonium hectorite was a minimal to mild ocular irritant to rabbits and humans. It was classified as a minimal to mild irritant in 3 Eyetex in vitro tests of products. Quaternium-18 hectorite was not an ocular irritant at 50% in rabbits and at 2 mg in humans. Dihydrogenated tallow benzylmonium hectorite at 0.5 g in 0.5 mL saline was practically nonirritating when administered to the eyes of rabbits.	[5]
Quaternium-18, quaternium-18 hectorite, and quaternium-18 bentonite	Safe as used; highest concentration of use: 10%; 19%. Absorption, distribution, metabolism, and excretion: Quaternium-18 hectorite and bentonite are chemically, physically, and biologically inert. Quaternium compounds are poorly absorbed through the skin. Single dose (acute) toxicity-oral and percutaneous: Acute oral and percutaneous toxicity tests in animals indicate that all three compounds exhibit little or no systemic toxic effects. Single dose (acute) toxicity-inhalation: Quaternium-18 hectorite was nontoxic in an acute inhalation study. Repeated dose toxicity- oral and dermal: Subchronic oral and dermal toxicity tests on quaternium-18 and quaternium-18 bentonite presented no evidence of systemic toxicity. Irritation and sensitization: All 3 quaternium compounds were considered to cause at	[2,4,9]

	most only slight irritation to animal skin. None has been reported to be skin sensitizing agents in animals. In clinical studies, quaternium-18 is practically nonirritating and nonsensitizing to the skin. Quaternium-18 hectorite and quaternium-18 bentonite can be classified as a nonirritating, "nonfatiguing," and nonsensitizing agent. Ocular irritation: In ocular irritation studies in rabbits, all 3 ingredients have been shown to be at most mild irritants. Quaternium-18 hectorite exhibits no ocular irritation in humans. Phototoxicity: Quaternium-18 Hectorite does not present any adverse phototoxic or photoallergenic effects.	
Hectorite, bentonite, montmorillonite, aluminum silicate, calcium silicate, magnesium aluminum silicate, magnesium silicate, magnesium trisilicate, sodium magnesium silicate, zirconium silicate, attapulgite, bentonite, fuller's earth, kaolin, lithium magnesium silicate, lithium magnesium sodium silicate, pyrophyllite, and zeolite	Safe as used; highest concentration of use: 100%. Absorption, distribution, metabolism, and excretion: No absorption of aluminum and elevated levels of silicon were recorded in assayed plasma samples of dogs given magnesium trisilicate and zeolite orally. The urinary excretion of silica was 5.2% in males given 20 g of magnesium trisilicate. Single-dose (acute) toxicity-oral: oral LD_{50} of hectorite, >5 g/kg in rats; calcium silicate, 3400 mg/kg in rats; magnesium aluminum silicate, 50000 mg/kg in mice; zirconium silicate, > 200 g/kg in mice; kaolin, 149 g/kg in rats (death due to bowel obstruction); 15 natural zeolites, 10 g/kg in rats. Single-dose (acute) toxicity-dermal: The acute dermal LD_{50} was >3.5 g/kg for rabbits exposed to 4% magnesium aluminum silicate. Repeated dose toxicity-oral: In short-term oral toxicity studies, no adverse effects were seen in mice or rabbits dosed up to 5 g/kg magnesium aluminum silicate; beagle dogs and rats fed aluminum silicate had no renal lesions. Dogs and rats fed magnesium trisilicate for 4 weeks had polydypsia and polyuria, and all dogs had renal cortical lesions. Guinea pigs had renal lesions after 4 months of drinking magnesium trisilicate in their tap water. Rats fed 10% magnesium aluminum silicate had slightly elevated silicon levels of the spleen and dogs and rats fed 10% magnesium aluminum silicate had no negative responses in 90-day feeding studies. No lesions were found in rats dosed up to 1000 mg/kg for 104 weeks. Various zeolites added to the diets of pigs caused no adverse effects. Repeated dose toxicity-inhalation: Small primary neoplastic lesions were found in 2 rats exposed to a calcium silicate sample in an inhalation chamber. The mass of silicate measured in the lungs ranged from 0.1-0.8 mg. Lebrija and Leichester Attapulgite samples caused 1 peritoneal mesothelioma, one adenocarcinoma, and 3 bronchoalveolar hyperplasia and 2 mesotheliomas, 1 peritoneal mesothelioma, 1 malignant alveolar tumor and eight bronchoalveolar hyperplasia (inhalation route) in rats, respectively. Both samples contained long fibers. Moderate to extensive respiratory disease was noted in rats chronically exposed to synthetic zeolite A by inhalation methods. Irritation and sensitization: Hectorite was nonirritating to the skin of rabbits in a Draize primary skin irritation study. 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. Sodium magnesium silicate (4%) had no primary skin irritation in rabbits and had no cumulative skin irritation in guinea pigs. Ocular irritation: Bentonite caused severe iritis after injection into the anterior chamber of the eyes of rabbits. 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. 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. Rats tolerated a single dose of zeolite A without any adverse reaction in the eye. Reproductive and developmental toxicity: Calcium silicate (250 to 1600 mg/kg) had no effect on nidation or on maternal or fetal survival in rabbits. Magnesium aluminum silicate (6000 mg/kg) had neither a teratogenic nor adverse effects on the mouse fetus. Female rats receiving a 20% kaolin diet exhibited maternal anemia but no reduction in birth weight of the pups was recorded. 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). Clinoptilolite had no effect on female rat reproductive performance. Genotoxicity: 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. No increase mutation frequencies were seen in the *Salmonella* TA-1530 or G-46 assay and no increase in recombinant activity in the *Saccharomyces* D3 assay treated with calcium silicate. 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 increase in the number of aberrations compared to controls and in a dominant lethal assay did not induce any dominant lethal mutations. In primary hepatocyte cultures, the addition of attapulgite had no significant unscheduled DNA synthesis (UDS) response or modulated response to AAF (a positive control); attapulgite at 10 $\mu g/cm^2$ caused increases in UDS in rat pleural mesothelial cells. Zeolite particles (<10 μm) produced an increase in the percentage of aberrant metaphases, mostly chromatid breaks. Irritation and sensitization: Applications of 2 g of magnesium aluminum silicate to the skin of 2 humans daily for 1 week caused no effects. In occupational exposure studies of mineral dusts, 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.	[6]

Benzalkonium chloride	Safe as used; highest concentration of use: 0.1%; 0.5% in a liquid towelette Single dose (acute) toxicity-oral: Acute oral LD_{50} for rats dosed with benzalkonium chloride ranged from 342 to 525 mg/kg. Single dose (acute) toxicity-dermal: Of 96 mice receiving dermal applications of 6.5 and 50% benzalkonium chloride, 29 died within 72 h after application. Repeated dose toxicity-oral: In a subchronic toxicity study, benzalkonium chloride solutions were administered via stomach tube to 40 albino rats for 12 weeks (once/day) at dosages of 50.0 mg/kg (1 :20 dilution) and 100.0 mg/kg (1:10 dilution). Two of 20 rats receiving the 100.0 mg/kg dosage died. In a chronic toxicity study, benzalkonium chloride (10.0%) was administered via stomach tube to 18 beagle dogs at dosages of 12.5, 25.0, and 50.0 mg/kg for 52 weeks (once daily). One of 6 dogs receiving 50 mg/kg dosages and 3 of 6 dogs receiving 25 mg/kg dosages died. Repeated dose toxicity-inhalation: No adverse effects were noted when rats and hamsters inhaled a conditioner containing 0.1% benzalkonium chloride over a period of 13 consecutive weeks (4 h/day). Irritation and sensitization-nonhuman: Benzalkonium chloride concentrations of l.0%-50% induced reactions ranging from erythema to necrosis when applied to the skins of rabbits. In another study, 24-h applications of 1.0% to 10.0% benzalkonium chloride to the skins of rabbits resulted in severe induration. Benzalkonium chloride concentrations of 1.0% and 5.0% induced epidermal necrosis when applied (24-h exposure) to the skins of albino guinea pigs. Applications of 2.0% benzalkonium chloride to the skins (abraded and intact) of rabbits resulted in severe erythema (2-day application period). Slight erythema was noted 7 days after application. Applications of 1.0% benzalkonium chloride to the skins of white rats during a 2-month period caused hyperemia and necrosis. Following applications of 0.5% benzalkonium chloride to the skins of rabbits (24 h exposure), severe erythema, moderate edema, and eschar formation were observed. Benzalkonium chloride (0.5%) resulted in practically no skin irritation when applied to the skins of albino rabbits (24-h exposure). When 0.1% benzalkonium chloride was applied to the skins of rabbits (5-day contact period), slight erythema and necrosis were observed. These reactions were observed for 3 weeks post-treatment. Irritation and sensitization-human: Cutaneous reactions were observed in 2 of 399 dermatitis patients patch tested with benzalkonium chloride over a period of 64 months. In separate studies, primary irritant dermatitis was observed in 13 patients and 12 patients patch tested with 10.0% benzalkonium chloride (24-h exposure). In another study, erythema was observed in 33 of 70 leprosy patients patch tested with 2.5% benzalkonium chloride. Benzalkonium chloride concentrations of 0.5%, 1.0%, and 2.0% induced several pustular and/or bullous reactions in 26 of 55 patients (48-h exposures). The application of 17.0% benzalkonium chloride (24-hour period) to the skin of each of 21 subjects resulted in well-defined erythema (13 subjects). Confluent erythema and edema were noted in the skin of subjects tested with 5.0% and 2.5% benzalkonium chloride (12-h exposure). Results from a 21-day skin irritation study of a cream containing 0.1% benzalkonium chloride indicated essentially no cumulative irritation. A cream containing 0.1% benzalkonium chloride did not induce skin irritation or sensitization reactions in 101 subjects patch tested during a 6-week period (24-h exposures). Sensitization reactions were observed in 6 of 100 patients patch-tested with 0.07% benzalkonium chloride. The 6 patients also had positive reactions to 0.05%, 0.025%, and 0.01% benzalkonium chloride. Sixty-six of 2,806 patients were sensitive to 0.1% benzalkonium chloride. In another study, allergic reactions were observed in 9 of 142 patients patch tested with 0.1% benzalkonium chloride. Sensitization reactions were not observed in normal subjects patch-tested with 0.1% benzalkonium chloride. Ocular irritation: Benzalkonium chloride at 1% and 2.0% aqueous induced severe iritis and severe conjunctival injection, respectively, when instilled into the conjunctival sac of rabbits twice daily for 7 days. Benzalkonium chloride (0.3%) induced minimal ocular irritation when instilled once into the eyes of rabbits. Single instillations of 0.1% benzalkonium chloride into the conjunctival sac of albino rabbits did not cause ocular irritation. The instillation of 0.1% benzalkonium chloride into the conjunctival sacs of rabbits 5 times daily for 1 week resulted in corneal damage. The instillation of 0.01% benzalkonium chloride into the conjunctival sacs of rabbits (5 min-6-h period) resulted in cornea1 damage. Four hours after the instillation of 0.5%, 1.0%, and 10% benzalkonium chloride, cornea1 damage was noted in rabbits and guinea pigs. The ocular administration of 0.5%, 1.0%, and 2.0% solutions twice daily for 7 days caused conjunctival damage in rabbits. Following the daily administration of 0.007% and 0.1% benzalkonium chloride for 2 weeks, retinal detachment was observed in pigmented but not albino rabbits. In in vitro intraocular toxicity studies, the exposure of rabbit corneas to benzalkonium chloride concentrations ranging from 0.0001% to 0.01% resulted in cornea1 damage. Exposure periods ranged from 2 min (0.01%) to 110 min (0.0001%). The longest exposure was 180 min (0.0065%). Slight conjunctival hyperemia was observed in 1 of 51 human subjects who received ocular instillations of 0.02% benzalkonium chloride. Reproductive and developmental toxicity: The instillation of 100 or 208 mg/kg of aqueous benzalkonium chloride into the vaginas of pregnant rats resulted in sternal defects in the offspring. Genotoxicity: Benzalkonium chloride was not mutagenic to *S. typhimurium* (strains TA1535, TA1536, TA1537, and TA1538) and *E. coli* (strains B/r WP2 her^+ and WP2 her^-) in microbial test systems making up the ret-assay in combination with reverse	[8]

	mutation systems. Mutagenic activity also was not demonstrated in reversion assays involving *S. typhimurium* (strains TA1535, TA1536, TA1537, and TA1538) and, in the ret-assay, with *Bacillus subtilis* (strains H17 Ret^+ and M45 Rec^-). In the plate incorporation assay, benzalkonium chloride was not mutagenic to *S. typhimurium* (strains TA98, TA1538, TA1537, and TA100). In the *E. coli* DNA polymerase assay benzalkonium chloride induced repairable DNA damage in strains W3110 (pol A+) and p3478 (pol A-). Carcinogenicity: The dermal application of 8.5% and 17% benzalkonium chloride to rabbits and mice did not result in tumor formation or systemic toxic effects, but did produce ulceration and inflammation at the application sites.	
Stearalkonium chloride	Safe as used; highest concentration of use: 5%, 7%. Single dose (acute) toxicity-oral: The oral LD_{50} of stearalkonium chloride in rats ranged from 0.5-1.25 g/kg. Repeated dose toxicity-oral: In mice, an LD_{50} value of 0.760-0.113 g/kg was reported in a 7-day oral study. Irritation and sensitization: In single application dermal studies with concentrations of up to 25%, stearalkonium chloride produced minor irritation in rabbits. A repeated insult patch test with a 1% aqueous solution of stearalkonium chloride on 50 human subjects showed the material to be neither a primary irritant nor a sensitizer. A single 48-hour patch test with challenge 2 weeks later indicated that 20% stearalkonium chloride was not a sensitizer. Ocular irritation: In acute eye studies in rabbits, a 25% solution of stearalkonium chloride was a severe irritant. Concentrations of 1.25% and less were slightly and transiently irritating to the rabbit eye.	[9]

Table 3. Chemical and physical properties of stearalkonium bentonite.

Property	Value	Reference
Stearalkonium bentonite		
Density/Specific Gravity @ 25 ºC	330-480	[24]
Melting Point ºC	> 390	[24]
Boiling Point ºC	> 500	[24]
Water Solubility g/L @ 20 ºC	< 0.04	[24]
log K_{ow} @ 25˚C	5.87 (estimated)	[24]

Table 4. Frequency of use according to duration and exposure of alkonium clays.[33,34]

Use type	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)
	Quaternium-90 bentonite		**Quaternium-90 montmorillonite**		**Quaternium-90 sepiolite**		**Stearalkonium bentonite**	
Total/range	**64**	**0.41-6.1**	**NR**	**0.4-0.8**	**NR**	**1.6-3.2**	**423**	**0.051-6.5**
Duration of use								
Leave-on	64	0.41-6.1	NR	0.4-0.8	NR	1.6-3.2	420	0.19-6.5
Rinse-off	NR	0.63	NR	NR	NR	NR	3	0.051
Diluted for (bath) use	NR	NR	NR	NR	NR	NR	NR	NR
Exposure type[a]								
Eye area	31	0.41-6.1	NR	NR	NR	NR	7	0.19-2.5
Incidental ingestion	16	6.1	NR	NR	NR	NR	64	0.5-2.4
Incidental Inhalation-sprays	2[b]	NR	NR	0.8	NR	3.2	1[d]	NR
Incidental inhalation-powders	2[b]	2.2; 0.88[c]	NR	NR	NR	NR	NR	NR
Dermal contact	35	0.41-4	NR	0.4-0.8	NR	1.6-3.2	19	0.19-2.5
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair-noncoloring	NR	NR	NR	NR	NR	NR	NR	NR
Hair-coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	0.46-0.5	NR	NR	NR	NR	340	0.051-6.5
Mucous Membrane	16	6.1	NR	NR	NR	NR	66	2.4
Baby	NR	NR	NR	NR	NR	NR	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.

[a] Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.

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

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

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

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Safety Assessment of Ammonium Hectorites as Used in Cosmetics

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Abstract

The Cosmetic Ingredient Review Expert Panel (Panel) reviewed the safety of 4 ammonium hectorite compounds used in cosmetics: disteardimonium hectorite, dihydrogenated tallow benzylmonium hectorite, stearalkonium hectorite, and quaternium-18 hectorite. These ingredients function in cosmetics mainly as nonsurfactant suspending agents. The Panel reviewed available animal and human data and concluded that these ammonium hectorite compounds were safe as cosmetic ingredients in the practices of use and concentration as given in this safety assessment.

Keywords

cosmetics, safety, ammonium hectorites

Introduction

This report assesses the safety of ammonium hectorites as used in cosmetics. The ingredients in this report are disteardimonium hectorite, dihydrogenated tallow benzylmonium hectorite, stearalkonium hectorite, and quaternium-18 hectorite. These ingredients function in cosmetics mainly as nonsurfactant suspending agents (Table 1).

Other hectorite ingredients, stearalkonium hectorite and quaternium-18 hectorite, have been reviewed by the Cosmetic Ingredient Review Expert Panel (Panel) and were found to be safe for use in cosmetics.[1,2] Summaries of the relevant data from these reports are included in the appropriate sections.

The silicate clay, hectorite, 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.[3] Quaternium-18 was also previously reviewed and was found to be safe as a cosmetic ingredient.[1]

Chemistry

Definition and Structure

Hectorite is part of a group of phyllosilicate, layered, clay-based minerals, the general term for which is smectites, the most prominent of which are montmorillonite, beidellite, nontronite, saponite, and hectorite.[4] As mentioned previously, hectorite and montmorillonite were included in the previous safety assessment of clays.[3] These various clays are differentiated by variations in chemical composition involving substitutions of aluminum for silicon in tetrahedral cation sites and aluminum, iron, magnesium, and lithium in octahedral cation sites (Figure 1).

Smectite minerals have a variable net negative charge, which is balanced by sodium, calcium, or magnesium ions adsorbed externally on interlamellar surfaces. The structure, chemical composition, exchangeable ion type, and small crystal size of smectite minerals are responsible for several unique properties, including a large chemically active surface area, a high cation exchange capacity, interlamellar surfaces having unusual hydration characteristics, and the ability to strongly modify the flow behavior of liquids. In the cosmetics industry, clay-based products are used to improve properties such as suspension, emulsion stability, viscosity, thermal stability, and spreadability.

Structurally, hectorite is a trioctahedral, magnesium/lithium silicate-based mineral that is amorphous and does not contain any crystalline silica.

Because of isomorphous substitution of lithium ions (a +1 charge) for magnesium ions (a +2 charge) in the octahedral sheet during hectorite formation, the surfaces of these minerals have a delocalized net negative charge in the lattice.[5] Cations

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Table 1. Definitions of Ammonium Hectorite Ingredients as in the *International Cosmetic Ingredient Dictionary and Handbook* Followed by the Definition Developed by the CIR Staff (in *italics*).[32]

Ingredient CAS No	Definition	Function
Quaternium-18 hectorite 12001-31-9 71011-27-3	Quaternium-18 hectorite is a reaction product of hectorite and quaternium-18. *Quaternium-18 hectorite is the cation exchange product of hectorite and quaternium-18. Essentially, some of the sodium cations of hectorite are replaced with di(hydrogenated tallow)dimethylammonium cations.*	Suspending agents—nonsurfactant
Disteardimonium hectorite 94891-31-3 (CAS no reflects dicetearimonium hectorite; ie, di-C16 18 dimethyl-ammonium hectorite)	Disteardimonium hectorite is the reaction product of distearyldimonium chloride and hectorite. *Disteardimonium hectorite is the cation exchange product of distearyldimonium chloride and hectorite. Essentially, some of the sodium cations of hectorite are replaced with distearyldimethylammonium cations.*	Suspending agents—nonsurfactant
Stearalkonium hectorite 12691-60-0 94891-33-5	Stearalkonium hectorite is a reaction product of hectorite and stearalkonium chloride. *Stearalkonium hectorite is a cation exchange product of hectorite and stearalkonium chloride. Essentially, some of the sodium cations of hectorite are replaced with benzyldimethylstearylammonium cations.*	Suspending agents—nonsurfactant
Dihydrogenated tallow benzylmonium hectorite	Dihydrogenated tallow benzylmonium hectorite is the reaction product of hectorite and a dihydrogenated tallow benzyl monomethyl quaternary ammonium salt. *Dihydrogenated tallow benzylmonium hectorite is the cation exchange product of hectorite and a di(hydrogenated tallow) benzyl monomethyl quaternary ammonium salt. Essentially, some of the sodium cations of hectorite are replaced with di(hydrogenated tallow)benzylmethylammonium cations.*	Suspending agents—nonsurfactant; viscosity increasing agents—aqueous; viscosity increasing agents—nonaqueous

Abbreviations: CIR, Cosmetic Ingredient Review; CAS, Chemical Abstracts Service.

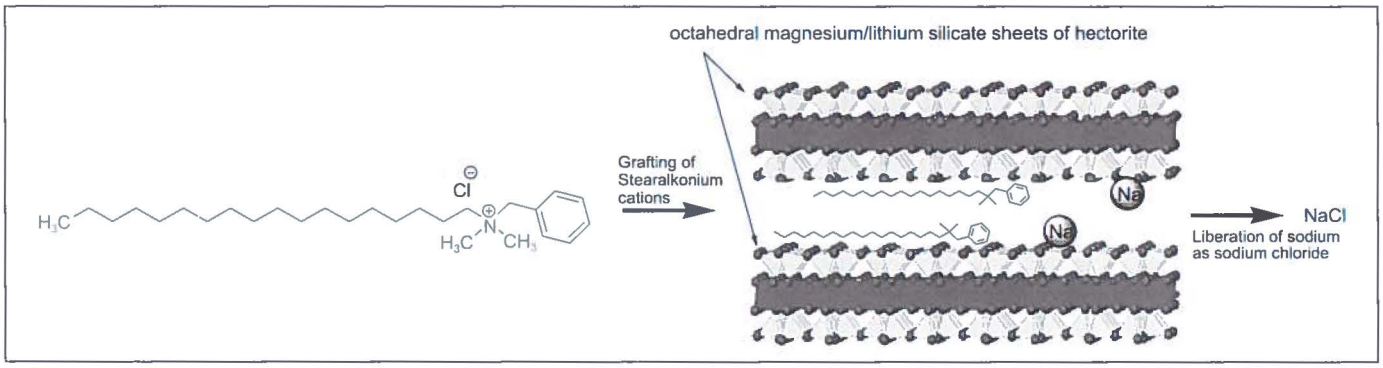
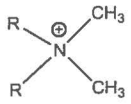


Figure 1. Synthesis of organoclay minerals.

located between 2 consecutive layers (octahedral sheets) contribute to compensate the structural charge and to keep the layers bound. Thus, cations like sodium are attracted to the mineral surface to counterbalance the interlayer charge. These cations can easily be exchanged, since they are retained by electrostatic attractions.

Organohectorite minerals, such as disteardimonium hectorite, stearalkonium hectorite, quaternium-18 hectorite, and dihydrogenated tallow benzylmonium hectorite, are synthesized by grafting cationic surfactants to hectorite (ie, exchanging the interlayer sodium cations with a cationic surfactant). These cationic surfactants are quaternary ammonium compounds with the template formulae $[(CH_3)_3NR]^+$, $[(CH_3)_2NRR']^+$, and $[CH_3NRR'R'']^+$, wherein R, R′, and R″ are alkyl or aromatic hydrocarbons. For instance, in the case of disteardimonium hectorite at least some of the sodium cations of hectorite have been exchanged for the $[(CH_3)_2NRR']^+$ cation, wherein both R and R′ are octadecyl alkyl chains (ie, stearyl groups). The exchange is typically carried out by the addition of the appropriate ammonium chloride (eg, disteardimonium chloride) to

Quaternium-18 Hectorite

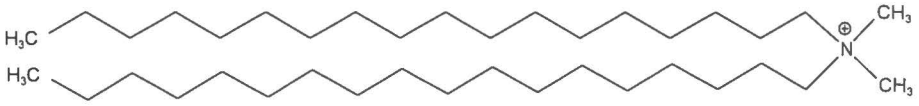


Dihydrogenated Tallow Dimonium cation: wherein R is the fatty acid chain residue of tallow

Hectorite formula: $Na_{0.33}[Mg_{2.67},Li_{0.33}]Si_4O_{10}[OH]_2$

Quaternium-18 Hectorite formula: $[Na,((CH_3)_2NR_2)]_{0.33}[Mg_{2.67},Li_{0.33}]Si_4O_{10}[OH]_2$

Disteardimonium Hectorite



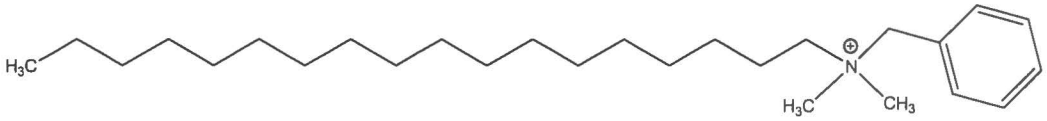
Disteardimonium cation:

Hectorite Formula: $Na_{0.33}[Mg_{2.67},Li_{0.33}]Si_4O_{10}[OH]_2$

Disteardimonium Hectorite formula: $[Na,((CH_3)_2N((CH_2)_{17}CH3)_2)]_{0.33}[Mg_{2.67},Li_{0.33}]Si_4O_{10}[OH]_2$

Stearalkonium Hectorite

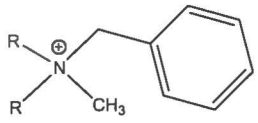
Stearalkonium cation:



Hectorite Formula: $Na_{0.33}[Mg_{2.67},Li_{0.33}]Si_4O_{10}[OH]_2$

Stearalkonium Hectorite formula: $[Na,((CH_3)_2N(CH_2)_{18}CH_3)(CH_2C_6H_5))]_{0.33}[Mg_{2.67},Li_{0.33}]Si_4O_{10}[OH]_2$

Dihydrogenated Tallow Benzylmonium Hectorite



Dihydrogenated Tallow Benzylmonium cation: wherein R is the fatty acid chain residue of tallow

Hectorite Formula:

Dihydrogenated Tallow Benzylmonium Hectorite formula: $[Na,(CH_3NR_2(CH_2C_6H_5)]_{0.33}[Mg_{2.67},Li_{0.33}]Si_4O_{10}[OH]_2$

Figure 2. Structures/Formulas of ammonium hectorite ingredients.

an alcohol/water slurry of hectorite.[6,7] The major by-product therein is sodium chloride, which is removed during processing (Figure 2). This cation exchange shifts the nature of these minerals from hydrophilic to lipophilic.[6]

Physical and Chemical Properties

The physical and chemical properties of the ingredients in this safety assessment are provided in Table 2.

Hectorite. The unique physicochemical properties of smectite clays, including hectorite, are the result of (1) extremely small crystal size, (2) variations in internal chemical composition, (3) structural characteristics caused by chemical factors, (4) large cation exchange capacity, (5) large surface area that is chemically active, (6) variations in types of exchangeable ions and surface charge, and (7) interactions with inorganic and organic liquids.[4]

Because of aggregation, the effective particle size will be larger and the surface area will be considerably smaller than the actual particle size and aggregated surface area. During the growth of hectorites, by either transformation or neoformation, crystals become interlocked and become difficult to separate except by a strong shearing force. Differences in the effective particle size of hectorites are extremely important in the determination of properties such as ion exchange, viscosity, and fluid loss.[4,8]

Quaternium-18 Hectorite. Quaternium-18 hectorite is reported to be an inert, chemically stable material. It is pH and heat stable under normal cosmetic use conditions.[9,10]

Table 2. Chemical and Physical Properties.

Property	Value	Reference
Disteardimonium hectorite		
Physical form	Organically modified hectorite/ finely divided powder	33
Color	Creamy white	33
Density/specific gravity	1.7	33
Dihydrogenated tallow benzylmonium hectorite		
Physical form	Smectite clay/finely divided powder	18
Color	Very light cream	18
Density/specific gravity	1.59	18
Stearalkonium hectorite		
Physical form	Fine powder	11
Color	Creamy white	11
Quaternium-18 hectorite		
Physical form	Powder	16,34
Color	White, light cream-colored	16,34
Odor	Faint	34
Water solubility, g/L	Insoluble	34

Impurities

Quaternium-18 Hectorite. Methyl ditallow amine, methyl ditallow ammonium hectorite, and sodium chloride are possible impurities in quaternium-18 hectorite.[11]

Stearalkonium Hectorite. Stearalkonium hectorite contains a maximum of 3 ppm and 20 ppm elemental arsenic and elemental lead, respectively.[12] Sodium chloride may be formed during the ionic exchange reaction of stearalkonium chloride and hectorite, which is washed out down to <0.5%. "Adsorbed" cations are between 3.0% and 5.0% in stearalkonium hectorite.

Use

Cosmetic

Data on ingredient usage as a function of cosmetic product type are provided to the Food and Drug Administration Voluntary Cosmetic Registration Program (VCRP), and a survey conducted by the Personal Care Products Council (Council) collected maximum use concentrations for ingredients in this group.[13-15] These data are combined in Table 3.

The VCRP reported that disteardimonium hectorite was used in 574 leave-on products (maximum of 28% in makeup preparations) and 10 rinse-off products (maximum of 4% in hair coloring preparations). Quaternium-18 hectorite was reported to be used in 106 leave-on products (maximum of 5% in mascara) and 5 rinse-off products (no concentrations of use for this category was reported by the Council). Stearalkonium hectorite was used in 467 leave-on products (maximum of 6% in nail polishes and enamels) and 2 rinse-off products (maximum of 3% in eye makeup remover). Of the 467 leave-on products, 277 were used in nail polish and enamels.

There were no reported uses of dihydrogenated tallow benzylmonium hectorite.

Noncosmetic

Quaternium-18 hectorite is used as a dispersant in volatile oils.[16] It has also been tested as granulators and binders in the production of tablets.

Toxicokinetics

Absorption, Distribution, Metabolism, and Excretion

There were no published studies on absorption, distribution, metabolism, or excretion discovered nor were unpublished data provided.

Toxicological Studies

Acute Toxicity

Dermal. There were no published acute dermal toxicity studies discovered nor were unpublished data provided.

Oral: Nonhumans

Quaternium-18 Hectorite. The oral median lethal dose (LD_{50}) of quaternium-18 was >10 g/kg for rats.[17]

Dihydrogenated Tallow Benzylmonium Hectorite. The oral LD_{50} for dihydrogenated tallow benzylmonium hectorite was >5.0 g/kg for Sprague-Dawley rats (n = 10).[18]

Inhalation: Nonhumans

Quaterium-18 Hectorite. Aerosolized quaternium-18 hectorite (202 mg/L in isopropyl myristate) was not toxic to rats (n = 10) after 1 hour.[7,17]

Dihydrogenated Tallow Benzylmonium Hectorite. The inhalation LC_{50} for dihydrogenated tallow benzylmonium hectorite was >5.2 mg/L for Sprague-Dawley rats (n = 5/sex) after 4 hours.[18]

Repeated Dose Toxicity

Dermal: Nonhumans

Quaternium-18 Hectorite. Quaternium-18 hectorite (up to 50%) applied, unoccluded, to the exposed skin of rabbits 3 times per day for 5 days per week for 3 weeks caused no toxic effects.[7,17] There was mild drying and scaling of the upper layers of the skin during the early days of the study.

Stearalkonium Hectorite. There were no toxic effects observed when stearalkonium hectorite (12.5% to 50%) was dermally applied to rabbits twice per day, unoccluded over 3 weeks.[19]

Table 3. Current Frequency and Concentration of Use According to Duration and Type of Exposure. There Were No Reported Uses of Dihydrogenated Tallow Benzylmonium Hectorite.[13-15,a,b]

	Disteardimonium Hectorite		Stearalkonium Hectorite		Quaternium-18 Hectorite	
	# of Uses	Concentration (%)	# of Uses	Concentration (%)	# of Uses	Concentration (%)
Duration of use						
Totals/conc range	584	0.04-28	469	0.006-6	111	0.05-5
Leave-on	574	0.04-28	467	0.006-6	106	0.05-5
Rinse-off	10	0.7-4	2	3	5	NR
Diluted for (bath) use	NR	3	NR	NR	NR	NR
Exposure type						
Eye area	202	0.02-15	40	0.2-3	42	1-5
Incidental ingestion	159	0.04-9	79	2-3	21	0.05
Incidental inhalation sprays	6	0.1-2	5	0.2-1[c]	6	0.02-3
Incidental inhalation powders		2	NR	NR	NR	NR
Dermal contact	329	0.07-28	84	0.006-3	68	0.02-3
Deodorant (underarm)	5	0.5-2[d]	NR	0.4[e]	4	0.02-3[f]
Hair—non coloring	1	0.3	1	NR	3	NR
Hair—coloring	NR	3-4	NR	NR	NR	NR
Nail	NR	NR	304	0.3-6	NR	NR
Mucous membrane	160	0.04-9	81	2-3	23	0.05
Baby products	NR	NR	NR	NR	NR	NR

Abbreviations: conc, concentration; NR, not reported.
[a] 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.
[b] Totals = rinse-off + leave-on product uses.
[c] 0.3% in a body and hand spray.
[d] 0.5% to 2% in aerosol sprays, 4% in nonspray products.
[e] 0.4% in both aerosol and pump sprays.
[f] 0.2% to 3% in aerosol sprays.

Reproductive and Developmental Toxicity

Dihydrogenated Tallow Benzylmonium Hectorite

Orally administered dihydrogenated tallow benzylmonium hectorite had a no effect level of 1000 mg/kg to Sprague-Dawley rats.[20] The test material was administered throughout the complete reproductive cycle for 1 generation. No further information was provided.

Genotoxicity

In Vitro

Stearalkonium Hectorite. Stearalkonium hectorite was not mutagenic to *Salmonella typhimurium* (TA98, TA100, TA1535, TA1537, and TA1538) up to 1500 µL/plate or mouse lymphoma cells up to 500 µL/plate.[21,22]

Dihydrogenated Tallow Benzylmonium Hectorite. Dihydrogenated tallow benzylmonium hectorite (concentration not provided) was not mutagenic in an Ames test using *Salmonella* with or without metabolic activation.[20]

Carcinogenicity

There were no published carcinogenicity studies discovered nor were unpublished data provided.

Irritation and Sensitization

Irritation

Dermal: Nonhumans

Quaternium-18 Hectorite. Quaternium-18 hectorite (50%) was not dermally irritating to rabbits.[17]

Stearalkonium Hectorite. Stearalkonium hectorite (50% w/v in water with 2.5% polysorbate 809) did not cause erythema or edema when administered to the skin of albino rabbits.[19]

Dihydrogenated Tallow Benzylmonium Hectorite. Dihydrogenated tallow benzylmonium hectorite (0.5 g in 0.5 mL saline) was not irritating when administered to the intact and abraded skin of New Zealand White rabbits (n = 6) for 24 hours.[20]

Dermal: Humans

Disteardimonium Hectorite. A patch test of a cosmetic preformulation containing disteardimonium hectorite (15% with cyclomethicone and PEG-10 dimethicone [Nikkol Group, 9999 4368/id];[23] diluted to 1.5% in mineral oil) was conducted in female subjects (n = 11) of various skin types.[24] The occlusive patches were left in place for 48 hours. The test site was examined at patch removal and 15 minutes later. There were no signs of irritation observed. A patch test of a cosmetic mixture product containing disteardimonium hectorite (15%) was conducted in subjects (n = 10).[25] The patches were left in place for 24

hours and the test sites observed at removal and after an additional 24 hours. There were no signs of irritation observed.

Stearalkonium Hectorite. Stearalkonium hectorite (50% w/v in water with 2.5% polysorbate 809; n = 50) was not irritating in a repeated insult patch test (100%) or in a facial mask containing stearalkonium hectorite (1.4%; n = 27).[26,27]

Ocular

Quaternium-18 Hectorite. Quaternium-18 hectorite (50%; 0.1 mL) was not irritating to rabbits.[7] Quaternium-18 hectorite (2 mg neat; 20 g in 100 mL physiological saline or corn oil) instilled in the eyes of subjects did not cause any abnormal ocular sensations.[17] No pain was reported. A "sand-like" feeling was reported in the saline sample. No damage to the eye was observed.

Dihydrogenated Tallow Benzylmonium Hectorite. Dihydrogenated tallow benzylmonium hectorite (0.5 g in 0.5 mL saline) was practically nonirritating when administered to the eyes of New Zealand White rabbits (n = 6 rinsed after 4 seconds; n = 3 not rinsed).[20]

Stearalkonium Hectorite. Stearalkonium hectorite (up to 100%; volumes not provided) was a minimal to mild ocular irritant to rabbits.[7,28] In an Eyetex in vitro test of products, an eyeliner containing stearalkonium hectorite (0.196%), a lipliner pencil (1.0%), and a face mask (5.0%) were classified as minimal to mild irritants.[29]

Sensitization

Dermal: Nonhumans

Dihydrogenated Tallow Benzylmonium Hectorite. It was reported that dihydrogenated tallow benzylmonium hectorite (concentration not provided) did not cause delayed contact hypersensitivity in albino guinea pigs (n not provided).[18]

Dermal: Humans

Quaternium-18 Hectorite. Quaternium-18 hectorite (100%) was not irritating or sensitizing in a repeated insult patch test (n = 50).[20] Quaternium-18 hectorite was not sensitizing in an eye shadow (n = 50), a blusher (n = 209), and 3 undisclosed products (n = 12) up to 10%.[17,30]

Disteardimonium Hectorite. A human repeated insult patch test (HRIPT; n = 112) of disteardimonium hectorite (100%; 20 µg) was conducted using an occlusive Finn chamber.[31] The test material was not sensitizing.

Stearalkonium Hectorite. Stearalkonium hectorite (50% w/v in water with 2.5% polysorbate 809) was not sensitizing in a repeated insult patch test (n = 50) or in a product containing stearalkonium hectorite (1.4%).[26]

Summary

Ammonium hectorites are a group of ingredients that function in cosmetics mainly as nonsurfactant suspending agents. The ingredients in this report are disteardimonium hectorite, dihydrogenated tallow benzylmonium hectorite, stearalkonium hectorite, and quaternium-18 hectorite.

Hectorite is a trioctahedral, magnesium/lithium silicate-based mineral that is amorphous and does not contain any crystalline silica. The relatively weak electrostatic interactions of thin crystalline layers can essentially be "propped open" to allow the insertion of certain molecules and atoms (ie, disteardimonium, quaternium-18).

Disteardimonium hectorite was used in 574 leave-on products up to 28% and in 10 rinse-off products up to 4%. Stearalkonium hectorite was used in 467 leave-on products up to 6% and 2 rinse-off products up to 3%. Quaternium-18 hectorite was reported to be used in 106 leave-on products up to 5% and 5 rinse-off products.

There were no published absorption, distribution, metabolism or excretion, acute dermal toxicity, or carcinogenicity studies discovered nor were unpublished data provided.

The oral LD_{50} for dihydrogenated tallow benzylmonium hectorite was 5.0 g/kg for rats. The oral LD_{50} of quaternium-18 was >10 g/kg. The inhalation LC_{50} for dihydrogenated tallow benzylmonium hectorite was >5.2 mg/L for rats after 4 hours. Aerosolized quaternium-18 hectorite was not toxic to rats at 202 mg/L after 1 hour.

Stearalkonium hectorite was not dermally toxic to rabbits at concentrations of 12.5% to 50% over 3 weeks. Quaternium-18 hectorite applied to the exposed skin of rabbits for 3 weeks was not toxic up to 50%.

Stearalkonium hectorite was not mutagenic to *S typhimurium* up to 1500 µL/plate or mouse lymphoma cells up to 500 µL/plate.

Stearalkonium hectorite did not cause erythema or edema to albino rabbits at 50% w/v. Quaternium-18 hectorite (50%) was not irritating to rabbits. Dihydrogenated tallow benzylmonium hectorite at 0.5 g in 0.5 mL saline was not irritating when administered to the intact and abraded skin of rabbits.

Disteardimonium hectorite was not irritating to humans in 2 patch tests at 15%. Stearalkonium hectorite was not irritating or sensitizing to humans at 100%. Dihydrogenated tallow benzylmonium hectorite (concentration not provided) did not cause delayed contact hypersensitivity in albino guinea pigs.

Stearalkonium hectorite was a minimal to mild ocular irritant to rabbits and humans. It was classified as a minimal to mild irritant in 3 Eyetex in vitro tests of products. Quaternium-18 hectorite was not an ocular irritant at 50% in rabbits and at 2 mg in humans. Dihydrogenated tallow benzylmonium hectorite at 0.5 g in 0.5 mL saline was practically nonirritating when administered to the eyes of rabbits.

Quaternium-18 hectorite was not irritating or sensitizing up to 100% in HRIPTs.

Discussion

Single-dose toxicity data were available for quaternium-18 hectorite and dihydrogenated tallow benzylmonium hectorite, and repeated-dose toxicity data were available for quaternium-

18 hectorite and stearalkonium hectorite. Genotoxicity data were available for stearalkonium hectorite and dihydrogenated tallow benzylmonium hectorite, and reproductive and developmental toxicity data were available for dihydrogenated tallow benzylmonium hectorite. Irritation and sensitization data were available for all of these ingredients. Overall, no significant toxicity was reported, and these ingredients were not dermal irritants or sensitizers. The Panel considered that the chemical structures of these clay-based ingredients were sufficiently similar, as was the pattern of use in cosmetics, to support using data on each individual ingredient to support the safety of the entire group.

The Panel noted that the hectorites in this safety assessment have high chemical stability and are biochemically inert. The Panel considered the lithium substitution for magnesium in the magnesium/lithium silicate sheet structure but concluded lithium is tightly bound and not likely to leach. The substitution of lithium for magnesium at many sites in the lattice structure gives the material a delocalized net negative charge in the lattice. Although no data were available on dermal penetration, the Panel considered that the charge properties and the large molecular weight of these clay-like ingredients would preclude significant dermal penetration. Because they are chemically inert, no metabolites are expected that would penetrate the skin.

Conclusion

The Panel concluded that disteardimonium hectorite, dihydrogenated tallow benzylmonium hectorite, stearalkonium hectorite, and quaternium-18 hectorite are safe in the present practices of use and concentration described in this safety assessment. Were dihydrogenated tallow benzylmonium hectorite (not in current use) to be used in the future, the expectation is that it would be used in product categories and at concentrations comparable to others in this group.

Authors' Note

Unpublished sources cited in this report are available from the Director, Cosmetic Ingredient Review, 1101 17th St, Suite 412, Washington, DC 20036, USA.

Declaration of Conflicting Interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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2015 VCRP for ALKONIUM CLAYS

03A - Eyebrow Pencil	QUATERNIUM-90 BENTONITE	2
03B - Eyeliner	QUATERNIUM-90 BENTONITE	2
03C - Eye Shadow	QUATERNIUM-90 BENTONITE	10
03D - Eye Lotion	QUATERNIUM-90 BENTONITE	1
03F - Mascara	QUATERNIUM-90 BENTONITE	13
03G - Other Eye Makeup Preparations	QUATERNIUM-90 BENTONITE	3
07C - Foundations	QUATERNIUM-90 BENTONITE	8
07E - Lipstick	QUATERNIUM-90 BENTONITE	16
07I - Other Makeup Preparations	QUATERNIUM-90 BENTONITE	4
12C - Face and Neck (exc shave)	QUATERNIUM-90 BENTONITE	2
12J - Other Skin Care Preps	QUATERNIUM-90 BENTONITE	3
		64

03B - Eyeliner	STEARALKONIUM BENTONITE	6
03C - Eye Shadow	STEARALKONIUM BENTONITE	1
07C - Foundations	STEARALKONIUM BENTONITE	3
07E - Lipstick	STEARALKONIUM BENTONITE	64
07I - Other Makeup Preparations	STEARALKONIUM BENTONITE	6
08A - Basecoats and Undercoats	STEARALKONIUM BENTONITE	11
08C - Nail Creams and Lotions	STEARALKONIUM BENTONITE	4
08E - Nail Polish and Enamel	STEARALKONIUM BENTONITE	310
08F - Nail Polish and Enamel Removers	STEARALKONIUM BENTONITE	1
08G - Other Manicuring Preparations	STEARALKONIUM BENTONITE	14
10E - Other Personal Cleanliness Products	STEARALKONIUM BENTONITE	2
12F - Moisturizing	STEARALKONIUM BENTONITE	1
		423

No uses were reported for:

Benzalkonium montmorillonite
Benzalkonium sepiolite
Hydrogenated tallowalkonium bentonite
Quaternium-18/benzalkonium bentonite
Quaternium-90 montmorillonite
Quaternium-90 sepiolite

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Lillian Gill, D.P.A.
Director - COSMETIC INGREDIENT REVIEW (CIR)

FROM: Beth A. Lange, Ph.D.
Industry Liaison to the CIR Expert Panel

DATE: January 6, 2015

SUBJECT: Concentration of Use by FDA Product Category: Alkonium Clays

Concentration of Use by FDA Product Category – Alkonium Clays*

Stearalkonium Bentonite
Hydrogenated Tallowalkonium Bentonite
Quaternium-18/Benzalkonium Bentonite
Quaternium-90 Bentonite
Quaternium-90 Montmorillonite
Quaternium-90 Sepiolite
Benzalkonium Montmorillonite
Benzalkonium Sepiolite

Ingredient	Product Category	Maximum Concentration of Use
Stearalkonium Bentonite	Eyeliner	0.19%
Stearalkonium Bentonite	Eye shadow	2.5%
Stearalkonium Bentonite	Foundation	0.47-1.1%
Stearalkonium Bentonite	Lipstick	0.5-2.4%
Stearalkonium Bentonite	Basecoats and undercoats (manicuring preparations)	1-1.3%
Stearalkonium Bentonite	Nail extenders	3.5%
Stearalkonium Bentonite	Nail polish and enamel	1.2-6.5%
Stearalkonium Bentonite	Nail polish and enamel removers	0.015%
Stearalkonium Bentonite	Other manicuring preparations	0.56-3.1%
Quaternium-90 Bentonite	Eyebrow pencil	0.81%
Quaternium-90 Bentonite	Eye shadow	4%
Quaternium-90 Bentonite	Eye lotion	0.41-3%
Quaternium-90 Bentonite	Mascara	3.5-6.1%
Quaternium-90 Bentonite	Face powder	2.2%
Quaternium-90 Bentonite	Foundation	0.78-4%
Quaternium-90 Bentonite	Lipstick	6.1%
Quaternium-90 Bentonite	Makeup bases	0.78%
Quaternium-90 Bentonite	Other makeup preparations	0.78%
Quaternium-90 Bentonite	Nail polish and enamel	0.5%
Quaternium-90 Bentonite	Other manicuring preparations	0.46%
Quaternium-90 Bentonite	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.63%
Quaternium-90 Bentonite	Face and neck products Not spray	0.88%
Quaternium-90 Bentonite	Other skin care preparations	1.3%
Quaternium-90 Bentonite	Suntan products Not spray	0.54%
Quaternium-90 Montmorillonite	Foundations	0.4%
Quaternium-90 Montmorillonite	Suntan products Aerosol	0.8%
Quaternium-90 Sepiolite	Foundations	1.6%
Quaternium-90 Sepiolite	Suntan products Aerosol	3.2%

*Ingredients included in the title of the table but not found in the table were included in the concentration of use survey, but no uses were reported.

Information collected in 2014; Table prepared January 5, 2015

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Lillian Gill, D.P.A.
Director - COSMETIC INGREDIENT REVIEW (CIR)

FROM: Beth A. Lange, Ph.D.
Industry Liaison to the CIR Expert Panel

DATE: March 11, 2015

SUBJECT: Stearalkonium Bentonite

TKL Research Inc. 2005. Human repeated insult patch study: Lipstick containing 1.452% Stearalkonium Bentonite

1620 L Street, N.W., Suite 1200 | Washington, D.C. 20036 | 202.331.1770 | 202.331.1969 (fax) | www.personalcarecouncil.org

HUMAN REPEATED INSULT PATCH STUDY

TKL STUDY NO. [redacted]

[redacted]

Lipstick containing 1.452% Stearalkonium Bentonite

CONDUCTED FOR:

[redacted]

DATE OF REPORT:

March 9, 2005

[redacted]

TKL Research, Inc., 4 Forest Avenue, Paramus, NJ 07652 Tel (201) 587-0500 Fax (201) 587-0878 Email: info@tklresearch.com

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SIGNATURES

Kathleen Georgeian
Kathleen Georgeian, Clinical Research Coordinator and Manager, Dermatologic Safety Testing

3/9/05
Date

Jonathan S. Dosik, MD
Principal Investigator
Dermatologist

3/8/05
Date

STATEMENT OF QUALITY ASSURANCE

This report has been reviewed by the TKL Research, Inc. (TKL) Corporate Quality Assurance Department and the report accurately reflects the raw data for this study.

Clinical research studies are performed by TKL in accordance with all applicable federal regulations and proposed guidelines for Good Clinical Practices, which include:

21 CFR Part 312,	Investigational New Drug Application
21 CFR Part 50,	Protection of Human Subjects
21 CFR Part 56,	Institutional Review Boards

Henry Briscoe
Quality Assurance

3/9/05
Date

TITLE OF STUDY

Human Repeated Insult Patch Study

SPONSOR

[redacted]

STUDY MATERIAL

[redacted] lipstick containing 1.452% stearalkonium bentonite

DATE STUDY INITIATED

December 13, 2004

DATE STUDY COMPLETED

January 20, 2005

DATE OF REPORT

March 9, 2005

INVESTIGATIVE PERSONNEL

Jonathan S. Dosik, MD
Principal Investigator
Dermatologist

Kathleen Georgeian
Clinical Research Coordinator and Manager, Dermatologic Safety Testing

Tina Kelly
Assistant Manager, Dermatologic Safety Testing

CLINICAL SITE

TKL RESEARCH, INC.
1099 Wall Street West
Lyndhurst, NJ 07652

SUMMARY

One study material, lipstick containing 1.452% stearalkonium bentonite [redacted], was evaluated neat to determine its ability to sensitize the skin of normal volunteer subjects using an occlusive repeated insult patch study. One hundred subjects completed the study. The dermatologist was in attendance for the 72-hour challenge evaluation.

Under the conditions employed in this study, there was no evidence of sensitization to study material [redacted].

1.0 OBJECTIVE

The objective of this study was to determine the ability of the study material to cause sensitization by repeated applications to the skin of humans under controlled patch study conditions.

2.0 RATIONALE

Substances that come into contact with human skin need to be evaluated for their propensity to irritate and/or sensitize. Once an appropriate pre-clinical safety evaluation has been performed, a reproducible, standardized, quantitative patch evaluation procedure must be used to demonstrate that a particular material can be applied safely to human skin without significant risk of adverse reactions. The method herein employed is generally accepted for such a purpose.

Repeated insult patch evaluation is a modified predictive patch study that can detect weak sensitizers that require multiple applications to induce a cell-mediated (Type IV) immune response sufficient to cause an allergic reaction. Irritant reactions may also be detected using this evaluation method, although this is not the primary purpose of this procedure. Results are interpreted according to interpretive criteria based upon published works, as well as the clinical experience of TKL Research, Inc. These interpretive criteria are periodically reviewed and amended as new information becomes available.

3.0 STUDY DESIGN

3.1 STUDY POPULATION

A sufficient number of subjects were to be enrolled to provide 100 completed subjects.

3.1.1 Inclusion Criteria

Individuals eligible for inclusion in the study were those who:

1. were males or females, 18 years of age or older, in general good health;
2. were free of any systemic or dermatologic disorder which, in the opinion of the investigative personnel, would have interfered with the study results or increased the risk of adverse events;
3. were of any skin type or race, providing the skin pigmentation would allow discernment of erythema;
4. had completed a medical screening procedure; and
5. had read, understood, and signed an informed consent agreement.

3.1.2 Exclusion Criteria

Individuals excluded from participation in the study were those who:

1. had any visible skin disease at the study site which, in the opinion of the investigative personnel, would have interfered with the evaluation;

2. were receiving systemic or topical drugs or medication which, in the opinion of the investigative personnel, would have interfered with the study results;

3. had psoriasis and/or active atopic dermatitis/eczema;

4. were females who were pregnant, planning to become pregnant during the study, or breast-feeding; and/or

5. had a known sensitivity to cosmetics, skin care products, or topical drugs as related to the material being evaluated.

3.1.3 Informed Consent

A properly executed informed consent document in compliance with FDA regulations (21 CFR Part 50) was obtained from each subject prior to entering the study. The signed informed consent document is maintained in the study file. In addition, the subject was provided with a copy of the informed consent document (see Appendix IV).

3.2 DESCRIPTION OF STUDY

3.2.1 Outline of Study Procedures

Subjects participated in the study over a 6-week period involving 3 phases: (1) Induction, (2) Rest, and (3) Challenge. Prior to study entry, the subjects were screened to assure that they met the inclusion/exclusion criteria. Informed consent was obtained. Each subject was provided with a schedule of the study activities. All subjects were told to avoid wetting the patches and were asked not to engage in activities that caused excessive perspiration. They were instructed to notify the staff if they experienced any discomfort beyond mild itching or observed any adverse changes at the patch sites, while on the study or within 2 weeks of completing the study.

The Induction Phase consisted of 9 consecutive applications of the study material and subsequent evaluations of the patch sites. Prior to application of the patches, the sites were outlined with a skin marker, eg, gentian violet. The subjects were required to remove the patches approximately 24 hours after application. They returned to the facility at 48-hour intervals to have the sites evaluated and identical patches applied to the same sites. Patches applied on Friday were removed by subjects after 24 hours. The sites were evaluated on the following Monday, ie, 72 hours after patch application*.

* A Monday or Friday holiday could result in evaluation at 96 hours after patch application.

Following the ninth evaluation, the subjects were dismissed for a rest period of approximately 10-15 days.

Subjects who were absent once during the induction phase received a make-up (MU) patch at the last induction visit. The MU applications were graded 48 hours later at the MU visit, or were recorded as N9G (no ninth grading).

The Challenge Phase was initiated during the sixth week of the study. Identical patches were applied to sites previously unexposed to the study material. The patches were removed by subjects after 24 hours and the sites graded after additional 24-hour and 48-hour periods (ie, 48 and 72 hours after application). Rechallenge was performed whenever there was evidence of possible sensitization.

To be considered a completed case, a subject must have had 9 applications and no fewer than 8 subsequent readings during induction, and a single application and 2 readings during challenge. Only completed cases were used to assess sensitization.

3.2.2 Definitions Used for Grading Responses

The symbols found in the scoring scales below were used to express the response observed at the time of examination:

- = No reaction
? = Minimal or doubtful response, slightly different from surrounding normal skin
\+ = Definite erythema, no edema
++ = Definite erythema, definite edema
+++ = Definite erythema, definite edema and vesiculation

SPECIAL NOTATIONS

E = Marked/severe erythema
S = Spreading of reaction beyond patch site (ie, reaction where material did not contact skin)
p = Papular response > 50%
pv = Papulovesicular response > 50%
D = Damage to epidermis: oozing, crusting and/or superficial erosions
I = Itching
X = Subject absent
PD = Patch dislodged
NA = Not applied
NP = Not patched (due to reaction achieved)
N9G = No ninth grading

3.2.3 Evaluation of Responses

All responses were graded by a trained dermatologic evaluator meeting TKL's strict certification requirements to standardize the assignment of response grades.

4.0 NATURE OF STUDY MATERIAL

4.1 Study Material Specifications

Identification	:	[redacted] Lipstick
Amount Applied	:	0.2 g
Special Instructions	:	Applied to patch pad and remained open to the air for at least 15 minutes, but no longer than 20 minutes prior to patch application.

4.2 Storage, Handling, and Documentation of Study Material

Receipt of the material used in this study was documented in a general logbook, which serves as a permanent record of the receipt, storage, and disposition of all study material received by TKL. On the basis of information provided by the sponsor, the study material was considered reasonably safe for evaluation on human subjects. A sample of the study material was reserved and will be stored for a period of 6 months. At the conclusion of the clinical study, the remaining study material was discarded or returned to the sponsor and the disposition documented in the logbook. All information regarding the receipt, storage, and disposition of the study material was also recorded on a Clinical Material Record form (see Appendix III), which is incorporated in this study report. All study material is kept in a locked product storage room accessible to clinical staff members only.

4.3 Application of Study Material

Study material was applied to the patch as instructed. The patch was applied to the infrascapular area of the back, either to the right or left of the midline, or to the upper arm.

4.4 Description of Patch Conditions

Materials evaluated under occlusive patch conditions are applied to a 2-cm x 2-cm Webril pad attached to a non-porous, plastic film adhesive bandage (3M medical tape). The patches are secured with hypoallergenic tape (Micropore), as needed.

Materials evaluated under semi-occlusive patch conditions are applied to a 2-cm x 2-cm Webril pad. The pads are affixed to the skin with hypoallergenic tape (Micropore).

5.0 INTERPRETATION

Sensitization is characterized by an acute allergic contact dermatitis. Typical sensitization reactions begin with an immunologic response in the dermis resulting in erythema, edema formation, and secondary epidermal damage (vesiculation), sometimes extending beyond the patch site and often accompanied by itching. Sensitization reactions tend to be delayed. The reaction typically becomes evident between 24 and 48 hours, peaks at 48-72 hours and subsequently subsides. The reaction is often greater at 72 hours than at 48 hours. The severity of the reaction is generally greater during the challenge phase of a Repeated Insult Patch Test (RIPT) than that seen during induction.

Irritant reactions are characterized as a non-immunologic, localized, superficial, exudative, inflammatory response of the skin due to an externally applied material. The typical initial reaction does not develop much edema or vesiculation but results in scaling, drying, cracking, oozing, crusting, and erosions. The reaction is usually sharply delineated, not spreading beyond the patch site. Irritant reactions are typically evident by 24 hours and diminish over the next 48-72 hours. Removal of the offending agent results in gradual improvement of the epidermal damage. The reaction seen at 72 hours is, therefore, less severe than that seen at 48 hours. Finally, the severity of the reaction experienced in the challenge phase is generally similar to that seen during induction.

If the results of the study indicate the likelihood of sensitization, the recommended practice is to rechallenge the subjects who have demonstrated sensitization-like reactions to confirm that these reactions are, indeed, associated with the product. Our preferred rechallenge procedure involves the application of the product to naïve sites, under both occlusive and semi-occlusive patch conditions. Use of the semi-occlusive patch condition helps to differentiate irritant and sensitization reactions. Generally speaking, if a product is a sensitizer it will produce a similar reaction under both occlusion and semi-occlusion. Whereas, if the product has caused an irritant reaction, the reactions will be less pronounced under the semi-occlusive condition.

6.0 PROTOCOL

See Protocol - Appendix V.

7.0 DOCUMENTATION AND RETENTION OF DATA

The case report forms (CRFs) are designed to identify each subject by subject number and initials, and to record demographics, examination results, adverse events, and end of study status. Originals or copies of all CRFs, correspondence, study reports, and all source data will be kept on hard-copy file for a minimum of 5 years from completion of the study. Storage is maintained either at a TKL facility in a secured room accessible only to TKL employees, or at an offsite location that provides a secure environment with burglar/fire alarm systems, camera detection and controlled temperature and humidity. Documentation will be available for the sponsor's review on the premises of TKL.

8.0 RESULTS AND DISCUSSION

One hundred eighteen subjects between the ages of 18 and 70 were enrolled and 100 completed the study (see Tables 1 and 2 in Appendix I and Data Listings 1 and 2 in Appendix II).

The following table summarizes subject enrollment and disposition.

Number enrolled:		118
Number discontinued		18
Lost to follow-up	18	
Number completed:		100

Source: Table 1, Appendix I

There were no adverse events.

The dermatologist was in attendance for the 72-hour challenge evaluation.

A summary of response data is provided in Table 3, Appendix I. Individual dermatological response grades are provided in Data Listing 3, Appendix II.

9.0 CONCLUSION

Under the conditions employed in this study, there was no evidence of sensitization to study material [redacted] lipstick containing 1.452% stearalkonium bentonite

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[redacted]

APPENDIX I

SUMMARY TABLES

TKL STUDY NO. [redacted]

TABLE 1: SUMMARY OF SUBJECT ENROLLMENT AND DISPOSITION

	N (%)
SUBJECTS ENROLLED	118
SUBJECTS COMPLETED ALL PHASES	100 (84.7)
TOTAL SUBJECTS DISCONTINUED	18 (15.3)
LOST TO FOLLOW-UP	18 (15.3)

NOTE: ALL PERCENTAGES ARE RELATIVE TO TOTAL SUBJECTS ENROLLED

SEE DATA LISTING 1 FOR FURTHER DETAIL

PROGRAM: DISPSMY.SAS/USES: FINAL/28JAN05:12:26:00

TKL STUDY NO. [redacted]
TABLE 2: SUMMARY OF SUBJECT DEMOGRAPHICS
ALL ENROLLED SUBJECTS

AGE	
N (%) 18 TO 44	55 (46.6)
N (%) 45 TO 64	56 (47.5)
N (%) 65 AND UP	7 (5.9)
MEAN (SD)	44.7 (14.1)
MEDIAN	46.2
RANGE	18.0 TO 70.8
GENDER	
N (%) MALE	37 (31.4)
N (%) FEMALE	81 (68.6)
RACE	
N (%) ASIAN	1 (0.8)
N (%) BLACK	1 (0.8)
N (%) CAUCASIAN	77 (65.3)
N (%) HISPANIC	38 (32.2)
N (%) OTHER	1 (0.8)

SEE DATA LISTING 2 FOR FURTHER DETAIL

PROGRAM: DEMOSMY.SAS/USES: DEMOGS/28JAN05:12:26:00

[redacted]

TKL STUDY NO. [redacted]

TABLE 3: SUMMARY OF DERMATOLOGIC RESPONSE GRADES
NUMBER OF SUBJECTS BY PRODUCT

PRODUCT= lipstick containing 1.452% stearalkonium bentonite

	INDUCTION READING									MAKE-	CHALLENGE PHASE		
RESPONSE	1	2	3	4	5	6	7	8	9	UP	48HR	72HR	96HR(*)
-	104	100	103	95	93	99	97	97	91	34	100	100	
TOTAL EVALUABLE	104	100	103	95	93	99	97	97	91	34	100	100	
NUMBER ABSENT	5	8	4	9	11	2	3	3	9		0	0	
NUMBER DISCONTINUED	9	10	11	14	14	17	18	18	18		18	18	

MAXIMUM ELICITED RESPONSE DURING INDUCTION
ALL SUBJECTS COMPLETING INDUCTION (N=100)

RESPONSE	N(%) SUBJECTS
-	100 (100.0%)

(*) WHEN REQUIRED

KEY TO SYMBOLS:
- = NO REACTION
? = MINIMAL OR DOUBTFUL RESPONSE, SLIGHTLY DIFFERENT FROM SURROUNDING NORMAL SKIN
+ = DEFINITE ERYTHEMA, NO EDEMA
++ = DEFINITE ERYTHEMA, DEFINITE EDEMA
+++ = DEFINITE ERYTHEMA, DEFINITE EDEMA AND VESICULATION
D = DAMAGE TO EPIDERMIS: OOZING, CRUSTING AND/OR SUPERFICIAL EROSIONS
P = PAPULAR RESPONSE >50%

PROGRAM: SUMMARY.SAS/USES: RESPONSE, PRODLIST, FINAL/28JAN05:12:26:08

APPENDIX II

DATA LISTINGS

TKL STUDY NO. [redacted]
DATA LISTING 1: SUBJECT ENROLLMENT AND DISPOSITION

SUBJECT NO.	STUDY DATES SCREENED	1ST APPLIC	CHALL APPLIC	ENDED	LAST READING #	COMPLETION STATUS	DAYS ON STUDY
1	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
2	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
3	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
4	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
5	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
6	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
7	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
8	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
9	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
10	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
11	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
12	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
13	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
14	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
15	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
16	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
17	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
18	12/13/04	12/13/04		12/17/04	I0	L	5
19	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
20	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
21	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
22	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
23	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
24	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
25	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
26	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
27	12/13/04	12/13/04		12/29/04	I5	L	17
28	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
29	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
30	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
31	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
32	12/13/04	12/13/04		12/22/04	I3	L	10
33	12/13/04	12/13/04		12/22/04	I3	L	10
34	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
35	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
36	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
37	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
38	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
39	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39

KEY: LAST READING # (I=INDUCTION PHASE, C=CHALLENGE PHASE)
COMPLETION STATUS (C=COMPLETED, L=LOST TO FOLLOW-UP, S=VOLUNTARY WITHDRAWAL
V=PROTOCOL VIOLATION, AE=ADVERSE EVENT, O=OTHER)

PROGRAM: DISPLIST.SAS/USES: DEMOGS, RESPONSE, FINAL/28JAN05:12:25:44

TKL STUDY NO. [redacted]
DATA LISTING 1: SUBJECT ENROLLMENT AND DISPOSITION

SUBJECT NO.	STUDY DATES: SCREENED	1ST APPLIC	CHALL APPLIC	ENDED	LAST READING #	COMPLETION STATUS	DAYS ON STUDY
40	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
41	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
42	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
43	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
44	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
45	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
46	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
47	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
48	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
49	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
50	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
51	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
52	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
53	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
54	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
55	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
56	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
57	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
58	12/13/04	12/13/04		12/22/04	I2	L	10
59	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
60	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
61	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
62	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
63	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
64	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
65	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
66	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
67	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
68	12/13/04	12/13/04		12/17/04	I0	L	5
69	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
70	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
71	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
72	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
73	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
74	12/13/04	12/13/04		12/17/04	I0	L	5
75	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
76	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
77	12/13/04	12/13/04		12/17/04	I0	L	5
78	12/13/04	12/13/04		12/22/04	I3	L	10

KEY: LAST READING # (I=INDUCTION PHASE, C=CHALLENGE PHASE)
COMPLETION STATUS (C=COMPLETED, L=LOST TO FOLLOW-UP, S=VOLUNTARY WITHDRAWAL
V=PROTOCOL VIOLATION, AE=ADVERSE EVENT, O=OTHER)

PROGRAM: DISPLIST.SAS/USES: DEMOGS, RESPONSE, FINAL/28JAN05:12:25:44

TKL STUDY NO. [redacted]
DATA LISTING 1: SUBJECT ENROLLMENT AND DISPOSITION

SUBJECT NO.	STUDY DATES SCREENED	1ST APPLIC	CHALL APPLIC	ENDED	LAST READING #	COMPLETION STATUS	DAYS ON STUDY
79	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
80	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
81	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
82	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
83	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
84	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
85	12/13/04	12/13/04		12/20/04	I1	L	8
86	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
87	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
88	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
89	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
90	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
91	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
92	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
93	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
94	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
95	12/13/04	12/13/04		12/17/04	I0	L	5
96	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
97	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
98	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
99	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
100	12/13/04	12/13/04		12/17/04	I0	L	5
101	12/13/04	12/13/04		12/17/04	I0	L	5
102	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
103	12/13/04	12/13/04	01/17/05	01/20/05	C2	C	39
104	12/15/04	12/15/04	01/17/05	01/20/05	C2	C	37
105	12/15/04	12/15/04	01/17/05	01/20/05	C2	C	37
106	12/15/04	12/15/04	01/17/05	01/20/05	C2	C	37
107	12/15/04	12/15/04	01/17/05	01/20/05	C2	C	37
108	12/15/04	12/15/04		12/29/04	I5	L	15
109	12/15/04	12/15/04		12/30/04	I6	L	16
110	12/15/04	12/15/04		12/20/04	I0	L	6
111	12/15/04	12/15/04		12/30/04	I5	L	16
112	12/15/04	12/15/04	01/17/05	01/20/05	C2	C	37
113	12/15/04	12/15/04		12/20/04	I0	L	6
114	12/15/04	12/15/04	01/17/05	01/20/05	C2	C	37
115	12/15/04	12/15/04	01/17/05	01/20/05	C2	C	37
116	12/15/04	12/15/04	01/17/05	01/20/05	C2	C	37
117	12/15/04	12/15/04	01/17/05	01/20/05	C2	C	37
118	12/15/04	12/15/04	01/17/05	01/20/05	C2	C	37

KEY: LAST READING # (I=INDUCTION PHASE, C=CHALLENGE PHASE)
COMPLETION STATUS (C=COMPLETED, L=LOST TO FOLLOW-UP, S=VOLUNTARY WITHDRAWAL
V=PROTOCOL VIOLATION, AE=ADVERSE EVENT, O=OTHER)

PROGRAM: DISPLIST.SAS/USES: DEMOGS, RESPONSE, FINAL/28JAN05:12:25:44

TKL STUDY NO. [redacted]
DATA LISTING 2: SUBJECT DEMOGRAPHICS

SUBJECT NO.	AGE	GENDER	RACE
1	59.7	FEMALE	CAUCASIAN
2	70.7	FEMALE	CAUCASIAN
3	66.9	FEMALE	HISPANIC
4	62.4	MALE	HISPANIC
5	60.0	FEMALE	CAUCASIAN
6	19.0	MALE	CAUCASIAN
7	49.0	FEMALE	CAUCASIAN
8	65.5	MALE	CAUCASIAN
9	50.4	MALE	HISPANIC
10	27.9	FEMALE	CAUCASIAN
11	50.6	FEMALE	CAUCASIAN
12	51.8	FEMALE	HISPANIC
13	40.2	MALE	CAUCASIAN
14	69.5	FEMALE	CAUCASIAN
15	44.5	FEMALE	CAUCASIAN
16	45.1	MALE	CAUCASIAN
17	55.7	FEMALE	HISPANIC
18	33.2	FEMALE	HISPANIC
19	29.3	FEMALE	CAUCASIAN
20	34.3	FEMALE	BLACK
21	37.3	FEMALE	CAUCASIAN
22	62.3	FEMALE	CAUCASIAN
23	18.0	FEMALE	CAUCASIAN
24	42.6	FEMALE	CAUCASIAN
25	27.4	MALE	CAUCASIAN
26	42.2	FEMALE	CAUCASIAN
27	57.4	MALE	ITALIAN
28	33.7	FEMALE	CAUCASIAN
29	57.2	FEMALE	CAUCASIAN
30	47.0	MALE	CAUCASIAN
31	43.1	FEMALE	HISPANIC
32	41.0	FEMALE	HISPANIC
33	39.6	FEMALE	HISPANIC
34	21.4	MALE	HISPANIC
35	26.4	MALE	CAUCASIAN
36	18.9	FEMALE	CAUCASIAN
37	28.9	FEMALE	CAUCASIAN
38	54.9	MALE	CAUCASIAN
39	48.0	MALE	CAUCASIAN
40	19.2	MALE	HISPANIC

TKL STUDY NO. [redacted]
DATA LISTING 2: SUBJECT DEMOGRAPHICS

SUBJECT NO.	AGE	GENDER	RACE
41	40.5	FEMALE	CAUCASIAN
42	59.2	FEMALE	CAUCASIAN
43	57.6	FEMALE	CAUCASIAN
44	67.5	FEMALE	CAUCASIAN
45	46.6	FEMALE	HISPANIC
46	42.1	FEMALE	HISPANIC
47	50.7	FEMALE	CAUCASIAN
48	42.2	FEMALE	CAUCASIAN
49	53.5	FEMALE	CAUCASIAN
50	61.7	FEMALE	HISPANIC
51	51.7	MALE	HISPANIC
52	33.0	FEMALE	CAUCASIAN
53	22.1	FEMALE	HISPANIC
54	70.8	FEMALE	CAUCASIAN
55	54.2	FEMALE	CAUCASIAN
56	34.2	FEMALE	CAUCASIAN
57	44.8	MALE	CAUCASIAN
58	34.5	MALE	HISPANIC
59	49.1	FEMALE	CAUCASIAN
60	58.8	FEMALE	CAUCASIAN
61	53.6	FEMALE	HISPANIC
62	56.2	MALE	HISPANIC
63	42.5	FEMALE	CAUCASIAN
64	49.8	FEMALE	CAUCASIAN
65	56.4	MALE	CAUCASIAN
66	59.4	FEMALE	CAUCASIAN
67	36.5	MALE	CAUCASIAN
68	41.1	MALE	CAUCASIAN
69	27.0	FEMALE	HISPANIC
70	52.2	FEMALE	CAUCASIAN
71	62.6	MALE	CAUCASIAN
72	28.6	FEMALE	CAUCASIAN
73	47.5	MALE	HISPANIC
74	22.0	MALE	HISPANIC
75	45.6	FEMALE	HISPANIC
76	26.2	FEMALE	HISPANIC
77	42.3	FEMALE	CAUCASIAN
78	50.0	FEMALE	HISPANIC
79	61.9	FEMALE	CAUCASIAN
80	55.8	FEMALE	CAUCASIAN

TKL STUDY NO. [redacted]
DATA LISTING 2: SUBJECT DEMOGRAPHICS

SUBJECT NO.	AGE	GENDER	RACE
81	54.0	FEMALE	CAUCASIAN
82	19.6	FEMALE	CAUCASIAN
83	28.3	FEMALE	CAUCASIAN
84	38.8	FEMALE	CAUCASIAN
85	33.6	MALE	CAUCASIAN
86	56.8	MALE	HISPANIC
87	62.4	FEMALE	HISPANIC
88	59.5	MALE	HISPANIC
89	45.8	FEMALE	CAUCASIAN
90	22.4	FEMALE	HISPANIC
91	37.8	FEMALE	CAUCASIAN
92	30.4	FEMALE	HISPANIC
93	58.7	FEMALE	CAUCASIAN
94	54.4	FEMALE	CAUCASIAN
95	22.5	FEMALE	HISPANIC
96	44.5	FEMALE	CAUCASIAN
97	29.5	MALE	HISPANIC
98	27.9	FEMALE	HISPANIC
99	55.1	FEMALE	HISPANIC
100	45.4	MALE	HISPANIC
101	47.1	FEMALE	CAUCASIAN
102	62.2	FEMALE	HISPANIC
103	24.4	MALE	HISPANIC
104	30.8	MALE	CAUCASIAN
105	55.8	FEMALE	CAUCASIAN
106	53.2	FEMALE	CAUCASIAN
107	69.4	FEMALE	CAUCASIAN
108	20.0	MALE	ASIAN
109	25.2	MALE	CAUCASIAN
110	56.0	FEMALE	CAUCASIAN
111	51.6	FEMALE	CAUCASIAN
112	51.9	FEMALE	CAUCASIAN
113	51.2	MALE	CAUCASIAN
114	49.7	FEMALE	CAUCASIAN
115	43.5	FEMALE	CAUCASIAN
116	18.0	MALE	CAUCASIAN
117	34.5	MALE	HISPANIC
118	57.8	MALE	CAUCASIAN

[redacted]

TKL STUDY NO. [redacted]

DATA LISTING 3: DERMATOLOGIC RESPONSE GRADES
BY PRODUCT AND SUBJECT

PRODUCT= lipstick containing 1.452% stearalkonium bentonite

SUBJECT NO.	INDUCTION READING 1	2	3	4	5	6	7	8	9	MU	CHALLENGE PHASE 48HR	72HR	96HR(*)
1	-	-	-	-	-	-	-	-	-		-	-	
2	-	-	-	-	-	-	-	-	-		-	-	
3	-	-	-	-	-	-	-	-	-		-	-	
4	-	-	-	-	-	-	-	-	-		-	-	
5	-	-	-	-	-	-	-	-	-		-	-	
6	-	-	-	-	-	-	X	-	-	-	-	-	
7	X	-	-	-	-	-	-	-	-	-	-	-	
8	-	-	-	-	-	-	-	-	-		-	-	
9	-	-	-	-	-	-	-	-	-		-	-	
10	-	-	-	X	-	-	-	-	-	-	-	-	
11	-	-	-	-	-	-	-	-	-		-	-	
12	-	-	-	-	-	-	-	-	-		-	-	
13	-	-	-	-	-	-	-	-	-		-	-	
14	-	X	-	-	-	-	-	-	-	N9G	-	-	
15	-	-	-	-	-	-	-	-	-		-	-	
16	-	-	-	-	-	-	-	-	-		-	-	
17	-	-	-	-	-	-	-	-	-		-	-	
18	X	X	X	X	X	X	X	X	X		X	X	
19	-	-	-	-	X	-	-	-	-	-	-	-	
20	-	-	-	-	X	-	-	-	-	-	-	-	

KEY TO SYMBOLS:

- = NO REACTION
? = MINIMAL OR DOUBTFUL RESPONSE, SLIGHTLY DIFFERENT FROM SURROUNDING NORMAL SKIN

+ = DEFINITE ERYTHEMA, NO EDEMA
++ = DEFINITE ERYTHEMA, DEFINITE EDEMA

+++ = DEFINITE ERYTHEMA, DEFINITE EDEMA AND VESICULATION

N9G = NO NINTH GRADING NA=NOT APPLIED NP=NOT PATCHED DUE TO REACTION ACHIEVED
X = READING NOT PERFORMED DUE TO MISSED VISIT OR SUBJECT DISCONTINUATION
D = DAMAGE TO EPIDERMIS: OOZING, CRUSTING AND/OR SUPERFICIAL EROSIONS
P = PAPULAR RESPONSE >50% NR=DATA NOT RECORDED
MU = MAKE-UP READING FOR MISSED INDUCTION VISIT

(*) WHEN REQUIRED

PROGRAM: DETAIL.SAS/USES: RESPONSE, PRODLIST/28JAN05:12:25:48

[redacted]

TKL STUDY NO. [redacted]

DATA LISTING 3: DERMATOLOGIC RESPONSE GRADES
BY PRODUCT AND SUBJECT

PRODUCT= lipstick containing 1.452% stearalkonium bentonite

SUBJECT	INDUCTION READING										CHALLENGE PHASE		
NO.	1	2	3	4	5	6	7	8	9	MU	48HR	72HR	96HR(*)
21	-	-	-	-	X	-	-	-	-	-	-	-	
22	-	-	-	-	X	-	-	-	-	-	-	-	
23	-	-	-	-	X	-	-	-	-	N9G	-	-	
24	-	-	-	-	-	-	-	-	-		-	-	
25	-	-	-	-	X	-	-	-	-	-	-	-	
26	X	-	-	-	-	-	-	-	-	-	-	-	
27	-	-	-	-	-	X	X	X	X		X	X	
28	-	-	-	-	X	-	-	-	-	-	-	-	
29	-	-	-	-	-	-	-	-	-		-	-	
30	-	-	-	X	-	-	-	-	-	-	-	-	
31	-	-	-	-	-	-	X	-	-	-	-	-	
32	X	-	-	X	X	X	X	X	X		X	X	
33	X	-	-	X	X	X	X	X	X		X	X	
34	-	-	-	-	X	-	-	-	-	-	-	-	
35	-	-	-	-	-	-	X	-	-	-	-	-	
36	-	-	-	-	-	-	-	-	-		-	-	
37	-	-	-	-	-	-	-	-	-		-	-	
38	-	-	-	-	-	-	-	-	-		-	-	
39	-	-	-	-	-	-	-	X	-	-	-	-	
40	-	-	-	-	-	-	-	-	-		-	-	
41	-	-	-	-	-	X	-	-	-	-	-	-	
42	-	-	-	-	-	-	-	-	-		-	-	
43	-	-	X	-	-	-	-	-	-	-	-	-	
44	-	-	-	-	-	-	-	-	-		-	-	
45	-	-	-	-	-	-	-	-	N9G		-	-	
46	-	-	-	-	-	X	-	-	-	-	-	-	
47	-	-	-	-	-	-	-	-	-		-	-	
48	-	-	-	-	-	-	-	X	-	-	-	-	
49	-	-	-	-	-	-	-	-	-		-	-	
50	-	-	-	-	-	-	-	-	-		-	-	
51	-	-	-	-	-	-	-	-	-		-	-	
52	-	-	X	-	-	-	-	-	-	-	-	-	

(*) WHEN REQUIRED

PROGRAM: DETAIL.SAS/USES: RESPONSE, PRODLIST/28JAN05:12:25:48

[redacted]

TKL STUDY NO. [redacted]

DATA LISTING 3: DERMATOLOGIC RESPONSE GRADES
BY PRODUCT AND SUBJECT

PRODUCT= lipstick containing 1.452% stearalkonium bentonite

SUBJECT	INDUCTION READING										CHALLENGE PHASE		
NO.	1	2	3	4	5	6	7	8	9	MU	48HR	72HR	96HR(*)
53	-	-	-	-	-	-	-	-	-		-	-	
54	-	-	X	-	-	-	-	-	-	N9G	-	-	
55	-	-	-	-	X	-	-	-	-	-	-	-	
56	-	-	-	-	-	-	-	-	-		-	-	
57	-	-	-	-	-	-	-	-	-		-	-	
58	-	-	X	X	X	X	X	X	X		X	X	
59	-	-	-	-	-	-	-	-	N9G		-	-	
60	-	-	-	-	-	-	-	-	-		-	-	
61	-	-	-	-	-	-	-	-	-		-	-	
62	-	-	-	-	-	-	-	-	-		-	-	
63	-	-	-	-	X	-	-	-	-	-	-	-	
64	-	-	-	-	-	-	-	-	-		-	-	
65	-	-	-	-	-	-	-	-	-		-	-	
66	-	-	-	-	-	-	-	-	-		-	-	
67	-	-	-	-	-	-	-	-	-		-	-	
68	X	X	X	X	X	X	X	X	X		X	X	
69	-	-	-	-	-	-	-	-	-		-	-	
70	-	-	-	-	-	-	-	-	-		-	-	
71	-	-	-	-	-	-	-	-	-		-	-	
72	-	-	-	-	-	-	-	-	-		-	-	
73	X	-	-	-	-	-	-	-	-	-	-	-	
74	X	X	X	X	X	X	X	X	X		X	X	
75	-	-	-	-	-	-	-	-	-		-	-	
76	-	-	-	-	-	-	-	-	-		-	-	
77	X	X	X	X	X	X	X	X	X		X	X	
78	-	X	-	X	X	X	X	X	X		X	X	
79	-	-	-	-	-	-	-	-	-		-	-	
80	-	-	-	-	-	-	-	-	-		-	-	
81	-	X	-	-	-	-	-	-	-	-	-	-	
82	-	-	-	-	-	-	-	-	-		-	-	
83	-	-	-	-	-	-	-	-	-		-	-	
84	-	-	-	-	-	-	-	-	-		-	-	

(*) WHEN REQUIRED

PROGRAM: DETAIL.SAS/USES: RESPONSE, PRODLIST/28JAN05:12:25:48

[redacted]

TKL STUDY NO. [redacted]

DATA LISTING 3: DERMATOLOGIC RESPONSE GRADES
BY PRODUCT AND SUBJECT

PRODUCT= lipstick containing 1.452% stearalkonium bentonite

SUBJECT	INDUCTION READING										CHALLENGE PHASE		
NO.	1	2	3	4	5	6	7	8	9	MU	48HR	72HR	96HR(*)
85	-	X	X	X	X	X	X	X	X		X	X	
86	-	-	-	-	-	-	-	-	-		-	-	
87	-	-	-	-	-	-	-	-	-		-	-	
88	-	-	-	-	-	-	-	-	-		-	-	
89	-	-	-	-	X	-	-	-	-	-	-	-	
90	-	X	-	-	-	-	-	-	-	-	-	-	
91	-	-	-	-	-	-	-	-	-		-	-	
92	-	-	-	-	-	-	-	-	N9G		-	-	
93	-	-	-	X	-	-	-	-	-	-	-	-	
94	-	-	-	X	-	-	-	-	-	-	-	-	
95	X	X	X	X	X	X	X	X	X		X	X	
96	-	X	-	-	-	-	-	-	-	-	-	-	
97	-	-	-	X	-	-	-	-	-	-	-	-	
98	-	-	-	X	-	-	-	-	-	-	-	-	
99	-	-	-	X	-	-	-	-	-	-	-	-	
100	X	X	X	X	X	X	X	X	X		X	X	
101	X	X	X	X	X	X	X	X	X		X	X	
102	-	X	-	-	-	-	-	-	-	-	-	-	
103	-	-	-	X	-	-	-	-	-	-	-	-	
104	-	-	X	-	-	-	-	-	-	N9G	-	-	
105	-	-	-	-	-	-	-	X	-	N9G	-	-	
106	-	X	-	-	-	-	-	-	-	N9G	-	-	
107	-	-	-	-	-	-	-	-	N9G		-	-	
108	-	-	-	X	-	X	X	X	X		X	X	
109	-	X	-	-	-	-	X	X	X		X	X	
110	X	X	X	X	X	X	X	X	X		X	X	
111	-	-	-	-	-	X	X	X	X		X	X	
112	-	-	-	-	-	-	-	-	N9G		-	-	
113	X	X	X	X	X	X	X	X	X		X	X	
114	-	-	-	-	-	-	-	-	N9G		-	-	
115	-	-	-	-	-	-	-	-	N9G		-	-	
116	-	-	-	-	-	-	-	-	N9G		-	-	
117	-	-	-	-	-	-	-	-	N9G		-	-	
118	-	-	-	-	-	-	-	-	-		-	-	

(*) WHEN REQUIRED

PROGRAM: DETAIL.SAS/USES: RESPONSE, PRODLIST/28JAN05:12:25:48

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Lillian Gill, D.P.A.
Director - COSMETIC INGREDIENT REVIEW (CIR)

FROM: Beth A. Lange, Ph.D.
Industry Liaison to the CIR Expert Panel

DATE: April 13, 2015

SUBJECT: Quaternium-90 Montmorillonite and Quaternium-90 Sepiolite

Clinical Research Laboratories, Inc. 2014. Summary of an HRIPT of a spray leave-on body product containing 0.8% Quaternium-90 Montmorillonite and 3.2% Quaternium-90 Sepiolite.

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The objective of this study was to determine the irritation and sensitization potential of spray leave-on body product containing 0.8% Quaternium-90 Montmorillonite and 3.2% Quaternium-90 Sepiolite.

The product was tested undiluted: 0.2ml on 3/4 inch x 3/4 inch occlusive patches.

The test material was applied to the upper back (between the scapulae) and was allowed to remain in direct contact for a period of 24 hours. Patches were applied to the same site on Monday, Wednesday and Friday for a total of 9 applications during the induction period. The sites were graded for dermal irritation 24 hours after removal of the patches by the subjects on Tuesday and Thursday and 48 hours after removal of the patches on Saturday.

Following approximately a 2-week rest period, the challenge patches were applied to a previously untreated test site on the back. After 24 hours, the patches were removed and the test sites were evaluated for dermal reactions. The test sites were re-evaluated 48 and 72 hours after patch removal.

There were 57 subjects in the study. One subject did not complete the study for reasons unrelated to the test material. A total of 56 subjects completed the study.

RESULTS

No adverse events were reported during the study.

CONCLUSION

Based on the 56 subjects completing the study, the test material containing 0.8% Quaternium-90 Montmorillonite and 3.2% Quaternium-90 Sepiolite did not demonstrate a potential for eliciting dermal irritation or sensitization.

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Lillian Gill, D.P.A.
Director - COSMETIC INGREDIENT REVIEW (CIR)

FROM: Beth A. Lange, Ph.D.
Industry Liaison to the CIR Expert Panel

DATE: April 17, 2015

SUBJECT: Comments on the Scientific Literature Review: Safety Assessment of Alkonium Clays as Used in Cosmetics

Key Issue

Although the report states that quaternium-90 and quaternium-18 are structurally similar, it does not actually describe or show the structures of these components. Please provide additional information about the structure/chemistry of quaternium-90 and quaternium-18 in this report.

Additional Comments

Cosmetic Use, Summary - Please provide more details about use reported to the VCRP. For example, not only is Stearalkonium Bentonite used predominantly in nail products, it is used predominantly in nail polish and enamel - 310 of 423 total uses (73.3%) of Stearalkonium Bentonite reported to the FDA were in the product category nail polish and enamel; lipstick with 64 (15.2%) uses was the product category with the second highest number of uses.

The 6.5% use concentration reported in the Council survey was in nail polish and enamel not basecoats and undercoats as stated in this section and the Summary.

Rather than stating that the Council survey reported use of Quaternium-90 Montmorillonite and Quaternium-90 Sepiolite "in two types of leave-on products", please name the product categories in which these ingredients were reported to be used. Both ingredients were reported to be used in foundations and aerosol suntan products.

Non-Cosmetic Use - For what use is bentonite considered GRAS by the FDA? FDA does not like CIR reports to imply that FDA may consider an ingredient GRAS for cosmetic use. Therefore,

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when discussing GRAS please be specific and indicate the use for which the substance is considered GRAS.

The OSHA regulation for occupational exposure to nuisance dust does not belong in the Non-Cosmetic Use section. Why does the exposure limit for nuisance dust only apply to sepiolite and not the other clays?

Repeated Dose Exposure, Dermal - As there is not a previous report on these ingredients, it is not clear why this section says "New data...".

Repeated Dose Exposure, Oral - Please indicate the method of oral treatment, e.g., gavage, used in the 28-day oral study of Stearalkonium Bentonite.