# Final Report on the Safety Assessment of Quaternium-26<sup>1</sup>

The quaternary ammonium salt Quaternium-26 is used as a film former, hair conditioning agent, and an antistatic agent in a variety of cosmetic products. Quaternium-26 is supplied as a 60% solution. It contains fatty acid groups derived from Mink Oil. Impurities include diethanolamine (0.4%) and 3-dimethylaminopropylamine (1.4%). Typical concentrations of use (of the solution as supplied) are 2% to 5%. There is no significant absorbance by Quaternium-26 in the UVA or UVB region of the spectrum. One acute oral toxicity study in 30 rats using Quaternium-26 at a concentration of 3.6% yielded an  $LD_{50}$  of 5.65 g/kg, whereas another using 1.8% failed to kill any of 10 rats. Ocular toxicity was evaluated in albino rabbits exposed to concentrations ranging from 1.8% to 3.0%; at most, mild irritation was noted over the concentration range studied. Quaternium-26 was a mild irritant over the concentration range 1.8% to 3.6%. It was not comedogenic at 1.8%. Quaternium-26 did not produce sensitization in a repeat insult patch test (RIPT) test, although irritation did persist throughout the induction phase of the study. In another sensitization study in which Quaternium-26 was injected into the skin, no sensitization reactions were observed. As with Mink Oil, the Cosmetic Ingredient Review (CIR) Expert Panel was concerned with the presence of halogenated environmental chemicals. Because only the fatty acid fraction of mink oil is used in a chemical reaction to form Quaternium-26, the Panel was of the opinion that such environmental chemicals would not likely carry over to Quaternium-26, but that Quaternium-26, as a cosmetic ingredient, should not contain halogenated environmental chemicals. The Expert Panel also considered previous safety assessments of Quaternium-18 and Quaternium-22 in which little evidence of toxicity was seen. Based on the available data, the CIR Expert Panel concluded that Quaternium-26 is safe in the present practices of use. Because of the presence of impurities, however, Quaternium-26 should not be used in products in which N-nitroso compounds may be formed.

# INTRODUCTION

The safety of Quaternium-26 in cosmetics is reviewed in this report. This quaternary ammonium salt is used as a film former, hair conditioning agent, and an antistatic agent in cosmetic products.

This document also contains summary information from Cosmetic Ingredient Review (CIR) safety assessments on the

International Journal of Toxicology, 19(Suppl. 1):69–75, 2000 Copyright © 2000 Cosmetic Ingredient Review 1071-7544/00 \$12.00 + .00 following quaternary ammounium compounds: Quaternium-18, Quaternium-18 Hectorite, and Quaternium-18 Bentonite (Elder 1982), and Quaternium-22 (Andersen 1995). Also included is the summary from the CIR safety assessment of Mink Oil (Andersen 1998). Each of these was considered relevant to the safety assessment of Quaternium-26. The previous assessments found the quaternary ammonium compounds to be safe as used in cosmetic formulations. The safety assessment of Mink Oil, however, found that the available data were insufficient to support safety.

## CHEMISTRY

# **Chemical and Physical Properties**

Quaternium-26 (CAS No. 68953-64-0) is the quaternium ammonium salt that conforms generally to the formula shown in Figure 1. Other names for this chemical are Minkamidopropyl Dimethyl 2-Hydroxyethyl Ammonium Chloride and Quaternary Ammonium Compounds, (Hydroxyethyl)Dimethyl(3-Mink Oil Amidopropyl), Chlorides (Wenninger, Canterbery, and McEwen 2000).

Quaternium-26 is marketed as a 60% solution (Ceraphyl 65) (International Specialty Products 1997). Throughout the text, this trade solution will be referred to as 60% Quaternium-26.

An ultraviolet (UV) spectral analysis of Quaternium-26 indicates maximum absorbance between 200 and 220 nm and minimum absorbance in the 280 to 320 nm range (CTFA no date).

#### **Methods of Production**

Quaternary compounds are normally synthesized by reacting a tertiary amine with an alkyl chloride or sulfate (Hunting 1983).

## Composition/Impurities

The typical fatty acid composition of the heavy fraction of mink oil used in the manufacture of 60% Quaternium-26 is as follows: myristic (4.29%), myristoleic (1.41%), palmitic (25.21%), palmitoleic (17.42%), stearic (0.63%), oleic (39.91%), linoleic (11.13%), and linolenic (trace) (Van Dyk & Company, Inc. no date).

Using gas chromatography (with flame ionization detection), the following two impurities have been detected in 60% Quaternium-26: diethanolamine (0.4%) and 3-dimethylaminopropylamine (1.4%) (Chemtest Laboratories Inc. 1992).

Received 3 February 2000; accepted 3 May 2000.

<sup>&</sup>lt;sup>1</sup>Reviewed by the Cosmetic Ingredient Review Panel. Wilbur Johnson, Senior Scientific Analyst and Writer. Address correspondence to him at Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 310, Washington, DC 20036, USA.



### FIGURE 1

Chemical formula for Quaternium-26. The RCO–group in the chemical structure represents the fatty acid groups derived from mink oil (Wenninger, Canterbery, and McEwen 2000).

#### Analytical Methods

Quaternium-26 (60%) has been identified by infrared spectroscopy (sample pH = 6.9 to 7.0) (Sadtler Research Laboratories Inc. 1982) and, as noted in the preceding section, has also been analyzed via gas chromatography (with flame ionization detection) (Chemtest Laboratories Inc. 1992).

# USE

#### **Purpose In Cosmetics**

Quaternium-26 is used as a film former, hair conditioning agent, and an antistatic agent in cosmetic products (Wenninger, Canterbery, and McEwen 2000).

## Scope and Extent of Use in Cosmetics

## United States

The product formulation data submitted to the Food and Drug Administration (FDA) in 1997 indicated that Quaternium-26 was used in as many as 25 cosmetic product formulations (Table 1) (FDA 1997).

Concentration of use values are no longer reported to FDA by the cosmetics industry (FDA 1992). However, product formulation data submitted to the FDA in 1984 indicated that Quaternium-26 was used at concentrations up to 5.0% (FDA 1984). Recent data indicates recommended uses of Ceraphyl 65 at concentrations between 2% and 5%, but because Ceraphyl 65 is sold as a 60% Quaternium-26 solution, the recommended concentrations (between 2% and 5%) correspond to 1.2% to 3.0% Quaternium-26 on an active basis (International Specialty Products 1997).

Cosmetic products containing Quaternium-26 are applied to the skin, hair, and most parts of the body, and can come in contact with the ocular and nasal mucosae. These products could be used on a daily basis, and have the potential for being applied frequently over a period of several years.

 TABLE 1

 Product formulation data on QUATERNIUM-26 (FDA 1997)

Product category	Total no. formulations in category	Total no. containing ingredient
Hair conditioners	596	3
Permanent waves	297	4
Shampoos (noncoloring)	825	5
Tonics, dressings, and other hair grooming aids	512	8
Other hair preparations	311	1
Bath soaps and detergents preparations (excluding shaving)	341	1
Cleansing skin care preparations 1997 totals	630	3 25

#### International

Quaternium-26 is not listed in the Japanese Comprehensive Licensing Standards of Cosmetics by Category (CLS) (Rempe and Santucci 1997).

Quaternium-26 is not included among the substances listed as prohibited from use in cosmetic products marketed in the European Union (European Economic Community 1995).

# TOXICOLOGY

#### Acute Oral Toxicity

The acute oral toxicity of a test solution (6% dilution of 60% Quaternium-26, effective concentration = 3.6%, in propylene glycol) was evaluated using 30 albino rats (males and females; weights = 200–300 g). Six groups of five rats received single doses (by stomach tube) of 2.0, 4.0, 5.0, 6.3, 8.0, and 16.0 g/kg, respectively, of the test solution. The animals were observed daily for 2 weeks, and neither postmortem nor microscopic examinations were performed at the end of the observation period. An LD<sub>50</sub> of 5.65 g/kg (95% confidence limits = 4.82–6.83 g/kg) was reported along with LD<sub>0</sub> and LD<sub>100</sub> values of 4.0 and 8.0 g/kg, respectively. Diarrhea (slight to severe) was observed in all dose groups, and nasal hemorrhage was observed in 5.0 to 16.0 g/kg dose groups (Bio-Toxicology Laboratories, Inc. 1976).

In another study, the acute oral toxicity of 60% Quaternium-26 (3% w/w in distilled water; effective concentration = 1.8%) was evaluated using 10 albino rats (5 males, 5 females; weights = 202–252 g). A single dose of 20 ml/kg body weight was administered to each animal. Observations for signs of pharmacologic activity and drug toxicity were made at 1, 3, 6, and 24 hours postadministration, and, thereafter, once daily for 14 days. Animals were then killed and necropsy completed. The LD<sub>50</sub> was not achieved at the administered dose of 20 ml/kg; only one death (one male rat) was reported. Consolidation of the inferior lobe of the right lung was the only alteration noted at necropsy (one female rat) (Consumer Product Testing Company, Inc. 1979a).

#### **Ocular Irritation**

The ocular irritation potential of 60% Quaternium-26 (3% w/w in deionized water; effective concentration = 1.8%) was evaluated using nine New Zealand white rabbits according to a modification of the procedure by Draize (1975). The test substance (0.1 ml) was instilled into the conjunctival sac of one eye of each animal; untreated eyes served as controls. Following instillation, the eyes of three rabbits were rinsed. Ocular irritation was scored at 24, 48, and 72 hours postinstillation (rinsed and unrinsed eyes) and at days 4 and 7 (unrinsed eyes), and the total Draize irritation score (scale = 0-110) calculated. In the group of six rabbits that was not subjected to ocular rinsing, the highest mean total Draize score (13.5) was noted at 24 hours postinstillation, and the lowest (0), at day 7. A Draize score of 0 (all observation periods) was reported for the three rabbits in which the eyes were rinsed. It was concluded that Quaternium-26 (effective concentration = 1.8%) induced mild ocular irritation in rabbits. Evidence that irrigation eliminated the ocular irritation reactions was obtained (Consumer Product Testing Company, Inc. 1979b).

Quaternium-26 was tested at greater concentrations in the following studies, which generally were conducted according to the preceding test procedure (modifications are indicated).

A 5% aqueous solution of 60% Quaternium-26 (effective concentration = 3%) was classified as a conjunctival irritant in unrinsed eyes. Reactions were scored at 1 hour postinstillation and daily thereafter for 7 days. Total Draize scores per rabbit ranged from 26 to 78 (110 = maximum score); the group mean Draize score was 46 (Bio-Toxicology Laboratories, Inc. 1977a). Another 5% aqueous solution of 60% Quaternium-26 (effective concentration = 3%) was not classified as an ocular irritant. Reactions were scored at the same intervals. Total Draize scores per rabbit ranged from 2 to 4, and the group mean Draize score was 2.3 (Bio-Toxicology Laboratories, Inc. 1977b).

A 4% aqueous solution of 60% Quaternium-26 (effective concentration = 2.4%) was not an ocular irritant in unrinsed eyes. Reactions were scored at 1 hour postinstillation and daily thereafter for seven days. Total Draize scores per rabbit ranged from 2 to 6; the group mean Draize score was 3.3 (Bio-Toxicology Laboratories, Inc. 1977c). Identical results were reported in another experiment in which a 4% aqueous solution of 60% Quaternium-26 (effective concentration = 2.4%) was tested (Bio-Toxicology Laboratories, Inc. 1977d).

In a third experiment, 60% Quaternium-26 (4% w/w in deionized water; effective concentration = 2.4%) was classified as a mild ocular irritant. Reactions (rinsed and unrinsed eyes) were scored on days 1 through 7 postinstillation. In the group of six rabbits that was not subjected to ocular rinsing, the highest mean total Draize score (22.3) was noted at day 1 postinstillation, and the lowest (1.8), at day 7. In the group of three rabbits subjected to ocular rinsing, the highest mean total Draize score (4.7) was noted at days 1 and 2 postinstillation, and the lowest (0), at day 7. Evidence that irrigation reduced the severity of ocular irritation was obtained (Consumer Product Testing Company, Inc. 1978).

## Skin Irritation

The skin irritation potential of 60% Quaternium-26 (3% w/w in deionized water; effective concentration = 1.8%) was evaluated using six New Zealand white rabbits according to a modification of the procedure of Draize (1975). The test substance, 0.5 ml, was applied to each of two skin sites (abraded and intact, clipped free of hair) on the mid-dorsal area of the trunk. Abraded and intact sites, on opposite sides of the vertebral column, were covered with a surgical gauze pad secured with adhesive tape. The trunk of each animal was also encased with an impermeable occlusive wrapping. Reactions were scored at 24 and 72 hours postapplication according to the following scales: 1 (very slight erythema-barely perceptible) to 4 (severe erythema to slight eschar formation) and 1 (very slight edema-barely perceptible) to 4 (severe edema, raised more than 1 mm and extending beyond area of exposure). Scores were averaged to determine the primary irritation index (PII); a PII of 5 or greater indicated primary dermal irritation. Quaternium-26 (effective concentration = 1.8%) had a PII of 0 (Consumer Product Testing Company, Inc. 1979c).

Quaternium-26 was tested at greater concentrations in the following studies, which generally were conducted according to the preceding test procedure (modifications are indicated).

A 6% solution of 60% Quaternium-26 (effective concentration = 3.6%) was classified as a mild irritant (PII = 0.33) in albino rabbits. In this study, except for the definition of reactions with a score of 1 as erythema and eschar formation and edema formation, the preceding grading scale was also used (Bio-Toxicology Laboratories, Inc. 1976).

Quaternium-26 (5% aqueous solution of 60% Quaternium-26; effective concentration = 3%) was also classified as a mild irritant in albino rabbits (PII = 0.71). The grading scale modifications in the preceding paragraph are also applicable to this study (Bio-Toxicology Laboratories, Inc. 1977a).

A PII of 0.88 was reported in another study in which 60% Quaternium-26 (4% w/w solution in deionized water; effective concentration = 2.4%) was tested using albino rabbits. It was concluded that the test substance had the potential for slight skin irritation (Consumer Product Testing Company, Inc. 1978).

#### Comedogenicity

The comedogenicity of a 3.0% solids solution of 60% Quaternium-26 (effective concentration = 1.8%) was evaluated using six female, New Zealand white rabbits. The test substance (0.5 ml) was applied to the external right ear of each of three rabbits 5 days per week for 2 consecutive weeks; left external ears were not treated. A 5% w/v solution of isopropyl myristate in cotton seed oil (control) was applied to the three control rabbits according to the same procedure. All animals were killed on day 14 of the study. Treated and untreated tissues from the right and left external ears, respectively, were excised and examined microscopically. On day 9 of the study, slight redness, with some flaking, was noted on the right external ears (application site) of two of three rabbits treated with Quaternium-26. The flaking had begun to subside by day 14. Similarly, on day 6, slight redness was noted on the right external ears (test site) of two of three rabbits treated with isopropyl myristate (control). By day 10, flaking (test site) was noted in one of the two rabbits. Both the redness and flaking induced by isopropyl myristate persisted for the remainder of the study. At microscopic examination of skin sites treated with Quaternium-26, minimal epidermal hyperplasia (mainly stratum granulosum and stratum corneum) was observed in all three rabbits, and minimal hyperkeratosis in one rabbit. Isopropyl myristate also induced epidermal hyperplasia (slight to mild) and hyperkeratosis (slight to mild) in the three control rabbits. In experimental and control groups, morphology of the sebaceous glands and ducts was considered normal. It was concluded that Quaternium-26 (effective concentration = 1.8%) and isopropyl myristate (5% w/v in cotton seed oil) were noncomedogenic (Food and Drug Research Laboratories, Inc. 1982).

## Skin Sensitization

The skin sensitization potential of a 25% aqueous solution of 60% Quaternium-26 (effective concentration = 15%) was evaluated according to the method of Buehler (1965) using 12 male Hartley guinea pigs. (The test concentration was determined to be the largest nonirritating concentration in a doseresponse, skin irritation pretest---one animal per concentration tested.) During induction, the test substance (0.5 ml under occlusive patch) was applied to the mid-dorsal area (clipped free of hair) of the trunk of each animal for a minimum of 6 hours. At the time of patch removal, reactions were scored according to the following scales: 1 (very slight erythema) to 4 (severe erythema to eschar formation) and 1 (very slight edema) to 4 (severe edema, raised more than 1 mm and extending beyond area of exposure). This procedure was repeated for a total of nine induction applications over a period of 3 weeks. Following a 2-week nontreatment period, challenge applications were made to two sites (original and new test sites). Reactions were scored at 6 and 24 hours postapplication. Slight to moderate irritation persisted throughout the induction period; however, no positive reactions were observed at challenge. It was concluded that Quaternium-26 (effective concentration = 15%) was not a sensitizer (Consumer Product Testing Company, Inc. 1979d).

In another study, the skin sensitization potential of a 0.1% solution or suspension of 60% Quaternium-26 (effective concentration = 0.06%) was evaluated using 10 male white guinea pigs. Physiological saline served as the control. The test substance was injected intracutaneously (shaved skin sites on back) three times weekly for a total of 10 sensitizing injections. The initial volume injected (0.05 ml) was increased to 0.1 ml for the remaining nine injections. Reactions were scored (reaction diameter, height, and redness) 24 hours after each injection . At 2 weeks after the tenth injection, an eleventh injection (challenge, 0.05 ml) was made immediately below the induction injection sites. The average induction score per animal (total of 10 injections) did not exceed 0.2. At challenge, none of the guinea pigs had scores that were greater than the average induction score per animal; all challenge scores were 0. Induction and challenge scores for the saline control were all 0. Quaternium-26 (effective concentration = 0.06%) was considered a nonsensitizer (Bio-Toxicology Laboratories, Inc. 1976).

## **PREVIOUS SAFETY ASSESSMENTS**

#### Quaternium-18 (Elder 1982)

Quaternium-18 is a mixture of quaternary ammonium chloride salts. Quaternium-18 Hectorite and Bentonite are the reaction products of Quaternium-18 and Hectorite or Bentonite clays, respectively. All three ingredients are used in cosmetic formulations at concentrations ranging from 0.1% to 10%. Cosmetics containing these compounds can come in contact with all body surfaces and can be used on a daily basis over extended periods of time.

Quaternium-18 Hectorite and Bentonite are chemically, physically, and biologically inert. Quaternium compounds are poorly absorbed through the skin. For example, <sup>14</sup>C-dimethyl, dioctadecyl ammonium chloride (DDAC) did not appreciably penetrate the skin (dorsal surface) of rabbits, after application according to an open patch test procedure. An evaluation of excreta collected over a 72-hour period indicated that approximately 89% of the delivered radioactivity was recovered, 88% of which was recovered from the skin test site. Acute oral and percutaneous toxicity tests in animals indicate that Quaternium-18, Quaternium-18 Bentonite, and Quaternium-18 Hectorite have little or no systemic toxic effects. Quaternium-18 Hectorite was also nontoxic in an acute inhalation study. Subchronic oral and dermal toxicity tests of Quaternium-18 and Quaternium-18 Bentonite produced no evidence of systemic toxicity. No chronic studies have been reported.

All three Quaternium compounds under review here can be considered to cause, at most, only slight irritation to animal skin. None has been reported to be a skin sensitizing agent. In ocular irritation studies in rabbits, all three compounds were, at most, mild irritants.

Clinical studies have determined that Quaternium-18 was practically nonirritating and nonsensitizing to the skin. Quaternium-18 Hectorite can be classified as a nonirritating, "nonfatiguing," and nonsensitizing agent; it did not present any adverse phototoxic or photoallergenic effects. Quaternium-18 Bentonite was not an irritating, "fatiguing," or sensitizing agent to human skin. Quaternium-18 Hectorite produced no ocular irritation in humans. No information is reported concerning any of the Quaternium-18 compounds with respect to absorption, metabolism, storage, excretion, teratology, mutagenesis, or carcinogenesis.

#### Quaternium-22 (Andersen 1995)

Quaternium-22 is a water-soluble ingredient that is used as a film former, hair conditioning agent, and an antistatic agent in cosmetic products. Quaternium-22 is commercially supplied as a 60% solids solution. Other cosmetic uses that have been reported include use as an emollient and skin and hair conditioner.

Quaternary compounds are normally synthesized by reacting a tertiary amine with an alkyl chloride or sulfate. The impurities 3-dimethylaminopropylamine and ethylene chlorohydrin have been detected in Quaternium-22 at concentrations up to 2.45% and 0.097%, respectively.

Product formulation data submitted to FDA in 1993 indicate that Quaternium-22 was used in 78 cosmetic products. Concentration of use values are no longer reported to the FDA by the cosmetics industry. However, in 1984, the maximum use concentration of Quaternium-22 that was reported to FDA was 5.0%.

In an acute oral toxicity study involving rats, Quaternium-22 (6.0% solids) was nontoxic. The  $LD_{50}$  was not achieved at a dose of 64.0 cc/kg, the highest dose tested.

In a 91-day dermal toxicity study involving male and female rabbits, 1% aqueous Quaternium-22 induced extreme dermal irritation on day 4, and the test concentration was reduced to 0.5% aqueous for the remainder of the study. Quaternium-22 (0.5% aqueous) was classified as a slight irritant. A different lot of 1% aqueous Quaternium-22 (diluted to 0.5% aqueous solution) was also classified as a slight irritant when the 91-day study was repeated using male rabbits only. In both experiments, the histopathological findings were considered unrelated to test substance administration.

Quaternium-22 (8.5%) induced minimal conjunctival irritation in two of three albino rabbits. Quaternium-22 (6.0% in deionized water) and Quaternium-22 (2.0% solids) did not induce ocular irritation in albino rabbits.

In occlusive 24-hour patch tests using albino rabbits, Quaternium-22 (6.0% gravimetric solution in deionized water) and Quaternium-22 (6.0% solids) were not irritating to intact or abraded skin.

Repeated intracutaneous injections of a 0.1% solution of Quaternium-22 (6.0% solids) did not induce irritation or sensitization reactions in white male guinea pigs.

In the Ames test, Quaternium-22 was not mutagenic to strains TA97, TA98, and TA100 of *Salmonella typhimurium*, the only bacterial strains tested.

Two formulations containing 1% Quaternium-22 were not classified as skin irritants in a 21-day cumulative skin irritation study involving 50 volunteers. Facial use and patch tests were conducted concurrently over a period of 3 weeks.

In a repeated insult patch test (RIPT), three product formulations containing 1% Quaternium-22 did not induce sensitization in a population of 106 volunteers. One of the products was diluted to a concentration of 0.03% during the induction phase, and was tested at this concentration for the remainder of the study.

Products containing 1% Quaternium-22 were not phototoxic when tested using 12 volunteers and also were not photoallergenic when tested using a group of 26 volunteers.

#### Mink Oil (Andersen 1998)

Mink Oil, obtained from the fatty tissues of minks, is a mixture of the natural glycerides of 14 to 20 carbon chain fatty acids. As of January 1995, it was reportedly used in 139 cosmetic formulations as a hair conditioning agent, an occlusive skin conditioning agent, and as a surfactant. In 1984 FDA data, Mink Oil was used at concentrations of 25% and less (1995 data from the cosmetics industry indicate use at  $\leq 2\%$  in two product types).

An attenuated total reflectance-infrared spectroscopy study found that 1 hour after application, Mink Oil was detected on the skin surface of all five panelists; it was detected within the stratum corneum in two of five panelists.

Mink Oil has an oral LD<sub>50</sub> of >64.0 cc/kg in albino rats.

No erythema or edema was noted after refined Mink Oil was applied for 24 hours to intact and scarified skin of albino rabbits.

Although reactions were noted during induction, a 50% dilution of a Mink Oil cream did not sensitize guinea pigs using the Buehler technique. In a second study, using the Magnusson-Kligman Maximization Procedure, 59% Mink Oil in petrolatum induced sensitization reactions.

Mink Oil was not an ocular irritant in albino rabbits.

Clinical studies using single occlusive patches found no irritation with up to 2.8% Mink Oil (PII scores of 0.08–0.10). Transient mild to no irritation was noted in two exaggerated use studies.

#### SUMMARY

Quaternium-26 is a quaternary ammonium salt that is used as a film former, hair-conditioning agent, and antistatic agent in cosmetic products.

Cosmetic grade Quaternium-26 (Ceraphyl 65) is marketed as a 60% solution. One company has recommended use of this solution at concentrations between 2% and 5%, which corresponds to 1.2% to 3.0% Quaternium-26 on an active basis. Product formulation data submitted to FDA in 1997 indicted that Quaternium-26 was used in as many as 25 cosmetic products.

The following two impurities have been detected in Quaternium-26: diethanolamine (0.4%) and 3-dimethylaminopropylamine (1.4%).

A UV spectral analysis of Quaternium-26 indicates maximum absorbance between 200 and 220 nm and minimum absorbance in the 280 to 320 nm range.

An LD<sub>50</sub> of 5.65 g/kg for Quaternium-26 (effective concentration = 3.6%) was reported in a study involving 30 rats. In another study (10 rats), the LD<sub>50</sub> for Quaternium-26 (effective concentration = 1.8%) was not achieved at a dose of 20 ml/kg.

In ocular irritation studies involving albino rabbits (nine per study), Quaternium-26 was tested at effective concentrations ranging from 1.8% to 3.0%. At most, mild ocular irritation was noted over the range of concentrations tested.

The skin irritation potential of Quaternium-26 in albino rabbits (six rabbits per study) was evaluated at effective concentrations ranging from 1.8% to 3.6% in single-insult, occlusive patch tests. Quaternium-26 was, at most, a mild skin irritant over the range of concentrations tested. Additionally, Quaternium-26 (effective concentration = 1.8%) was noncomedogenic in six albino rabbits.

Quaternium-26 (effective concentration = 15%) did not induce sensitization in any of the 12 guinea pigs tested (RIPT, occlusive patches). Slight to moderate irritation persisted throughout the induction phase.

In another sensitization study, 10 guinea pigs received repeated intracutaneous injections of Quaternium-26 (effective concentration = 0.06%). Sensitization reactions were not observed, and the average induction score (10 injections) per animal did not exceed 0.2.

#### DISCUSSION

Data from previous reviews of Quaternium-18 and Quaternium-22 suggest little toxicity. Likewise, the available data on Quaternium-26 show low toxicity. Because Quaternium-26 contains fatty acids derived from Mink Oil, the Expert Panel also reviewed its previous safety assessment of Mink Oil. During deliberations on the safety of Mink Oil in cosmetics, the Panel determined that the available data were insufficient to support safety. For Mink Oil, the additional data needed included method of ingredient manufacture/extraction and 28-day dermal toxicity and UV absorption data. Independent of these data needs, however, it was also determined that the total polychlorinated biphenyl (PCB)/pesticide contamination of mink oil should not exceed 40 ppm, with not more than 10 ppm for any specific residue. Although concern over the potential pesticide contamination of Mink Oil-derived components of Quaternium-26 was expressed, the Expert Panel concluded that such contamination would not carry over to the fatty acid fraction as it appears in Quaternium-26. As with Mink Oil, however, the Panel determined that, as a cosmetic ingredient, Quaternium-26 should not contain halogenated environmental chemicals.

Taking into consideration that data on mutagenicity/carcinogenicity or reproductive and developmental toxicity were not available for inclusion in this safety assessment, the Panel agreed that the chemical structure of Quaternium-26 does not suggest that these end points would be of concern, except for a concern about impurities. Because the impurities diethanolamine (0.4%)and 3-dimethylaminopropylamine (1.4%) have been detected in Quaternium-26, the Panel expressed concern over the potential for formation of *N*-nitroso compounds in product formulations containing this ingredient and agreed to restrict its cosmetic use.

# CONCLUSION

Based on the available animal and clinical data in this report, the CIR Expert Panel concludes that Quaternium-26 is safe in the present practices of use. Quaternium-26 should not be used in products in which *N*-nitroso compounds may be formed.

#### REFERENCES

- Andersen, F. A. 1995. Final report on the safety assessment of Quaternium-22. J. Am. Coll. Toxicol. 14:485–497.
- Andersen, F. A. 1998. Final report on the safety assessment of Mink Oil. J. Am. Coll. Toxicol. 17(Suppl. 4):71–82.
- Bio-Toxicology Laboratories, Inc. 1976. Primary skin irritation and acute oral toxicity studies on Quaternium-26 (6%) and guinea pig sensitization study on Quaternium-26. Unpublished data submitted by CTFA. (18 pages.)<sup>2</sup>
- Bio-Toxicology Laboratories, Inc. 1977a. Draize eye irritation and skin irritation tests on quaternium-26 (5% aqueous) in rabbits. Unpublished data submitted by CTFA. (20 pages.)<sup>2</sup>
- Bio-Toxicology Laboratories, Inc. 1977b. Eye irritation study on quaternium-26 (5% aqueous) in rabbits. Unpublished data submitted by CTFA. (15 pages.)<sup>2</sup>
- Bio-Toxicology Laboratories, Inc. 1977c. Eye irritation study on quaternium-26 (4% aqueous) in rabbits. Unpublished data submitted by CTFA. (15 pages.)<sup>2</sup>
- Bio-Toxicology Laboratories, Inc. 1977d. Eye irritation study on quaternium-26 (4% aqueous) in rabbits. Unpublished data submitted by CTFA. (14 pages.)<sup>2</sup>
- Buehler, E. V. 1965. Delayed contact hypersensitivity in the guinea pig. Arch. Dermat. 91:171–175.
- Chemtest Laboratories Inc. 1992. Certificate of analysis on quaternium-26 (ceraphyl 65). Unpublished data submitted by CTFA. (2 pages.)<sup>2</sup>
- Consumer Product Testing Company, Inc. 1978. Primary dermal irritation and ocular irritation studies on quaternium-26 (4% w/w in deionized water) in rabbits. Unpublished data submitted by CTFA. (14 pages.)<sup>2</sup>
- Consumer Product Testing Company, Inc. 1979a. Acute oral toxicity study on quaternium-26 (3% w/w in deionized water) in rats. Unpublished data submitted by CTFA. (7 pages.)<sup>2</sup>
- Consumer Product Testing Company, Inc. 1979b. Primary ocular irritation study on quaternium-26 (3% w/w in deionized water) in rabbits. Unpublished data submitted by CTFA. (10 pages.)<sup>2</sup>
- Consumer Product Testing Company, Inc. 1979c. Primary dermal irritation study on quaternium-26 (3% w/w in deionized water) in rabbits. Unpublished data submitted by CTFA. (9 pages.)<sup>2</sup>
- Consumer Product Testing Company, Inc. 1979d. Guinea pig sensitization test on 25% aqueous quaternium-26. Unpublished data submitted by CTFA. (10 pages.)<sup>2</sup>
- Cosmetic, Toiletry, and Fragrance Association (CTFA). (No date) UV absorption spectrum on quaternium-26. Unpublished data submitted by CTFA. (1 page.)<sup>2</sup>
- Draize, J. H. 1975. Dermal toxicity. In Appraisal of the safety of chemicals in foods, drugs and cosmetics, 47, 49–51. Austin, TX: The Association of Food and Drug Officials of the United States.
- Elder, R. L., ed. 1982. Final report on the safety assessment of quaternium-18, quaternium-18 hectorite, and quaternium-18 bentonite. J. Am. Coll. Toxicol. 1:71-83.
- European Economic Community (EEC). 1995. EEC Cosmetics Directive 76/768/EEC, as amended, Annexes I through VII. Brussels; EEC.
- Food and Drug Administration (FDA). 1984. Frequency and concentration of use of cosmetic ingredients. *FDA database*. Washington, DC: FDA.
- FDA. 1992. Modification in voluntary filing of cosmetic product ingredient and cosmetic raw material composition statements. *Fed. Register* 57:3128– 3130.

<sup>&</sup>lt;sup>2</sup>Available for review from the Director, Cosmetic Ingredient Review, 1101 17th Street, NW Suite 310, Washington, DC 20036, USA.

FDA. 1997. Frequency of use of cosmetic ingredients. *FDA database*. Washington, DC: FDA.

•

- Food and Drug Research Laboratories, Inc. 1982. Comedogenic assay on 3% solids solution of Quaternium 26 in rabbits. Unpublished data submitted by CTFA. (16 pages.)<sup>2</sup>
- Hunting, A. L. L., ed. 1983. Encyclopedia of shampoo ingredients, 341. Port Washington, NY: Micelle Press.
- International Specialty Products. 1997. Composition of Ceraphyl 65, tradename for Quaternium-26. Personal communication. Letter from David Bower to Gerald McEwen. Unpublished data submitted by CTFA. (1 page.)<sup>2</sup>
- Rempe, J. M., and L. G. Santucci, eds. 1997. CTFA list of Japanese cosmetic ingredients, 3rd ed. Washington, DC: CTFA.
- Sadtler Research Laboratories, Inc. 1982. Infrared spectrum on ceraphyl 65 (mink-amidopropyl dimethyl 2-hydroxyethyl ammonium chloride, pH 6.9 to 7.9). Unpublished data submitted by CTFA. (1 page.)<sup>2</sup>
- Van Dyk & Company, Inc. (No date.) A typical fatty acid composition of the heavy fraction of mink oil used in the manufacture of foamole B and ceraphyl 65. Unpublished data submitted by CTFA. (1 page.)<sup>2</sup>
- Wenninger, J. A., R. C. Canterbery, and G. N. McEwen, eds. 2000. International cosmetic ingredient dictionary and handbook, 8th ed., Vol 2, 1261. Washington, DC: CTFA.