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# Final Report on the Safety Assessment of Petroleum Distillate

Cosmetic grade Petroleum Distillate consists predominantly of  $C_{10}$ – $C_{16}$  paraffinic, naphthenic, and isoparaffinic hydrocarbons. The Distillate is used in a variety of cosmetic products at concentrations up to 50%. Undiluted Petroleum Distillate had an acute oral  $LD_{50}$  in rats of  $>25$  ml/kg. Subchronic animal tests on a formulation containing 41.75% Petroleum Distillate were uneventful. Moderate skin irritation and mild, transient eye irritation were observed in rabbits following a single exposure to undiluted Petroleum Distillate. Cosmetic formulations containing 29.2–55% Petroleum Distillate were generally nonirritating, nonsensitizing, and nonphotosensitizing to human skin. It is concluded that Petroleum Distillate, as characterized in the report, is safe as a cosmetic ingredient at the current concentrations of use.

## INTRODUCTION

The following report is a summary of the chemistry, use, animal toxicology, and clinical safety of cosmetic grade Petroleum Distillate. Although numerous studies on "petroleum distillate" toxicity were reported in the published literature, many of these investigations failed to provide an adequate chemical description of the specific petroleum distillate fraction tested. Therefore, many of these studies were considered inadequate for evaluating the safety of Petroleum Distillate as it is used in cosmetic products.

"Petroleum Distillate" is a broad term that can imply any one of numerous petroleum fractions. Among some of the major petroleum distillates are petroleum ether, rubber solvent, varnish makers' and painters' naphtha, stoddard solvent, mineral spirits, gasoline, kerosene, fuel oil, mineral seal oil, mineral oil, and various lubricating oils. The chemistry and toxicology of these several petroleum fractions, which include several fractions closely related to the cosmetic grade Petroleum Distillate, are reviewed elsewhere.<sup>(1-9)</sup>

## CHEMISTRY

### Definition and Method of Manufacture

Petroleum Distillate (CAS No. 8002-32-4) is defined by the *CTFA Cosmetic Ingredient Dictionary* as a mixture of volatile hydrocarbons obtained from petro-

leum.<sup>(10)</sup> The ingredient is prepared by fractional distillation of crude petroleum, followed by acid or hydrotreatment to complete saturation and to remove odor-causing impurities. This process may be followed by solvent or catalytic dewaxing and a clay or hydrotreatment finishing step.<sup>(11,12)</sup> Other names for the cosmetic ingredient include Penreco Oil No. 2251, Penreco Oil No. 2263, Shell Sol 71 (CAS No. 64741-65-7) and Shell Sol 72.<sup>(10,12)</sup>

### Chemical and Physical Properties

Cosmetic grade Petroleum Distillate is a clear, colorless, low viscosity, combustible liquid having a slight characteristic odor. It consists predominantly of C<sub>10</sub>–C<sub>16</sub> paraffinic, naphthenic, and isoparaffinic hydrocarbons. It is soluble in most organic solvents and is insoluble in water. This highly refined hydrocarbon solvent is stable and does not undergo "hazardous" polymerization. Carbon monoxide, carbon dioxide, and unidentified organics are formed during combustion of this material.<sup>(11,14–16)</sup>

The numerous fractions and grades of petroleum distillate frequently are differentiated and defined on the basis of their boiling points or distillation range. In the case of cosmetic grade Petroleum Distillate, reported boiling points are inconsistent. The *CTFA Cosmetic Ingredient Descriptions* published in 1974 and 1982 report that cosmetic grade Petroleum Distillate has a boiling range of 340° to 406°F.<sup>(14,15)</sup> On the other hand, in unpublished data submitted to the Cosmetic Ingredient Review by CTFA, the distillation range of cosmetic grade Petroleum Distillate is reported as both 350–500°F and 355–500°F.<sup>(11)</sup> Further, Mineral Spirits is listed as a synonym for Petroleum Distillate in the 1974 and 1982 *CTFA Cosmetic Ingredient Descriptions*; however, the 1982 *CTFA Cosmetic Ingredient Dictionary* reports the distillation range for Mineral Spirits as 318 to 400°F.<sup>(10,14,15)</sup>

Table 1 presents chemical and physical data typical of cosmetic grade Petroleum Distillate. These data are not representative of a specific Petroleum Distillate product but instead represent a general description of the various cosmetic grades used by a variety of formulators and manufacturers. Thus, data in Table 1 are typical of this cosmetic ingredient and should not be considered as product specifications. The specifications and properties of three specific Petroleum Distillate products supplied to cosmetic firms are presented in Tables 2, 3, and 4. For convenience, the three commercial products have been referred to as Product A, Product B, and Product C, respectively. These three products are purported to be the three predominant grades used by the cosmetic industry.<sup>(17)</sup> Products A, B, and C fit the general description of cosmetic grade Petroleum Distillate presented in Table 1.

### Aromatic Hydrocarbon Content

Four samples of cosmetic grade petroleum Distillate (Product C/Table 4) were examined by means of EI mass, NMR, and UV spectroscopy to determine the presence of aromatic hydrocarbons. NMR and UV spectroscopic analyses established the presence of substituted benzenes and/or naphthalenes; tri- or

**TABLE 1.** Chemical and Physical Data Typical of Cosmetic Grade Petroleum Distillate<sup>(11,12)</sup>

<i>Characteristic<sup>a</sup></i>	<i>Value</i>
API gravity (D287)	46–55
Specific gravity at 60/60°F (D1250)	0.76–0.79
Distillation (D86)	
Initial boiling point	355–393°F
End point	400–500°F
Color, Saybolt (D156)	+30
Viscosity at 100°F (SUS)	30
Flash point (COC)	175°F
Composition	
Paraffins, naphthenes, isoparaffins	96–99%
Olefins	1.0–4.0%
Total aromatics	<2.0%

<sup>a</sup>These data are not representative of a particular Petroleum Distillate product but are instead a general description of the various cosmetic grades used by a variety of formulators and manufacturers. Thus, the data are “typical” of this cosmetic ingredient and are not to be considered as a product specification.

**TABLE 2.** Chemical and Physical Data for Cosmetic Grade Petroleum Distillate: Product A<sup>(21,23)</sup>

<i>Characteristic</i>	<i>Value</i>
Estimated aromatic content	<0.5%
API gravity at 60°F	46/50
Specific gravity at 60/60°F	0.779/0.797
Distillation (ASTM D86)	
Initial boiling point	375°F
End point	500°F max
Viscosity at 100°F (SUS)	30.5
Pounds per gallon at 60°F	6.56
Flash point (COC)	165°F
Pour point (ASTM D97)	–40°F
Benzene content <sup>a</sup>	None
Carbon distribution	Similar to that of Product B (Table 3)
Meets federal regulations	21 CFR 172.884
for odorless light petroleum	21 CFR 178.3650
hydrocarbons	21 CFR 573.740

<sup>a</sup>As determined by gas chromatographic analysis.

**TABLE 3.** Chemical and Physical Data for Cosmetic Grade Petroleum Distillate: Product B<sup>(21,23)</sup>

Characteristic	Value
Estimated aromatic content	<2.0%
API gravity at 60°F	46/50
Specific gravity at 60/60°F	0.779/0.797
Distillation (ASTM D86)	
Initial boiling point	375°F
End point	500°F max
Viscosity at 100°F (SUS)	30.5
Pounds per gallon at 60°F	6.56
Flash point (COC)	165°F
Pour point (ASTM D97)	–40°F
Benzene content <sup>a</sup>	None
Total isomers (weight %) <sup>a,b</sup>	
C-10 to C-11	10.22%
C-11 to C-12	34.13%
C-12 to C-13	42.48%
C-13 to C-14	11.17%
C-14 to C-15	1.17%
Normal paraffins (weight %) <sup>a</sup>	
C-11	5.0%
C-12	14.5%
C-13	11.8%
C-14	2.2%
Meets federal regulations	21 CFR 172.884
for odorless light petroleum	21 CFR 178.3650
hydrocarbons	21 CFR 573.740

<sup>a</sup>As determined by gas chromatographic analysis.<sup>b</sup>Total isomers includes branched, cyclic, and straight chain structures.

tetracyclic molecules were not identified. Mass spectroscopy indicated an alkylbenzene of molecular weight 120 (possibly isopropylbenzene and/or trimethylbenzene). The possible presence of naphthalene (molecular weight 128) was not ruled out but was considered unlikely. The maximum trimethylbenzene concentration for one sample was estimated at approximately 0.26%. No “condensed aromatic systems” were detected.<sup>(18)</sup>

A fifth Petroleum Distillate sample (Product C/Table 4) was also examined by EI mass, NMR, and UV spectroscopy in a second study. The NMR method employed was sufficiently sensitive to detect aromatic hydrocarbons at concentrations as low as 1.0%. No aromatic compounds were detected.<sup>(19)</sup>

The aromatic hydrocarbon content of cosmetic grade Petroleum Distillate varies not only according to the sample tested but also to the particular product supplied to the cosmetic manufacturer. Petroleum Distillate products A, B, and C (Tables 2, 3, and 4) have typical aromatic contents of <0.5, <2.0, and <0.1%, respectively.<sup>(13,16,20–22)</sup>

**TABLE 4.** Chemical and Physical Data for Cosmetic Grade Petroleum Distillate: Product C <sup>(13,16,20,22)</sup>

Characteristic	Value
Specific gravity at 60°F (ASTM D-1250)	0.759
API gravity (ASTM D-287)	55.0
Pounds per gallon at 60°F (ASTM D-1250)	6.32
Color, Saybolt (ASTM D-156)	+ 30
Kauri-butanol number (ASTM D-1133)	26
Aniline point (ASTM D-611/D-1012)	184°F
Flash point, TCC (ASTM D-56)	125°F
Autoignition temperature (ASTM D-2155)	586°F
Reid vapor pressure (ASTM D-323)	<0.1 psia
Vapor pressure at 100°F	4 mm Hg
Vapor density (air = 1)	5.3
Distillation (ASTM D-86)	
Initial Boiling point	355°F
10% recovered	360°F
30%	362°F
50%	364°F
70%	370°F
90%	376°F
End point	400°F
Evaporation rate (butyl acetate = 1)	<0.1
Evaporation rate in seconds (ASTM D-3539)	
10%	330 seconds
30%	1080 seconds
50%	1960 seconds
70%	3010 seconds
90%	4510 seconds
100%	6870 seconds
Composition (% volume)	
Paraffins (saturates)	95.9%
Naphthenes	—
Olefins	4.1%
Total aromatics	<0.1%
Benzene	Nil
Toluene plus ethyl benzene	0.0
C <sub>8</sub> plus aromatics excluding ethyl benzene	<0.1%
Meets federal regulations	21 CFR 172.882
for synthetic isoparaffinic	21 CFR 178.3530
petroleum hydrocarbons	

### Analytical Methods

Refined petroleum solvents with boiling points between 120 and 200°C may be analytically determined by gas chromatography.<sup>(3)</sup>

### USE

#### Noncosmetic Use

Cosmetic grade Petroleum Distillate (Product A/Table 2) is used as a foam control agent for newspaper print, as a solvent for waterless hand cleansers, and as a solvent for carbonless paper.<sup>(11,23)</sup>

Federal regulations permit the use of certain petroleum distillate grades to be used as direct and indirect food additives.<sup>(24-27)</sup> Food additive uses for cosmetic grade Petroleum Distillate are summarized in Tables 5 and 6. Cosmetic grades of Petroleum Distillate complying with Title 21 Part 573.740 of the Code of Federal Regulations may also be used as a component of insecticide formulations "in an amount not in excess of that required."<sup>(28)</sup>

### Cosmetic Use

Petroleum Distillate is used in cosmetic products as a solvent or as a component of solvent systems.<sup>(11,12)</sup> Data submitted to the Food and Drug Administration (FDA) in 1981 by cosmetic firms participating in the voluntary cosmetic registration program indicated that Petroleum Distillate was used that year as an ingredient in 113 cosmetic formulations (Table 7). Product types in which Petroleum Distillate was most frequently used included eye shadow (78 products) and mascara (18 products). One hundred five formulations contained this ingredient

**TABLE 5.** Permitted Direct Food Additive Uses of Cosmetic Grade Petroleum Distillate<sup>a</sup>

<i>Direct food additive use</i>	<i>Limitations</i>
As a component of insecticide formulations for use on processed foods	In an amount not to exceed good manufacturing practice
As a component of coatings on fruits and vegetables	In an amount not to exceed good manufacturing practice
In the froth-flotation cleaning of vegetables	In an amount not to exceed good manufacturing practice
As a coating on shell eggs	In an amount not to exceed good manufacturing practice
As a float on fermentation fluids in the manufacture of vinegar and wine and on brine used in curing pickles to prevent or retard access of air, evaporation, and contamination with organisms during fermentation	In an amount not to exceed good manufacturing practice
As a defoamer in processing beet sugar and yeast	Compliance with 21 CFR 173.340
As a float on fermentation fluids in the manufacture of vinegar and wine to prevent or retard access of air, evaporation, and yeast contamination during fermentation	In an amount not to exceed good manufacturing practice
As a component of insecticide formulations used in compliance with Title 21, Parts 170 through 189 of the Code of Federal Regulations	In an amount not to exceed good manufacturing practice

<sup>a</sup>Title 21 Parts 172.882 and 172.884 of the Code of Federal Regulations allows synthetic isoparaffinic petroleum hydrocarbons and odorless light petroleum hydrocarbons to be used as direct additives to food provided that certain conditions are met. Petroleum Distillate product C (Table 4) meets 21 CFR 172.882 for synthetic isoparaffinic petroleum hydrocarbons. Petroleum Distillate products A and B (Tables 2 and 3) meet 21 CFR 172.884 for odorless light petroleum hydrocarbons.<sup>(24,25)</sup>

**TABLE 6.** Permitted Indirect Food Additive Uses of Cosmetic Grade Petroleum Distillate<sup>a</sup>

<i>Indirect food additive use</i>	<i>Limitations</i>
As a plasticizer and absorber oil in the manufacture of polyolefin articles authorized for food contact use	In an amount not to exceed that required to produce intended effect, consistent with good manufacturing practice
As a lubricant of fibers of textiles authorized for food contact use	At a level not to exceed 0.15% by weight of finished fibers
As a component of adhesives	Compliance with 21 CFR 175.105
As a defoamer in the manufacture of paper and paperboard	Compliance with 21 CFR 176.210
As a defoamer in coatings	Compliance with 21 CFR 176.200

<sup>a</sup>Title 21 Parts 178.3530 and 178.3650 of the Code of Federal Regulations allows synthetic isoparaffinic petroleum hydrocarbons and odorless light petroleum hydrocarbons to be used as indirect additives to food provided that certain conditions are met. Petroleum Distillate product C (Table 4) meets federal regulation 21 CFR 178.3530 for synthetic isoparaffinic petroleum hydrocarbons. Petroleum Distillate products A and B (Tables 2 and 3) meet 21 CFR 178.3650 for odorless light petroleum hydrocarbons. <sup>(26,27)</sup>

at concentrations of >50% (8 products), >25–50% (75 products), >10–25% (3 products), >5–10% (18 products), and >1–5% (1 product); the concentration of Petroleum Distillate in 8 formulations was not reported. <sup>(29,30)</sup>

Bentone Gel SS 71 is a cosmetic raw material containing Petroleum Distillate as a component ingredient. <sup>(10)</sup> This raw material is sold by chemical suppliers to cosmetic formulators for use in finished cosmetic products. Bentone Gel SS 71 contains other ingredients in addition to Petroleum Distillate; however, the concentration of each component ingredient within the raw material mixture is not readily available from the FDA. Thus, eight Petroleum Distillate concentrations in Table 7 are listed as unreported.

Voluntary filing of product data with the FDA by cosmetic manufacturers and formulators conforms to the prescribed format of preset concentration ranges and product categories as described in Title 21 Part 720.4 of the Code of Federal Regulations. <sup>(31)</sup> Because data are only submitted within the framework of preset concentration ranges, opportunity exists for overestimation of the actual concentration of an ingredient in a particular product. An entry at the lower end of a concentration range is considered the same as one entered at the higher end of that range, thus introducing the possibility of a 2- to 10-fold error in the assumed ingredient concentration.

Cosmetic products containing Petroleum Distillate are applied to or have the potential to come in contact with eyes, skin, hair (scalp), and nails (Table 7). Frequency and duration of application of these products will vary. Formulations incorporating Petroleum Distillate as an ingredient may be expected to remain in contact with the skin for as briefly as a few hours to as long as a few days. Each cosmetic product containing Petroleum Distillate has the potential for repeated application over the course of several years.

**TABLE 7.** Product Formulation Data on Petroleum Distillate<sup>(29,30)</sup>

<i>Product category<sup>a</sup></i>	<i>Total no. of formulations in category</i>	<i>Total no. containing ingredient</i>	<i>No. of product formulations within each concentration range (%)<sup>a</sup></i>					
			<i>Unreported concentration</i>	<i>&gt;50</i>	<i>&gt;25-50</i>	<i>&gt;10-25</i>	<i>&gt;5-10</i>	<i>&gt;1-5</i>
Eyeliner	396	1	—	1	—	—	—	—
Eye shadow	2582	78	5	1	58	—	13	1
Eye makeup remover	81	1	—	—	1	—	—	—
Mascara	397	18	—	4	13	1	—	—
Other eye makeup preparations	230	3	—	1	1	—	1	—
Hair dyes and colors (all types requiring caution statement and patch test)	811	1	—	—	1	—	—	—
Other hair coloring preparations	49	3	3	—	—	—	—	—
Makeup bases	831	4	—	—	—	—	4	—
Other makeup preparations	530	1	—	—	—	1	—	—
Nail polish and enamel	767	1	—	—	—	1	—	—
Skin cleansing preparations (cold creams, lotions, liquids, and pads)	680	1	—	1	—	—	—	—
Depilatories	32	1	—	—	1	—	—	—
1981 TOTALS		113	8	8	75	3	18	1

<sup>a</sup>Preset product categories and concentration ranges are used by firms in reporting to FDA in order to conform to federal filing regulations outlined in 21 CFR 720.4.<sup>(31)</sup>



## ANIMAL TOXICOLOGY

### Acute Oral Toxicity

The acute oral LD<sub>50</sub> in rats of undiluted Petroleum Distillate (Product C/Table 4) is >25 ml/kg.<sup>(16)</sup> According to the toxicity classification system of Hodge and Sterner,<sup>(32)</sup> this cosmetic ingredient is "relatively harmless" to rats when given in a single oral dose.

The acute oral toxicity of cosmetic products formulated with 35% Petroleum Distillate (Table 1) has also been determined. Fasted Harlan Fischer 344 rats (5 of each sex) were each given a single oral 5 ml/kg dose of a mascara as a 50% solution in corn oil. No mortality or signs of toxicity were observed during the 2 weeks following administration.<sup>(33)</sup> An eye shadow cream was administered by oral intubation in a single 60 ml/kg dose to each of 5 male and 5 female fasted Wistar rats. One female died on day 4 of the 14-day observation period.<sup>(34)</sup> A single 25 ml/kg oral dose of the same eye shadow was given to each of 4 Beagle dogs (2 males and 2 females). During the first 24 h following treatment, all dogs had loose brown stools consisting entirely of the test material; stools were normal thereafter. All 4 dogs survived and had normal taxis, behavior, appetite, and body weight throughout the 14-day study. Necropsy was negative for lesions.<sup>(35)</sup>

### Skin Irritation

Undiluted Petroleum Distillate (Product A/Table 2) was evaluated for primary skin irritation by means of the Draize procedure outlined in 16 CFR 1500.41.<sup>(36)</sup> The cosmetic ingredient (0.5 ml) was applied under a surgical gauze to the intact and abraded shaved back of 6 adult albino rabbits. The gauze dressing was removed after 24 h and the test sites were subsequently graded for erythema, eschar formation, and edema. Test sites were graded a second time 72 h after exposure. Petroleum Distillate produced erythema on the intact and abraded skin of all 6 rabbits at the 24- and 72-h evaluations. Edema was observed on the intact skin of 5 of 6 rabbits at the 24-h grading, as well as on the intact skin of 2 of 6 rabbits at the 72-h grading. On abraded skin, edema was observed in 5 of 6 rabbits and 4 of 6 rabbits at the 24- and 72-h evaluations, respectively. The average skin irritation score (Primary Irritation Index) was 2.5 on a scale of 0 (no irritation) to 8.0 (severe irritation), indicating that undiluted Petroleum Distillate was a moderate irritant to rabbit skin.<sup>(37)</sup>

Two mascara products containing either 35 or 35.5% Petroleum Distillate (Table 1) also were tested for skin irritation. Minor abrasions were made in the skin of 3 albino rabbits to be tested with the product containing 35.5% Petroleum Distillate. The test material was then applied as a single 0.5 ml dose to the scarified skin for 24 h. Skin responses were evaluated 24 and 48 h after application. The other product was administered in "four daily 0.5 ml doses" to the clipped, intact skin of 3 New Zealand rabbits. Skin reactions were graded thereafter every day for 7 days. No skin irritation was produced by either cosmetic product.<sup>(33,38)</sup>

### Acute Dermal Toxicity

The acute dermal LD<sub>50</sub> in rabbits of undiluted Petroleum Distillate (Product C/Table 4) is >5 ml/kg.<sup>(16)</sup>

### Eye Irritation

The procedures described in 16 CFR 1500.42<sup>(39)</sup> were used to assess the ocular irritating effects of undiluted Petroleum Distillate (Product A/Table 2). The test material (0.1 ml) was instilled into the conjunctival sac of one eye of each of 6 adult albino rabbits; the untreated eye of each animal served as a control. Treated eyes received no water rinse. Corneal, iridial, and conjunctival reactions were graded 24, 48, and 72 h postinstillation. Petroleum Distillate produced conjunctival irritation in 3 of the 6 rabbits. Scores at the first two evaluations for these 3 rabbits ranged from 2 to 4 (maximum score/animal/evaluation = 110). Conjunctival irritation was evident in only 1 rabbit by the 72-h evaluation (score = 2). It was concluded that undiluted Petroleum Distillate was a mild, transient irritant to the rabbit eye.<sup>(40)</sup>

The ocular irritating effects of a mascara containing 35.5% Petroleum Distillate (Table 1) were evaluated in three separate investigations. In each study, the undiluted product was instilled in a single 0.1 ml dose into the right eyes of a group of albino rabbits. Treated eyes received no water rinse following product exposure. The untreated left eye of each animal served as a control. Eyes were examined thereafter every 24 h for 4 days and then again on the seventh day. In the first investigation, no irritation was observed in the 3 animals tested. In each of the other two investigations, 6 rabbits were evaluated (12 total: 6 animals/study). Minimal ocular irritation was observed 1 h after treatment; however, no irritation was evident at the 1, 2, 3, 4, or 7 day evaluations.<sup>(41-43)</sup>

Slight conjunctivitis developed in 6 New Zealand rabbits when the animals were treated once in one eye with 0.1 ml of an undiluted mascara containing 35% Petroleum Distillate (Table 1). There were no signs of irritation to the cornea or iris.<sup>(33)</sup>

Nine albino New Zealand rabbits were treated with an eye shadow product for evaluation of eye irritation. One-tenth milliliter of the undiluted product containing 35% Petroleum Distillate (Table 1) was placed into the conjunctival sac of one eye of each rabbit; the contralateral eye served as untreated control. The treated eye was closed for one second. In 3 rabbits, the treated eyes were given a water rinse 30 seconds after product exposure. In the other 6 rabbits, the treated eyes received no water rinse. Ocular reactions were scored 1, 2, 3, 4, and 7 days posttreatment. In the no rinse group, 4 of 6 rabbits had minimal conjunctival irritation at the 72-h evaluation. Similar ocular responses were observed in 2 of 3 rabbits given the water rinse.<sup>(44)</sup>

Rhesus monkeys were used to assess the ocular irritating effects of two eye shadow products containing 35% Petroleum Distillate (Table 1). Twelve monkeys were divided into two groups for testing of the two products (6 animals/product). The test material was instilled in a single 0.1 ml dose into the conjunctival sac of the left eye; the right eye served as an untreated control. The treated eyes of 3 monkeys in each group were not rinsed. Eyes of the remaining 3 monkeys of each group were rinsed with water 30 seconds postinstillation. Ocular responses were graded 24, 48, and 72 h following product exposure. No evidence of ocular irritation or corneal damage was noted with either product.<sup>(45)</sup>

### Mucous Membrane Irritation

Six New Zealand albino rabbits (3 of each sex) were used to evaluate a mascara containing 35% Petroleum Distillate (Table 1) for mucous membrane irrita-

tion. The undiluted formulation was applied in a single 0.1 ml dose to the genital mucosa. Animals were observed thereafter for 7 days. No irritation developed.<sup>(33)</sup>

### Inhalation

Rats were exposed in an inhalation study to undiluted Petroleum Distillate (Product C/Table 4) for 4 h. The  $LC_{50}$  was  $>592$  ppm.<sup>(16)</sup>

### Subchronic Dermal and Ocular Toxicity

A mascara solvent system containing 41.75% Petroleum Distillate (Product C/Table 4), 8.25% dodecane, and 50% mineral oil was evaluated in a 3-month dermal and ocular toxicity study.<sup>(46)</sup> Thirty-six New Zealand rabbits were randomly divided into four groups. Each group contained 8 or 10 animals and had an equal distribution of males and females. In the two treatment groups, the test material was applied to the clipped skin daily for 3 months at doses of either 60 mg/kg per 5% body surface area (10 rabbits) or 120 mg/kg per 10% body surface area (10 rabbits). These doses represented multiples of 120 and 240, respectively, over anticipated human exposure to the solvent system of 0.5 mg/kg per day. Felt collars were used to prevent ingestion of the test material. Rabbits receiving dermal exposures were also given ocular treatments. The test material was instilled into the conjunctival sac in daily doses of 20 mg (0.05 ml) for 3 months. A third group of 8 rabbits served as the vehicle control group and was administered mineral oil each day at a topical dose of 0.30 ml/kg per 10% body surface area and a daily ocular dose of 20 mg. A fourth group consisting of 8 rabbits served as the untreated control group.

Exposure to both dose regimens of the solvent system produced slight to well-defined skin erythema, slight skin edema, and mild desquamation; the mineral oil vehicle was slightly more irritating to rabbit skin than the solvent system. Epidermal fissures with occasional bleeding were observed in 4 rabbits treated with the mineral oil vehicle and in 2 rabbits treated with the high dose of mascara solvent system; papuloerythema occurred occasionally in both the vehicle and solvent system treated groups. Ocular exposure of both treatment groups to the solvent system resulted in slight conjunctivitis; there was no indication of irritation to the cornea or iris. A similar ocular response was noted in the vehicle control group. No deaths occurred that were attributed to administration of the solvent system. All surviving animals gained weight, and food consumption data reflected expected variability. Hematological and clinical chemistry measurements revealed no toxicologically important changes. A significant increase in relative heart weight was observed in male rabbits of the two treatment groups when compared to heart weights in the untreated control group. The increase in heart weight was not significant when compared to the vehicle control group. No treatment-related dermal or ocular lesions were found except mild skin inflammation at the application site in both solvent system and mineral oil treated animals.

Organs and tissues examined microscopically included kidney, liver, heart, lung, spleen, thymus, lymph node, salivary gland, pancreas, stomach, duodenum, jejunum, ileum, colon, ovary, uterus, adrenal, thyroid, testis, prostate,

skin, mammary gland, skeletal muscle, urinary bladder, cerebrum, cerebellum, brainstem, bone, bone marrow, eye, application site, gallbladder, and conjunctiva. Organs weighed included adrenals, heart, kidneys, liver, ovary, spleen, testes, and thyroids. Hematological and serological studies included measurements of hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, erythrocyte and leukocyte count, differential leukocyte count, erythrocyte morphology, glucose, blood urea nitrogen, creatine, total bilirubin, alkaline phosphatase and serum glutamic pyruvic transaminase.<sup>(46)</sup>

### Carcinogenicity

Although numerous studies were reported in the literature regarding the carcinogenicity of various petroleum products, no direct information was available on cosmetic grade Petroleum Distillate. However, it is the opinion of the CIR Panel that data relating to the carcinogenicity of white oils and petrolatums, as reviewed by the International Agency for Research on Cancer (IARC), are the most applicable to cosmetic grade Petroleum Distillate. White oils and petrolatums suitable for food and/or medicinal use are produced from oils that have "undergone the most severe acid and/or hydrogen treatment." Medicinal white oils are made from paraffinic and naphthenic crudes and contain hydrocarbons predominantly with carbon numbers in the range 15–50. Technical grade white oils are also made from naphthenic or paraffinic crudes but are less refined than medicinal oils. Medicinal and technical grade white oils are both reported to be used in cosmetics (cold creams, hair preparations, hair oils).<sup>(7)</sup> Selected studies from the IARC literature review on these materials are summarized below.

No tumors were observed in CF1 mice following skin applications of white oils once or twice weekly (or once every 2 weeks) for 78 weeks.<sup>(47)</sup> Administration of three different grades of medicinal petrolatum by subcutaneous injection produced no tumors in Swiss-Webster mice over an 18-month observation period.<sup>(48)</sup> Administration of two food grade mineral oils by three intraperitoneal (ip) injections at 2 month intervals or by a single ip injection induced plasma-cell neoplasms and reticulum-cell sarcomas in BALB/c mice.<sup>(49)</sup> Groups of BD and W strain rats were given ip injections of liquid paraffin to give a total dose of 9 ml over a 40-week period. Four male rats developed sarcomas in the abdominal cavity, two of which appeared to be of testicular origin. Yellow petrolatum was similarly injected into rats; however, no tumors developed.<sup>(50)</sup> No significant increase in tumor incidence was observed in a 2-year study in which three different samples of medicinal grade petrolatum were fed to FDRL rats.<sup>(48)</sup> Inhalation, aspiration, or ingestion of white oils and petrolatums by humans produced lipid pneumonia and lipid granuloma of the lung.<sup>(51)</sup>

On the basis of their review, the International Agency for Research on Cancer concluded<sup>(7)</sup>:

There is no evidence for the carcinogenicity to experimental animals of white oils [class 5] when administered by routes other than intraperitoneal injection; when white oils were given by intraperitoneal injection to mice, plasma-cell tumors were produced in repeated experiments. The significance of the latter findings is difficult to interpret.

The reader is referred to the IARC monograph for a further chemical and physical description of white oils and for additional studies on the carcinogenicity of these materials.<sup>(7)</sup>

## CLINICAL ASSESSMENT OF SAFETY

### Acute Exposure

Acute overexposure to cosmetic grade Petroleum Distillate by inhalation or ingestion can lead to central nervous system depression, headache, dizziness, nausea, and loss of consciousness. Ingestion of the liquid may cause vomiting. "High airborne concentrations" or "lower airborne concentrations for a prolonged exposure" are slightly irritating to mucous membranes. Aspiration of the liquid into the lungs can result in chemical pneumonitis, pulmonary edema, and/or pulmonary hemorrhage. Short-term liquid or vapor contact with the eye produces slight irritation; prolonged and repeated contact increases the severity of the ocular reaction. Prolonged and repeated liquid contact with the skin causes defatting, drying, irritation, and/or dermatitis. No occupational exposure limits for cosmetic grade Petroleum Distillate have been established.<sup>(16)</sup>

One Petroleum Distillate product available to cosmetic formulators (Product C/Table 4) has a health hazard rating of 2 (moderate health hazard) on a scale of 0 ("least" hazard) to 4 (extreme hazard). This rating is used by the manufacturer as a safety guide for employees handling the chemical.<sup>(16)</sup>

### Skin Irritation, Sensitization, and Photosensitization

Cosmetic products containing Petroleum Distillate have been evaluated in a number of studies for skin irritation, sensitization, and photosensitization. These studies are discussed in detail below, and results are summarized in Table 8.

Two cream eye shadows were evaluated for skin irritation in two "in-home" use tests. Each product was formulated with 35% Petroleum Distillate (Table 1). No skin irritation was reported from the groups of 197 or 170 women who were instructed to apply one of the products daily for 2 weeks.<sup>(52,53)</sup>

The cumulative skin irritant effects of 7 eye shadow creams containing Petroleum Distillate were evaluated on 8 women and 2 men. The method employed was a modification of the procedure described by Phillips et al.<sup>(54)</sup> Each product containing 35% Petroleum Distillate (Table 1) was applied by patch to the back daily for 21 consecutive days. Patches were allowed to remain in place 1 h prior to application to permit evaporation of the solvents. After 23 h, patches were removed. Panelists were instructed to bathe or shower following patch removal and keep the patch areas dry at other times. Reactions to the 7 products were evaluated 24 h following application. All products were "essentially nonirritating" to the skin; the maximum total score reported for any one product was 29 on a scale of 0–630.<sup>(55)</sup>

Three hundred nine women were treated with three mascaras, each containing 35% Petroleum Distillate (Table 1), to determine whether the products cause skin irritation or sensitization. Preinduction patches containing the products were applied to the upper back for 48 h. After removal of the patches, the

**TABLE 8.** Clinical Studies on Cosmetic Products Containing Petroleum Distillate

<i>Type of study</i>	<i>Test material</i>	<i>Petroleum Distillate concentration (%)</i>	<i>No. of subjects</i>	<i>Methods</i>	<i>Results</i>	<i>Reference</i>
Skin irritation	Two cream eye shadows	Each product: 35	Two groups consisting of 197 and 170 women	Products applied daily for 2 weeks	No skin irritation	52, 53
Skin irritation	Seven eye shadow creams	Each product: 35	10	Products applied daily for 21 days	All products were "essentially nonirritating" to skin	55
Skin irritation/sensitization	Three mascaras	Each product: 35	309	Unsupervised daily use of products for 4 weeks; following this induction period, a 48-h challenge patch applied	No skin reactions during 4-week induction phase; eight subjects developed erythema at challenge to one or more products; however, investigator considered reactions to challenge patch as being irritant, not allergic in nature	56
Skin irritation/sensitization	Mascara	35	97	Unsupervised daily use of product for 4 weeks (induction period) followed by 48-h postinduction challenge patch	No skin irritation or sensitization	57

Skin irritation/sensitization	Mascara	35	166	Unsupervised daily use of product for 4 weeks (induction period) followed by 48-h postinduction challenge patch	No skin reactions during induction phase; 2 subjects developed erythema to challenge patch	58
Skin irritation/sensitization	Two cream eye shadows	Each product: 35	22	Kligman Maximization Test: Products applied for 5 alternate day 48-h periods; following 10–14-day nontreatment period, 48-h challenge patch applied; challenge patch and initial induction patch preceded by skin treatment with 5% aqueous sodium lauryl sulfate (SLS)	No significant skin irritation or evidence of sensitization was produced by either product	59
Skin irritation/sensitization	Two cream eye shadows	Each product: 35	30	Kligman Maximization Test: 5 48-h induction patches, 10–14-day nontreatment period, 48-h challenge patch; challenge and initial induction patch preceded by skin exposure to 5% aqueous SLS	No skin irritation or sensitization	60
Skin irritation/sensitization	Two eye shadows	Each product: 35	25	Kligman Maximization Test: 5 48-h induction patches, 10–14-day nontreatment period, 48-h challenge patch; challenge and initial induction patch preceded by skin exposure to 5% aqueous SLS	No skin irritation or sensitization	61

TABLE 8. (Continued)

<i>Type of study</i>	<i>Test material</i>	<i>Petroleum Distillate concentration (%)</i>	<i>No. of subjects</i>	<i>Methods</i>	<i>Results</i>	<i>Reference</i>
Skin irritation/sensitization	Mascara	35	205	Product applied every other day for 3 weeks for total of 10 induction patches; following 2-week nontreatment period, 48-h challenge patch applied to original and previously untreated site; beginning with fourth insult, patches volatilized 30 minutes prior to application	Erythema generally noted throughout induction phase, but with less frequency following fourth insult; one sensitization reaction noted on original test site	62
Skin irritation/sensitization	Mascara	35.5	113	A total of 10 48-h induction patches applied; induction patches were nonocclusive with the exception of the initial patch, which consisted of an occlusive dressing; a 48-h patch applied following induction phase	Nine subjects developed either doubtful erythema and/or vesicular reactions during the induction phase; a single doubtful reaction observed at challenge	63
Skin sensitization	Mascara in mineral oil	29.2	151	Jordan-King Repeat Insult Patch Procedure: patches applied every other day for 3 weeks; following a 2-week nontreatment period, two consecutive 48-h patches applied	No sensitization reactions	64



Skin sensitization	mascara	55	202	Patches applied every other day for 3 weeks; following a 2-week nontreatment period, two consecutive 48-h challenge patches applied	No skin sensitization	65
Skin sensitization/phototosensitization	Two cream eye shadows	Each product: 35	98	Schwartz-Peck Prophetic Patch Test with UV exposure: open and closed patches applied for 48 h; after a 2-week nonexposure period, a second set of open and closed patches applied; following evaluation of second set of patches, closed patch sites were exposed to UV light	No skin reactions noted to either product	66
Skin sensitization/phototosensitization	Mascara	53.25	52 hyperreactive subjects	Open induction patches applied twice a week for 3 weeks; 7 days after last induction patch, a 48-h challenge patch was applied; challenge and initial induction patches preceded by skin exposure to 5% aqueous SLS; duplicate patch test sites were exposed to UV light	No skin sensitization or phototosensitization	67

subjects were divided into three groups and then were instructed to use the product(s) once a day for the next 4 weeks. Following the 4-week induction period, a 48-h challenge patch was applied. Evaluations of the treated skin were made 48 and 72 h after challenge. Four subjects developed erythema or erythema and papules to one or more of the mascaras as a result of the preinduction patch. Eight individuals had reactions to one or more products at the 48- or 72-h challenge evaluations; these reactions generally consisted of erythema or erythema and papules. In 1 individual, erythema, papules, and vesicles were observed. The investigator considered that all the reactions to the challenge patch were irritant, not allergic, in nature. Skin reactions during the 4-week induction phase were not reported.<sup>(56)</sup>

Another mascara containing 35% Petroleum Distillate (Table 1) was evaluated for skin sensitization and irritation in two separate studies. As in the previous investigation, each study consisted of three phases: (1) a 48-h preinduction patch, (2) unsupervised daily use of the product for 4 weeks (induction period), and (3) a 48-h postinduction challenge patch. The product was volatilized prior to application to the upper arm. In the first study, no skin irritation or sensitization was noted among the 97 women evaluated.<sup>(57)</sup> In the second study, 2 of 166 subjects developed skin erythema by the 48-h challenge reading; these reactions cleared by the 72-h evaluation. No skin reactions were observed to the preinduction application or during the 4-week "home use" induction phase.<sup>(58)</sup>

Twenty-two subjects participated in a Kligman Maximization Test to determine the irritation and sensitization potential of two cream eye shadows, each containing 35% Petroleum Distillate (Table 1). Initially, 5% aqueous sodium lauryl sulfate (SLS) was applied under occlusive patches to the back of each subject for a 24-h period. The two formulations were then applied under occlusive patches to the forearms for "five alternate day 48 hour periods." Following a 10–14 day nontreatment period, a 48-h challenge patch of each product was applied under occlusive patches to a previously untreated site on the left or right side of the back. Challenge applications to the left side of the back were preceded by a 30-minute treatment with SLS. Challenge applications to the right side of the back consisted of the test material alone, with no SLS pretreatment. The SLS-treated sites developed notable burns in over half the subjects; however, no significant skin irritation or skin sensitization was produced by the two products.<sup>(59)</sup>

No skin irritation or sensitization was observed in a second Kligman Maximization Test when 30 women were exposed to two cream eye shadows, each containing 35% Petroleum Distillate (Table 1). The procedures employed were similar to those as described in the previous study (five 48-h induction patches, and aqueous sodium lauryl sulfate treatments prior to the first induction application and prior to the challenge application).<sup>(60)</sup> A third Kligman Maximization Test involving 25 subjects and two eye shadows formulated with 35% Petroleum Distillate (Table 1) also was negative for skin irritation and sensitization.<sup>(61)</sup>

Two hundred five subjects were tested for skin irritation and sensitization with a mascara containing 35% Petroleum Distillate (Table 1). The product (0.1 g) was applied under an occlusive patch to the upper back for 24 h. Applications were made every Monday, Wednesday, and Friday for 3 weeks for a total of 10 induction patches. Two weeks after the last induction application, 48-h chal-

lenge patches were applied to the original test site and to a previously untreated site. Skin reactions were graded on a scale of 0 (no irritation) to 4 (erythema, edema, and blisters). Seven subjects had 2+ skin reactions (erythema and edema) after the second insult, whereas 1 subject developed a 2+ reaction as a result of the third insult. These reactions were judged by the investigator as irritant in nature and due to insufficient volatilization of the product. Beginning with the fourth insult, patches containing the product were volatilized for 30 minutes prior to application. Two subjects subsequently developed single 2+ induction reactions. Grade 1+ skin reactions (erythema) were generally noted throughout the induction phase, but with less frequency following the fourth insult. One sensitization reaction (1+) was observed at the original test site 48 h after challenge; this reaction had dissipated by the 72-h evaluation.<sup>(62)</sup>

One hundred thirteen panelists were exposed in a repeated insult patch test to a mascara containing 35.5% Petroleum Distillate (Table 1). A total of ten 48-h induction applications of the test material were made to the back of each subject. Patches applied on Friday remained in place for 72 h instead of 48 h. The initial induction application consisted of an occlusive dressing. This initial patch was made in error, since the solvent system of the mascara was a known skin irritant. Therefore, subsequent induction patches were nonocclusive. A 48-h challenge patch containing the material was applied to a fresh site on the back (whether there was a nontreatment period prior to the single challenge application was not specified). Test sites were graded 15 minutes and 24 h after challenge patch removal. Nine subjects developed singular skin reactions during the induction phase. Responses consisted of 5 single "doubtful" reactions, 1 single erythema reaction, and 3 single vesicular reactions. The 3 vesicular reactions all were the result of the initial induction patch. A single "doubtful" reaction was noted on challenge in 1 individual.<sup>(63)</sup>

A Jordan-King repeat insult patch procedure was used to evaluate the sensitization potential of a mascara containing 58.37% Petroleum Distillate (Table 1). The mascara was tested at a 50% concentration in mineral oil, which provided a final Petroleum Distillate concentration of 29.2%. Occlusive patches containing the test material were applied to the upper backs of 151 subjects on Monday, Wednesday, and Friday for 3 consecutive weeks. The induction patches were removed and the sites evaluated on the same day as the next patch was applied. After a 2-week nontreatment period, two consecutive 48-h challenge patches were applied adjacent to the original induction site. No skin reactions were noted in any of the test subjects.<sup>(64)</sup>

A test similar to the previous study was conducted on a panel of 202 subjects with a mascara containing 55.0% Petroleum Distillate (Table 1). In this test, the mascara was applied full strength under gauze dressings. No skin reactions were observed.<sup>(65)</sup>

A Schwartz-Peck Prophetic Patch Test involving UV light exposure was conducted on 98 panelists. The products tested consisted of two cream eye shadows each containing 35% Petroleum Distillate (Table 1). Open and closed patches containing the products were applied behind the left ear or to the wrist for 48 h. After a 2-week nonexposure period, the subjects were given a second set of open and closed patches. Following evaluation of the second insult, closed patch sites were exposed to UV light (Hanovia Tanette Mark I Lamp) at a dis-

tance of 12 inches for 1 minute. No skin reactions were noted to either product in response to open or closed patches or to UV irradiation.<sup>(66)</sup>

A combination skin sensitization/photosensitization test was conducted on 52 "hyperreactive" subjects with a mascara containing 53.25% Petroleum Distillate (Table 1). Open induction patches containing the product were applied to the skin on Monday and Wednesday for 3 consecutive weeks; evaluations were made on Wednesday and Friday. Six to eight h prior to the initial induction patch, the test site was treated for 30 minutes with a closed patch containing 5% aqueous sodium lauryl sulfate. Seven days following application of the last induction patch, the test sites were again exposed to a 30-minute closed patch impregnated with the sodium lauryl sulfate solution. Six to eight h after the last sodium lauryl sulfate treatment, a 48-h open patch containing the product was applied as a challenge. "Duplicate" patch test sites were exposed to UV light (Hanovia Tanette Mark I Lamp) at a distance of 12 inches for 1 minute at applications 1, 4, 7, and challenge. No skin sensitization or photosensitization reactions were noted in any of the 52 test subjects.<sup>(67)</sup>

## SUMMARY

Cosmetic grade Petroleum Distillate consists predominantly of  $C_{10}$ – $C_{16}$  paraffinic, naphthenic, and isoparaffinic hydrocarbons. It is prepared by the fractional distillation of crude petroleum, followed by acid or hydrotreatment to complete saturation and to remove odor-causing impurities. This process may be followed by solvent or catalytic dewaxing and a clay or hydrotreatment finishing step. Typical values for aromatic hydrocarbon content and distillation range are <2.0% and 355–500°F, respectively; however, these values may vary depending on the specific Petroleum Distillate product.

Cosmetic grade Petroleum Distillate is used as a foam control agent for newspaper ink, as a solvent for waterless hand cleansers, and as a solvent for carbonless paper. With certain limitations, federal regulations permit use of cosmetic grade Petroleum Distillate as a direct and indirect food additive and as a component of insecticide formulations. Petroleum Distillate is used in cosmetic products as a solvent or as a component of solvent systems.

Data submitted to the FDA by firms participating in the voluntary cosmetic registration program indicated that Petroleum Distillate was used in 1981 in 113 cosmetic products. Product categories in which this ingredient was used most frequently included eye shadow (78 products) and mascara (18 products). Reported concentrations of Petroleum Distillate were as follows: >50% (8 products); >25–50% (75 products); >10–25% (3 products); >5–10% (18 products); and >1–5% (1 product). The concentration of Petroleum Distillate in 8 formulations was not reported. Cosmetic products containing this ingredient are normally applied to or have the potential to come in contact with eyes, skin, hair, and nails.

Undiluted Petroleum Distillate (Product C/Table 4) had an acute oral  $LD_{50}$  in rats of >25 ml/kg, an acute dermal  $LD_{50}$  in rabbits of >5 ml/kg, and an inhalation  $LC_{50}$  in rats of >592 ppm. Moderate skin irritation and mild, transient eye ir-

ritation were observed in rabbits following a single exposure to undiluted Petroleum Distillate (Product A/Table 2).

Rabbits were exposed in a subchronic study to a mascara solvent system containing 41.75% Petroleum Distillate (Product C/Table 4). The solvent system was applied to the skin or instilled into the eye daily for 3 months. Animals treated with the solvent system were comparable to controls with respect to survival, food consumption, body weight gain, skin and eye irritation, hematological and serological measurements, organ weights, and tissue changes.

Results of clinical studies were mixed. Eye area products formulated with 29.2–55% Petroleum Distillate (Table 1) were generally nonirritating, nonsensitizing, and nonphotosensitizing to the skin. In other studies, eye products containing 35% Petroleum Distillate (Table 1) produced irritation and minimal sensitization; however, it was not ascertained whether these skin reactions were a result of Petroleum Distillate or other ingredients in the formulation.

Acute overexposure of humans to cosmetic grade Petroleum Distillate by inhalation or ingestion can cause central nervous system depression, headache, dizziness, nausea, and coma. Airborne concentrations can cause eye and mucous membrane irritation. Prolonged and repeated contact with the human skin produces defatting, drying, and irritation. No occupational exposure limits for cosmetic grade Petroleum Distillate have been established.

## DISCUSSION

Petroleum Distillate, cosmetic grade, is a general term that is applicable to several petroleum fractions that are defined variously with respect to chemical and physical characteristics. This safety review and conclusion are limited to cosmetic grade Petroleum Distillate as defined in this report. These petroleum distillates are used in cosmetics as solvents or as components of solvent systems. Petroleum Distillate could be mildly irritating to the eyes and to the respiratory tract if inhaled. Although Petroleum Distillate is used in cosmetic products at concentrations as great as 25–50%, it is tolerated satisfactorily by the skin, though such products in the form of eye shadow, mascara, or other eye makeup can be irritating to the eye.

## CONCLUSION

The CIR Expert Panel concludes that Petroleum Distillate, as characterized in this report, is safe as a cosmetic ingredient at the current concentrations of use.

## ACKNOWLEDGMENT

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