

3

Final Report on the Safety Assessment of Polyquaternium-10

Polyquaternium-10 is a polymeric quaternary ammonium derivative of hydroxyethyl cellulose that is used in cosmetics as a conditioner, thickener, and emollient at concentrations of $\leq 0.1\%$ – 5% . Polyquaternium-10 has, at most, only a low potential to penetrate the stratum corneum but is adsorbed by keratinous surfaces. The oral LD_{50} of Polyquaternium-10 was not obtained at 16 g/kg in rats. Inhalation, dermal, and ocular animal test data indicated, at most, only a low degree of toxicity at test concentrations of Polyquaternium-10 greater than that used in cosmetic products. Polyquaternium-10 with and without metabolic activation was not a mutagen in three separate assay systems. Polyquaternium-10 was neither an irritant nor a human sensitizer when tested at 2.0%. Cosmetic products containing up to 1% Polyquaternium-10 were not human irritants, sensitizers, or photosensitizers. On the basis of the information presented, it is concluded that Polyquaternium-10 is safe as a cosmetic ingredient in the present practices of use.

INTRODUCTION

Polyquaternium-10 is a cationic form of hydroxyethyl cellulose that adsorbs and sorbs well to proteinaceous surfaces. It is used in cosmetics as a conditioner, thickener, and emollient in hair care products, lotions, and makeup.

CHEMISTRY

Definition

Polyquaternium-10, also known as Quaternium-19, is a polymeric quaternary ammonium salt of hydroxyethyl cellulose reacted with a trimethyl ammonium substituted epoxide. There are various grades of Polyquaternium-10 with different average molecular weights generally ranging from 250,000 to 600,000. Polyquaternium-10 has three CAS numbers: 53568-66-4, 54351-50-7, and 55353-19-0.⁽¹⁻³⁾

Chemical and Physical Properties

Polyquaternium-10 is a white granular powder with a characteristic amine odor. It is soluble in water and insoluble in alcohol and nonpolar organic sol-

vents. Polyquaternium-10 used in cosmetics has 0.5% maximum water insolubles, 1.7 to 2.2% nitrogen-containing components, 2% maximum ash (NaCl), and 6% maximum volatile material. The particle size specifications are 95% minimum through a 20 mesh filter and 85% minimum through a 40 mesh filter. The viscosity of a 2% aqueous solution (25°C) is between 60 and 150 centipoises.⁽⁴⁾

Polyquaternium-10 alters the surface tension of aqueous solutions of anionic surfactants. Addition of 1% and 2% Polyquaternium-10 lowered the surface tension of aqueous solutions of sodium lauryl sulfate, sodium tridecylbenzenesulfonate, and potassium laurate.⁽⁵⁾

Reactivity

Polyquaternium-10 is a cationic, surface-active polymer that is adsorbed by keratinous surfaces, such as hair and skin (stratum corneum). The adsorption of the polymer was not readily affected by pH in the range of 4 to 10. It undergoes slow hydrolytic cleavage outside this pH range. Sorption of Polyquaternium-10 to keratinous surfaces was decreased by the addition of electrolytes (salts), such as aluminum, iron, calcium, or sodium. Polyquaternium-10 is biologically degradable. The presence of ethyl alcohol or propylene glycol adds to the stability of Polyquaternium-10.⁽⁶⁻⁹⁾

Analytical Methods

The most common analytical method for quaternary ammonium compounds is colorimetric testing following separation by acid extraction.⁽¹⁰⁾

Method of Manufacture

Polyquaternium-10 is generally produced by reacting hydroxyethylcellulose with epichlorhydrin, followed by quaternization using trimethylamine. It is stable within a pH range of 4 to 8.

Impurities

Inorganic impurities of Polyquaternium-10 used in cosmetics include water (up to 0.5%), nitrogen (1.7 to 2.2%), and ash (NaCl up to 2%). Information was not available on organic impurities of Polyquaternium-10.⁽⁴⁾ Epichlorhydrin was not detected in any of six different Polyquaternium polymers analyzed with an average detection limit of about 0.5 ppm.⁽¹¹⁾ A maximum of 10.8 ppm Trimethylamine was detected in lots of Polyquaternium-10 that were produced and sold during 1985.⁽¹²⁾

USE

Purpose in Cosmetics

Polyquaternium-10 is used as a conditioner, emollient and viscosity controlling agent in cosmetics.^(3,13,14)

Scope and Extent of Use in Cosmetics

Polyquaternium-10 is used primarily in hair care products, skin cleansers, and skin moisturizers in concentrations of $\leq 0.1\%$ –5%. One hundred thirty-nine (139) of the voluntarily filed cosmetic product formulations were reported to the Food and Drug Administration to contain Polyquaternium-10.⁽¹⁵⁾ The cosmetic product formulation data that are made available by the FDA are compiled through voluntary filing of such data in accordance with Title 21 part 720.4 of the Code of Federal Regulations.⁽¹⁶⁾ Ingredients are listed in prescribed concentration ranges under specific product type categories. Since certain cosmetic ingredients are supplied by the manufacturer at less than 100% concentration, the value reported by the cosmetic formulator may not necessarily reflect the actual concentration found in the finished product; the actual concentration would be a fraction of that reported to the FDA. Data submitted within the framework of preset concentration ranges provide the opportunity for overestimation of the actual concentration of an ingredient in a particular product. An entry at the lowest end of a concentration range is considered the same as one entered at the highest end of that range, thus introducing the possibility of a 2- to 10-fold error in the assumed ingredient concentration (Table 1).

Polyquaternium-10 has been generally or individually approved for use in cosmetic formulations marketed in Japan.⁽¹⁷⁾

Surfaces, Frequency, and Duration of Application

The hair care products containing Polyquaternium-10 are, for the most part, applied for a few minutes, then rinsed off. However, Polyquaternium-10 is incorporated in these products for its "substantivity" (sorption) and would be expected to remain in contact with the hair between treatments. Skin cleansers and moisturizers have the potential to remain in continuous contact with the skin and nails for extended periods of time.

BIOLOGY

Penetration, Sorption, and Permeation Through Stratum Corneum

Approximately 1 ml of a 5% (w/v) water solution of ¹⁴C-Polyquaternium-10 (uniformly labeled on the pendant side chain) was applied to the backs of 12 Fischer 344 rats. The total dose of 4.0 ml/kg was occluded for the test period 1, 3, and 24 h. Six rats were placed in Roth-type glass metabolism cages designed for the separate collection of urine, feces, and expired air for the entire 24-h exposure period. The remaining 6 exposed animals were killed, 3 at 1 h and 3 at 6-h postexposure. Blood measured at 1 h and 3 h for the interim sacrifices and for the 6 material balance rats killed at 24 h had no radioactivity above background. There was no radioactivity above background in any of 9 tissues examined in the 6 animals that were killed at 24 h. Less than 0.02% of the administered dose was found in the urine and less than 0.1% in the feces; no radioactivity was recovered in CO₂. Of the 83.7% of the total dose that was recovered from the male rats, 75.2% was from the occlusive materials and 7.1% was found

TABLE 1. Product Formulation Data for Polyquaternium-10⁽¹⁵⁾

Product category	Total no. of formulations in category	Total no. containing ingredient	No. of product formulations within each concentration range (%)			
			Unreported concentration	>1-5	>0.1-1	≤0.1
Bubble baths	475	1	—	—	1	—
Mascara	397	5	—	—	—	5
Hair conditioners	478	16	—	6	9	1
Hair sprays (aerosol fixatives)	265	1	—	—	1	—
Permanent waves	474	6	—	1	5	—
Hair shampoos (noncoloring)	909	62	—	9	46	7
Tonics, dressings, and other hair grooming aids	290	4	—	—	3	1
Wave sets	180	6	—	2	3	1
Other hair preparations (noncoloring)	177	1	—	—	1	—
Hair shampoos (coloring)	16	3	—	—	3	—
Makeup bases	831	2	—	—	—	2
Bath soaps and detergents	148	1	—	—	1	—
Skin cleansing preparations (cold creams, lotions, liquids, and pads)	680	6	2	—	1	3
Face, body, and hand skin care preparations (excluding shaving preparations)	832	8	—	—	3	5
Moisturizing skin care preparations	747	12	1	—	3	8
Night skin care preparations	219	1	—	—	—	1
Paste masks (mud packs)	171	1	—	—	—	1
Skin fresheners	260	1	—	—	—	1
Wrinkle smoothers (removers)	38	1	—	—	—	1
Other skin care preparations	349	1	—	—	1	—
1981 TOTALS		139	3	18	81	37

in or around the skin at the dose site. The fraction of the applied material that did penetrate the skin amounted to less than 1.5% of the administered radioactivity. The investigators noted the low total recovery of the applied radioactivity; however, if the data were normalized to 100%, less than 1.75% of the applied dose would have penetrated the skin. The authors concluded that Polyquaternium-10 is unlikely to penetrate the human skin in toxicologically significant amounts.^(18,19)

The anti-irritant effect of hydroxyl and quaternary ammonium compounds, including Polyquaternium-10, has been investigated in recent years. It has been hypothesized that the sorption properties of Polyquaternium-10 enable the polymer to block keratin reactive sites, thus reducing the topical and eye irritant effects of surfactants in shampoo and cleanser formulations.^(20,21)

Several studies have investigated the passage of Polyquaternium-10 and surfactants, such as sodium lauryl sulfate, into and through isolated stratum corneum from the skin of fetal pigs, neonatal rats, and adult humans. The fetal pig-skin was frozen, and on warming, the stratum corneum was gently separated from the underlying epidermis. Neonatal rat skin was removed following death by CO₂ inhalation. The skin was placed in a desiccator jar and exposed to ammonia vapor for 1–3 h, then put in water to remove the epidermis from the dermis. After 1 h the epidermis was recovered on a paper towel, and the malpighian layer was scraped off, leaving the stratum corneum to dry. The various preparations were exposed to ¹⁴C-Polyquaternium-10 and/or surfactant (in aqueous solution) in vials or permeability cells⁽²²⁾ to quantify sorption and permeability and to evaluate the effects of the polymer on the preparations. The results indicated that Polyquaternium-10 slowly diffused into the outer layer of the stratum corneum (all three species) rather than forming multilayers on the surface. Although ionic surfactants did reduce polymer sorption, pretreatment of the stratum corneum with 1% Polyquaternium-10 greatly reduced the amount of surfactant that passed through the preparation. This reduction in permeation of surfactant supported the hypothesis that Polyquaternium-10 is an anti-irritant in the presence of ionic (i.e., irritant) surfactants. The kinetics of polymer/surfactant sorption and permeation indicated that the polymer did not act primarily as a barrier to penetration, but rather it helped to maintain the physical integrity of the stratum corneum preparation.

Pretreatment of the stratum corneum of neonatal rats with Polyquaternium-10 slightly increased the hydration of the membrane and reduced swelling after surfactant exposure.^(2,9,23,24)

ANIMAL TOXICOLOGY

Oral Toxicity

Three lots of Polyquaternium-10 were tested for acute oral toxicity by intubation in rats. Three studies at maximum doses of 16 g/kg, 13.1 g/kg, 16 g/kg did not achieve the LD₅₀.^(25–27)

The acute oral toxicity of 1.0% Polyquaternium-10 in a shampoo and a conditioner was tested by gavage. The LD₅₀ of the two formulations was not reached at 5 g/kg.^(28,29) Results are summarized in Table 2.

TABLE 2. Acute Oral Toxicity

<i>Compound</i>	<i>No. of rats</i>	<i>Vehicle</i>	<i>LD₅₀</i>	<i>Comments</i>	<i>Reference</i>
Polyquaternium-10 (Lot 1)	10	Corn oil	>16 g/kg	3/10 died; sluggish, wet fur and diarrhea on one day; low order of toxicity	25
Polyquaternium-10 (Lot 1)	3	Water	Not reached	None died; sluggish at 4 g/kg	25
Polyquaternium-10 (Lot 2)	10	Corn oil	13.1 g/kg	7/10 died; sluggish, wet fur, nose covered with blood on 1 day	26
Polyquaternium-10 (Lot 2)	10	Corn oil	Not reached	None died at 8 g/kg; appeared normal	26
Polyquaternium-10 (Lot 2)	5	Water	Not reached	None died at 2 g/kg; appeared normal	26
Polyquaternium-10 (Lot 3)	5	Corn oil	>16.0 g/kg	None died at 16.0 g/kg; wet fur and diarrhea at 1 day	27
Polyquaternium-10 (Lot 3)	3	Water	Not reached	None died at 4 g/kg; animals sluggish	27
<hr/>					
Polyquaternium-10 1% in shampoo	10	Formulation	>5 g/kg	None died; nontoxic	28
Polyquaternium-10 1% in conditioner	10	Formulation	>5 g/kg	None died; nontoxic	29

Inhalation Toxicity

Inhalation tests of three lots of Polyquaternium-10 were conducted using individual groups of 6 rats and an exposure period of 8 h. The rats were exposed to a substantial aerosol concentration that was prepared by placing 50 g of test material on a 200 cm² tray for 16 h before testing in a sealed chamber and during the 8-h exposure period. A fan was operated intermittently to agitate the internal chamber atmosphere. No signs of toxicity were observed during the exposure period.⁽²⁵⁾

Dermal Toxicity and Irritation

Three lot samples of Polyquaternium-10 were tested individually using three groups of 5 rabbits each. No deaths occurred when 4.0 g/kg was applied directly to the skin and the application site covered. Erythema developed, but no other remarkable gross lesions were observed. The three lot samples were considered, at most, slightly toxic.⁽²⁵⁻²⁷⁾

Three lots of Polyquaternium-10 were tested on the clipped uncovered intact skin of the abdomen of 5 rabbits at individual lot concentrations of 2%, 5%,

and 10% (in water). At 2% concentration, no irritation was observed in 4 rabbits, and moderate erythema was seen in 1 rabbit. At 5.0% concentration, no irritation was observed in 3 rabbits, and moderate erythema was seen in 2 rabbits. At 10% concentration, no irritation was observed in 2 rabbits, and moderate erythema was observed in 3 rabbits. The investigator termed the observed irritation a trace reaction.⁽²⁵⁻²⁷⁾

A shampoo containing 0.5% Polyquaternium-10 had a primary irritation index (PII) of 5.37 (max. 8) in a study performed according to CFR Title 16:1500.3(c)(4) and 1500.41.⁽³⁰⁾ The test used 12 rabbits, dosed at 0.5 ml of the shampoo, with 6 having intact skin and 6 having abraded skin. The shampoo was a severe skin irritant.^(28,31)

The dermal toxicity of a shampoo containing 0.5% Polyquaternium-10 was evaluated according to the procedures in the CFR Title 16:1500.3(c)(1)(ii)(c) and 1500.40.⁽³⁰⁾ The product was tested on the clipped skin of 5 rabbits and 5 that were both clipped and abraded. The dermal LD₅₀ of the formulation was greater than 2 g/kg.^(28,31)

A 21-day subchronic dermal toxicity study was conducted with a conditioner containing 1% Polyquaternium-10. Five male and five female rabbits were given 0.5 ml undiluted product once a day for 21 consecutive days. The test material was applied to the clipped dorsal trunk of the rabbits, and the skin of 5 of 10 animals was abraded before application of the test material. The test material remained in contact with the skin 6 h daily, and sites were uncovered. A control group of 5 male and 5 female rabbits had tap water applied to intact and abraded skin. No rabbits died during the test period, both groups had normal weight gains, and no lesions were observed at necropsy. Initial and terminal hematological and urinalysis values were within normal range. The product was not a cumulative dermal toxin.⁽³²⁾

Six New Zealand rabbits were used to evaluate the primary skin irritation of a conditioner containing 1% Polyquaternium-10. One-half (0.5) milliliter of the test material was administered to 1 intact and 1 abraded test site per animal. The clipped test sites were covered by occlusive patches for 24 h, and test sites were scored for irritation immediately after patch removal and 48 h later. The group PII was 0.0 (max. 8). The product was not a primary skin irritant⁽²⁹⁾ (Table 3).

Ocular Toxicity

Three lots of Polyquaternium-10 were tested for ocular toxicity, both as a dry powder and as an aqueous solution using groups of 5 animals. No irritation was produced by the powder form of any lot. When applied as the aqueous solution, no irritation was produced by lot 1 at a 20% concentration or by lot 2 at a 5% concentration. A trace of irritation was produced by lot 3 at a 10% concentration.⁽²⁵⁻²⁷⁾

A shampoo containing 0.5% Polyquaternium-10 was tested for ocular irritation in two groups of 12 rabbits according to the procedures given in the CFR Title 16:1500.3(c)(4) and 1500.42.⁽³⁰⁾ One group received full-strength instillations of the shampoo; a second received instillation of a 5% dilution. The eyes of half of the rabbits of each group were rinsed after product instillation. No irri-

TABLE 3. Dermal Toxicity and Irritation

<i>Compound</i>	<i>No. of rabbits</i>	<i>Vehicle</i>	<i>Concentration</i>	<i>Method</i>	<i>Results</i>	<i>Reference</i>
Polyquaternium-10 (Lot 1)	5	None	4 g/kg	Applied directly to clipped intact skin, occluded for 24 h	No deaths; erythema at 24 h; no remarkable gross pathological results	25
Polyquaternium-10 (Lot 2)	5	None	4 g/kg	Applied directly to clipped intact skin, occluded for 24 h	No deaths; erythema at 24 h; no remarkable gross pathological results	26
Polyquaternium-10 (Lot 3)	5	None	4 g/kg	Applied directly to clipped intact skin, occluded for 24 h	No deaths; erythema at 24 h; no remarkable gross pathological results	27
Polyquaternium-10 (Lot 1)	5	Water	2%	0.01 ml applied to clipped intact bellies for 24 h	No irritation in 4; moderate capillary injection in 1 rabbit	25
Polyquaternium-10 (Lot 2)	5	Water	5%	0.01 ml applied to clipped intact bellies for 24 h	No irritation in 3; moderate capillary injection in 2 rabbits	26
Polyquaternium-10 (Lot 3)	5	Water	10% (suspension)	0.01 ml applied to clipped intact bellies for 24 h	No irritation in 2; moderate capillary injection in 3 rabbits	27
Shampoo containing 1.0% Polyquaternium-10	12	Direct	1.0%	CFR 16:1500.3(C)(4), 1500.41; 6 with intact and 6 with abraded skin	PII 5.37 (max. 8); shampoo was classified as severe irritant	28, 31
Conditioner containing 1.0% Polyquaternium-10	6	Direct	1.0%	0.5 ml applied to each intact and abraded area; occluded for 24 h	PII 0.0 (max. 8); conditioner was not skin irritant	29

tation was observed in the eyes of any animal. The full-strength shampoo was not an eye irritant.^(31,33)

The ocular irritation of a conditioner containing 1% Polyquaternium-10 was evaluated in 9 New Zealand rabbits. One-tenth (0.1) milliliter of the test material was instilled into one eye of each rabbit, and the other eye served as an untreated control. The eyes of 3 rabbits were rinsed 15 sec after application of the test solution. No irritation was observed in rinsed or unrinsed eyes 1, 2, 3, 4, and 7 days after application of the product. The conditioner was not an eye irritant.⁽²⁹⁾ A summary of ocular test data is given in Table 4.

MUTAGENICITY AND GENOTOXICITY

Polyquaternium-10 was tested in triplicate and at five concentrations for mutagenic activity in the *Salmonella typhimurium* assay (Ames test) on TA-98, TA-100, TA-1535, TA-1537, and TA-1538 tester strains without and with metabolic activation. The metabolic activation was induced with S9 liver homogenate from male Sprague-Dawley rats pretreated with Aroclor 1254. In this setting, Polyquaternium-10 was not mutagenic in any of the five bacterial strains tested with and without metabolic activation.⁽³⁴⁾

Chinese hamster ovary (CHO) cells were exposed for 5 h to five concentrations of Polyquaternium-10 (0.12–0.285% in DMSO) without and with addition of S9 liver homogenate for metabolic activation (as in the Ames assay). Although some degree of mutagenicity was observed in both of the duplicate assays in the absence as well as in the presence of S9 homogenate, the response was not dose dependent. Polyquaternium-10 was thus considered to be nonmutagenic in the CHO test. In sister chromatid exchange (SCE) assays, Polyquaternium-10 in CHO cells both with and without enzyme induction by S9 liver homogenate did not increase the frequency of SCE over the range of concentrations tested (0.14–0.23%).⁽³⁴⁾

Polyquaternium-10 was evaluated also for its genotoxic effect in the rat hepatocyte primary culture/DNA repair test in six concentrations between 0.0009 and 0.23%. The results from duplicate samples indicate significant genotoxicity of this cosmetic ingredient at three of six doses. However, the measured activity, which was not dose dependent, was determined with hepatocytes from a single preparation and quantitated by liquid scintillation counting rather than by the more reproducible quantitative autoradiography.⁽³⁴⁾ The results of this study do not allow a valid conclusion about the activity of Polyquaternium-10 in hepatocyte DNA repair test.

Polyquaternium-10 was tested for its in vivo clastogenic activity in female Swiss mice by injecting single doses of 0.125, 0.25, and 0.4 g/kg, respectively, into the peritoneal cavity of 5 males and 5 females. Blood samples were collected 24, 48, and 72 h after the injection. Blood smears were prepared and stained for evaluating the possible presence of micronuclei. No statistically significant increases in micronucleated polychromatophilic erythrocytes were reported.⁽³⁴⁾

TABLE 4. Ocular Toxicity

<i>Compound</i>	<i>No. of rabbits</i>	<i>Vehicle</i>	<i>Concentration</i>	<i>Method</i>	<i>Results</i>	<i>Reference</i>
Polyquaternium-10 (Lot 1)	5	Powder	Direct	Single instillation into conjunctival sac	No irritation	25
Polyquaternium-10 (Lot 1)	5	Water	2%	0.5 ml single instillation into conjunctival sac	No irritation	25
Polyquaternium-10 (Lot 2)	5	Powder	Direct	0.5 ml single instillation into conjunctival sac	No irritation	26
Polyquaternium-10 (Lot 2)	5	Water	5%	0.5 ml single instillation into conjunctival sac	No irritation	26
Polyquaternium-10 (Lot 3)	5	Powder	Direct	0.5 ml single instillation into conjunctival sac	No irritation	27
Polyquaternium-10 (Lot 3)	5	Water	10% (suspension)	0.5 ml single instillation into conjunctival sac	Trace irritation in 1 eye, none in 4	27
Shampoo containing 0.5% Polyquaternium-10	12	Direct and 5% dilution	1.0 and 0.05%	CFR 16:1500.3(C)(4) and 1500.42; half of test eyes were rinsed	No irritation at either concentration, rinsed or unrinsed	28, 31
Conditioner containing 1.0% Polyquaternium-10	9	Direct	0.1 ml of conditioner	Direct application, 3 eyes rinsed	No irritation, not an eye irritant	29

CLINICAL ASSESSMENT OF SAFETY

Primary Skin Irritation, Sensitization, and Photosensitization

A lot of Polyquaternium-10 was tested for primary skin irritation on 106 subjects. A 5% w/v solution in water was applied to the skin under occlusive patches for 48 h. No skin irritation was observed at 48 and 72 h after application.⁽³⁵⁾ No irritation was observed when a 5% Polyquaternium-10 solution was applied daily under occlusive conditions for 21 days to 27 subjects.⁽³⁶⁾

Three separate lots of Polyquaternium-10 were tested by a repeated insult patch test (RIPT) protocol using 50 subjects. A 2% w/v solution in water was applied to the skin on lintine disks under occlusive patches for 24 h. The treatment reaction sites were scored at 24 h. Following a 24-h nontreatment period, the sites were again exposed to the test samples. A 2-week nontreatment period followed the 15th application. The test sites were evaluated and then treated in a similar manner and scored at 24 and 48 h. No evidence of either irritation or sensitization was observed in any subject when exposed to the three lot samples of Polyquaternium-10.⁽³⁷⁻³⁹⁾

There was no irritation or sensitization when a 5% w/v solution of Polyquaternium-10 was used in an RIPT on 203 subjects.⁽⁴⁰⁾

A shampoo containing 0.5% Polyquaternium-10 was evaluated for primary irritation and sensitization by a prophetic patch test⁽⁴¹⁾ and an RIPT.⁽⁴²⁾ One hundred subjects participated in the prophetic patch test, and no reactions were observed to either of the two closed patches applied. Fifty-three subjects completed the RIPT, and no reactions were observed during induction or at challenge. Photosensitization also was evaluated in these two studies by exposure of the sites to UV light during the induction phase of the RIPT study and during the challenge phase of the prophetic patch test. The undiluted shampoo was not a primary skin irritant, sensitizer, or photosensitizer.^(31,43)

The primary irritation, sensitization, and photosensitization of an undiluted shampoo containing 0.5% Polyquaternium-10 was evaluated in an RIPT according to the procedures of Shelanski and Shelanski⁽⁴²⁾ using a 25-member panel. The UV light was applied during the induction phase of the study. The shampoo was tested at full strength. The product was nonirritating, nonsensitizing, and nonphotosensitizing.⁽⁴⁴⁾

Forty-six panelists participated in an RIPT of a conditioning product containing 1% Polyquaternium-10. Patches containing 0.2 ml undiluted conditioner were applied to the inner arm or back of each subject on Mondays, Wednesdays, and Fridays for a total of 10 induction patches. After a 10–20 day nontreatment period, two challenge patches were applied simultaneously, one to the original test site and the other to an untreated site. One panelist had minimal erythema (score of \pm on a 0–4 scale) to induction patch 9, and another panelist had a \pm reaction to induction patch 10. Two panelists reacted at challenge; 1 had \pm reactions at the 24-h reading of both challenge patches, and another had scores of 1 and 2, and 2 and 2 at the 24-h and 48-h readings of the original site patch and untreated site patch, respectively. After rechallenge, the same panelist had no reactions. The conditioner was not an irritant or sensitizer.⁽⁴⁵⁾

A controlled use study following CTFA guidelines⁽⁴⁶⁾ was performed using a shampoo containing 0.5% Polyquaternium-10. Eighty-three subjects participated

in the 4-week study, which required daily product use. The scalp, neck, face, and hair of each subject were examined for irritation. The shampoo was nonirritating under the conditions of this test.^(31,47) Results are summarized in Table 5.

Moderation of Skin Irritants

An extensive study was undertaken to determine the capacity of Polyquaternium-10 to moderate reactions to skin irritants. The first phase of the study ex-

TABLE 5. Clinical Assessment of Safety

Test type ^a	No. of subjects	Product type	Polyquaternium-10 concentration (%)	Comments	Reference
RIPT	50	Polyquaternium-10 (Lot 1)	2	No reactions; not an irritant or sensitizer	37
RIPT	50	Polyquaternium-10 (Lot 2)	2	No reactions; not an irritant or sensitizer	38
RIPT	50	Polyquaternium-10 (Lot 3)	2	No reactions; not an irritant or sensitizer	39
Prophetic patch test	100	Shampoo	0.5	No reactions; not an irritant, sensitizer, or photosensitizer	43
RIPT	53	Shampoo	0.5	No reactions; not an irritant, sensitizer, or photosensitizer	43
RIPT	25	Shampoo	0.5	No reactions; not an irritant, sensitizer, or photosensitizer	44
RIPT	46	Conditioner	1	Two minimal reactions during induction, one minimal and one moderate reaction at challenge; rechallenge to moderate reactor was negative; not an irritant or sensitizer	45
Controlled use	83	Shampoo	0.5	No reactions; not an irritant	31, 47

^aSee text for details of experimental procedure.

aminated the cutaneous toxicity and effects on wound healing of Polyquaternium-10. The Polyquaternium-10 used in this study had a molecular weight of approximately 400,000. Six subjects were given single 0.1 ml intradermal injections of 0.25% and 1.0% aqueous Polyquaternium-10 into the back. The injection sites were observed daily for 1 week, and no reactions were observed at the 0.25% Polyquaternium-10 sites. The 1.0% injections produced small (5 mm) inflamed nodules within 24 h. The nodules disappeared without residue within a few days.

The effect of Polyquaternium-10 on wound healing was studied by applying 1% or 2% Polyquaternium-10 to raw blisters produced by 15% ammonia solutions. A single application or five daily applications enhanced wound healing if the 2% Polyquaternium-10 was allowed to dry before the site was bandaged. If the test site was bandaged before the polymer dried, healing was slower than untreated control sites. These studies suggest that Polyquaternium-10 protected the wound surface and promoted reepithelialization.

The second phase of this study evaluated moderation by Polyquaternium-10 of inflammatory reactions to sodium lauryl sulfoacetate, shampoos, a depilatory cream, *Rhus* (poison ivy) dermatitis, and soap. In all cases, pretreatment and/or concurrent treatment of the test site with Polyquaternium-10 resulted in less severe reactions to the irritants⁽⁴⁸⁾ (Table 6).

SUMMARY

Polyquaternium-10, a white granular powder, is a polymeric quaternary ammonium derivative of hydroxyethyl cellulose with cationic surface-active properties. The product for cosmetic use varies in molecular weight from 250,000 to 600,000. Polyquaternium-10 is soluble in water and insoluble in alcohol and nonpolar organic solvents. Results of studies in rats indicated that Polyquaternium-10 has, at most, only a low potential to penetrate the stratum corneum. It is adsorbed by keratinous surfaces. The ingredient is used in cosmetics as a conditioner, thickener, and emollient in hair care products, lotions, and makeup products at reported ranges of concentration of $\leq 0.1\%$ –5%.

Polyquaternium-10 with and without metabolic activation was assayed for mutagenicity in 5 *S. typhimurium* tester strains, in Chinese hamster ovarian cells, for in vitro sister chromatid exchange in CHO cells, and for clastogenic activity in female Swiss mice. Polyquaternium-10 was negative for mutagenicity in these four short-term tests. In the rat hepatocyte primary culture/DNA repair test, genotoxicity was present but was not dose related.

Polyquaternium-10 permeates and adsorbs into isolated stratum corneum obtained from fetal pigs, neonatal rats, and humans. LD₅₀s for lots of Polyquaternium-10 in corn oil were not obtained at 16 g/kg in two lots or 13.1 g/kg in a third lot. Signs of toxicity were not observed when rats were exposed for 8 h to a vapor containing Polyquaternium-10. Acute dermal exposure of rats to undiluted Polyquaternium-10 produced erythema only. In other skin irritation studies using rabbits, 2%, 5%, and 10% concentrations of Polyquaternium-10 produced only slight irritation. Polyquaternium-10 was not an irritant when tested for ocular irritation in powder form and aqueous solutions at concentrations up to 10%.

TABLE 6. Moderation of Irritant Reactions by Polyquaternium-10⁽⁴⁸⁾

<i>Irritant</i> ^a	<i>No. of subjects</i>	<i>Group average without Polyquaternium-10 (0-4 scale)</i>	<i>Group average with 2% Polyquaternium-10 (0-4 scale)</i>
5% sodium lauryl sulfate (pre-treated with polymer)	10	3.6	1.1
5% sodium lauryl sulfate	10	3.6	1.4
Shampoo	5	2.6 ^b	1.4 ^b
Shampoo	5	3.0 ^b	1.6 ^b
Depilatory cream	6	2.0	0.8
<i>Rhus</i> (poison ivy) (pretreated with polymer)	5	3.6	1.4
<i>Rhus</i>	5	3.8	1.2 ^c
Soap	5	3.4	1.8 ^d

^aConcurrent treatment with polymer unless otherwise noted.

^b1-3 scale.

^c1% Polyquaternium-10.

^d2.5% Polyquaternium-10.

Products containing up to 1% Polyquaternium-10 were practically nontoxic to rats when given by acute oral and dermal routes. These products were not skin or eye irritants, except for one shampoo that was a primary skin irritant in rabbits. Polyquaternium-10 was neither an irritant nor a sensitizer for humans when it was tested using a 50-member panel and at 2.0% in a repeat insult patch test.

Products containing up to 1% Polyquaternium-10 were nontoxic in clinical studies. Conditioners and shampoos containing Polyquaternium-10 were not irritants, sensitizers or photosensitizers in a prophetic patch test, repeat insult patch tests, and a controlled use study. Polyquaternium-10 at 1% concentration was minimally irritating when administered as a single intradermal injection. The polymer enhanced wound healing of minor skin lesions. Pretreatment and concurrent treatment with 1-2% Polyquaternium-10 reduced inflammatory and/or dermatitic reactions to known irritants, such as sodium lauryl sulfate and *Rhus* (poison ivy).

DISCUSSION

Acute toxicity studies indicate that Polyquaternium-10 has a low order of toxicity. Subchronic studies were not available; however, skin penetration studies indicate that Polyquaternium-10 adsorbs on keratin tissue and is poorly absorbed.

Animal studies using up to 5.0% Polyquaternium-10 indicate that this cosmetic ingredient is at most only mildly irritating to skin or eye. The severe skin irritation reported in one study, but not all studies, was most likely due to the shampoo ingredients and not the Polyquaternium-10. Studies of the ingredient at 2.0%, using human subjects, indicate that this ingredient was neither an irritant nor a sensitizer. Similar negative results were obtained from product formulations at 0.5%, including data that indicate the ingredient is not a photosensitizer.

CONCLUSION

On the basis of the information presented in this report, the CIR Expert Panel concludes that Polyquaternium-10 is safe as a cosmetic ingredient in the present practices of use.

REFERENCES

1. ESTRIN, N.F., CROSLY, P.A., and HAYNES, C.R. (eds.). (1982). *CTFA Cosmetic Ingredient Dictionary*. Washington, DC: The Cosmetic, Toiletry and Fragrance Association, Inc.
2. FAUCHER, J.A., and GODDARD, E.D. (1976). Sorption of a cationic polymer by stratum corneum. *J. Soc. Cosmet. Chem.* **27**, 543-53.
3. HUNTING, A.L.L. (1983). *Encyclopedia of Shampoo Ingredients*. Cranford, NJ: Micelle Press.
4. ESTRIN, N.F., HAYNES, C.R., and WHELAN, J.M. (eds.). (1982). *CTFA Compendium of Cosmetic Ingredient Composition: Cosmetic Ingredient Descriptions*. Washington, DC: Cosmetic Toiletry and Fragrance Association, Inc.
5. GODDARD, E.D., PHILLIPS, T.S., and HANNAN, R.B. (1975). Water-soluble polymer-surfactant interaction—Part I. *J. Soc. Cosmet. Chem.* **26**, 461-75.
6. GODDARD, E.D., FAUCHER, J.A., SCOTT, R.J., and TURNEY, M.E. (1975). Adsorption of polymer JR on keratinous surfaces. II. *J. Soc. Cosmet. Chem.* **26**(11), 539-50.
7. FAUCHER, J.A., GODDARD, E.D., and HANNAN, R.B. (1977). Sorption and desorption of a cationic polymer by human hair: Effects of salt solutions. *Text. Res. J.* **47**(9), 616-20.
8. GODDARD, E.D., and LEUNG, P.S. (1980). Cationic cellulosics in lotions. *Cosmet. Toilet.* **95**, 67-9.
9. GODDARD, E.D., and LEUNG, P.S. (1982). Protection of the skin by cationic cellulosics: In vitro testing methods. *Cosmet. Toilet.* **97**(7), 55-6, 58, 60-2, 64-5, 68-9.
10. SENZEL, A.J. (1977). *Newburger's Manual of Cosmetic Analysis*, 2nd ed. Washington, DC: Association of Official Analytical Chemists, Inc.
11. UNION CARBIDE CORPORATION. (Jan. 27, 1986). Submission of unpublished data on Epichlorohydrin in Polyquaternium-10 polymer samples.*
12. UNION CARBIDE CORPORATION. (Jan. 7, 1986). Submission of unpublished data on Trimethylamine in Polyquaternium-10 lot samples.*
13. CANNELL, D.W. (1979). Split ends and their repair. *Cosmet. Toilet.* **94**, 29-31.
14. WILKINSON, J.B., and MOORE, R.J. (eds.). (1982). *Harry's Cosmetology*, 7th ed. New York: Chemical Publishing Company, Inc.
15. FOOD AND DRUG ADMINISTRATION (FDA). (1981). Computer printout of voluntary submission of cosmetic ingredient data.

*Available for review: Director, Cosmetic Ingredient Review, 1110 Vermont Ave., NW, Suite 810, Washington, DC 20005.

16. CODE OF FEDERAL REGULATIONS, TITLE 21. (1982). Washington, DC: U.S. Government printing Office.
17. COSMETIC, TOILETRY AND FRAGRANCE ASSOCIATION (CTFA). (1984). Polyquaternium-10: Cosmetic Ingredient Safety Analysis. (Received July 23, 1984).*
18. UNION CARBIDE CORPORATION. (Aug. 27, 1986). Submission of unpublished data on the skin penetration potential of ¹⁴C-Polyquaternium-10.*
19. UNION CARBIDE CORPORATION. (Dec. 10, 1986). Letter on radioactive labeling of test compound.*
20. GOLDEMBERG, R.L., and SAFRIN, L. (1977). Reduction of topical irritation. *J. Soc. Cosmet. Chem.* **28**, 667-79.
21. GOLDEMBERG, R.L. (1979). Anti-irritants. *J. Soc. Cosmet. Chem.* 30:415-27. In: Haynes, C.R., and Estrin, N.F. (eds.). (1981). *CTFA Technical Guidelines: CTFA Safety Testing Guidelines*. Washington, DC: Cosmetic, Toiletry and Fragrance Association.
22. LOVEDAY, D.E. (1961). An in vitro method for studying percutaneous absorption. *J. Soc. Cosmet. Chem.* **12**, 224.
23. FAUCHER, J.A., and GODDARD, E.D. (1978). Interaction of keratinous substrates with sodium lauryl sulfate. II. Permeation through stratum corneum. *J. Soc. Cosmet. Chem.* **29**, 339-52.
24. FAUCHER, J.A., and GODDARD, E.D. (1978). Diffusion and sorption phenomena in neonatal rat stratum corneum. *J. Coll. Interface Sci.* **65**(3), 444-50.
25. CARNEGIE-MELLON UNIVERSITY. (1973). Submission of unpublished data by CTFA. Range finding toxicity studies (Polyquaternium-10, JR-400).
26. CARNEGIE-MELLON UNIVERSITY. (1973). Submission of unpublished data by CTFA. Range finding toxicity studies (Polyquaternium-10, JR-30M).
27. CARNEGIE-MELLON UNIVERSITY. (1973). Submission of unpublished data by CTFA. Range finding toxicity studies (Polyquaternium-10, JR-125).
28. CTFA. (1972). Submission of unpublished data by CTFA. Acute oral and dermal toxicity and skin irritation of a shampoo containing 0.5% Polyquaternium-10. (2-48-1).*
29. CONSUMER PRODUCT TESTING COMPANY (CPT). (1980). Submission of unpublished data by CTFA. Animal dermal, ocular and acute oral toxicity of a conditioner containing 1% Polyquaternium-10. (2-48-6).*
30. CODE OF FEDERAL REGULATIONS, TITLE 16. (1982). Washington, DC: U.S. Government Printing Office.
31. CTFA. (1985). Memorandum to G.N. McEwen, Jr., clarifying CTFA submission of unpublished data. (Received Jan. 14, 1985).*
32. CPT. (1980). Submission of unpublished data by CTFA. Rabbit subacute dermal toxicity study on a conditioner containing 1% Polyquaternium-10. (2-48-8).*
33. CTFA. (1973). Submission of unpublished data by CTFA. Rabbit ocular irritation study on a shampoo containing 0.5% Polyquaternium-10. (2-48-2).*
34. UNION CARBIDE CORPORATION. (May 23, 1985). Submission of unpublished mutagenicity data.*
35. UNION CARBIDE CORPORATION. (Aug. 6, 1985). Submission of unpublished data on primary human skin irritation of a Polyquaternium-10 polymer.*
36. UNION CARBIDE CORPORATION. (Sept. 12, 1985). Submission of unpublished data on cumulative human skin irritation.*
37. PRODUCT INVESTIGATIONS, INC. (1976). Evaluations of potential hazards by dermal contact. (Polyquaternium-10, Lot JR-125).
38. PRODUCT INVESTIGATIONS, INC. (1976). Evaluations of potential hazards by dermal contact. (Polyquaternium-10, Lot JR-400).
39. PRODUCT INVESTIGATIONS, INC. (1976). Evaluations of potential hazards by dermal contact. (Polyquaternium-10, Lot JR-30M).
40. UNION CARBIDE CORPORATION. (Oct. 25, 1985). Submission of unpublished data on human repeat insult patch testing.*
41. SCHWARTZ, L., and PECK, S.M. (1944). The patch test in contact dermatitis. *Public Health Rep.* **59**, 546-57.
42. SHELANSKI, H.A., and SHELANSKI, M.V. (1953). A new technique of human patch tests. *Proc. Sci. Sect. Toilet Goods Assoc.* **19**, 46-9.
43. CTFA. (1972). Submission of unpublished data by CTFA. Human prophetic patch test and RIPT on a shampoo containing 0.5% Polyquaternium-10. (2-48-3).*
44. CTFA. (1973). Submission of unpublished data by CTFA. Human RIPT on a shampoo containing 0.5% Polyquaternium-10. (2-48-4).*

45. FOOD AND DRUG RESEARCH LABORATORIES. (1980). Submission of unpublished data by CTFA. Human RIPT on a conditioner containing 1% Polyquaternium-10. (2-48-7).*
46. HAYNES, C.R., and ESTRIN, N.F. (eds.). (1981). *CTFA Technical Guidelines: CTFA Safety Testing Guidelines*. Washington, DC: Cosmetic, Toiletry and Fragrance Association.
47. CTFA. (1973). Submission of unpublished data by CTFA. Human controlled use study on a shampoo containing 0.5% Polyquaternium-10. (2-48-5).*
48. FAUCHER, J.A., GODDARD, E.D., HANNAN, R.B., and KLIGMAN, A.M. (1977). Protection of the skin by a cationic cellulose polymer. *Cosmet. Toilet.* **92**, 39-44.