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Final Report on the Safety Assessment of Phenyl Trimethicone

Phenyl Trimethicone is a silicon polymer used in a variety of cosmetic products at concentrations up to 5%.

In acute oral studies, Phenyl Trimethicone was relatively nontoxic in rats and was nontoxic in acute and subchronic dermal studies. Phenyl Trimethicone was nonirritating to the skin of rabbits under both intact and abraded conditions and was not a sensitizer to guinea pigs. The ingredient was not an eye irritant when evaluated by the Draize ocular irritation test.

Phenyl Trimethicone was nonmutagenic both with and without metabolic activation when evaluated in the Ames assay. Phenyl Trimethicone was not teratogenic in rats and rabbits when applied dermally at doses of up to 500 mg/kg per day, although an increase in the number of resorptions was noted in two of three studies (statistically significant in only one). A dose of 200 mg/kg per day indicated that a fetotoxic dose was being approached. The doses tested are comparatively greater than the concentrations used in cosmetic products.

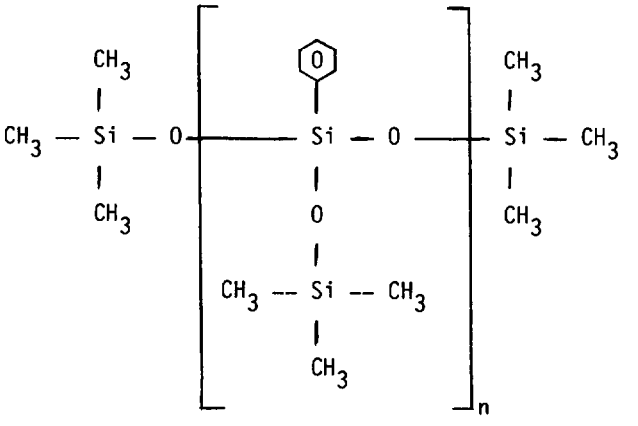
Phenyl Trimethicone is neither an irritant nor a sensitizer to humans. No photosensitization data are available on Phenyl Trimethicone; however, the UV absorption spectrum indicated only weak absorbance at 327 nm.

Based on the animal and human data included in this report, it is concluded that Phenyl Trimethicone is safe as a cosmetic ingredient in the present practices of use and concentration.

CHEMICAL AND PHYSICAL PROPERTIES

Definition and Structure

Phenyl Trimethicone is a water white, almost odorless, fluid silicone polymer.[1] It conforms to the formula[2]:



This compound is a tris(trimethylsiloxy)-phenylsilane and is also known as Dow Corning® 556 fluid (defined as mixed oligomers).[2-4] The ultraviolet (UV) spectrum for Phenyl Trimethicone indicates weak absorbance centered at approximately 327 nm.[5] No data on impurities were available. The chemical and physical characteristics of Phenyl Trimethicone are presented in Table 1.

Analytical Method

Identification is by infrared spectroscopy.[1] The compound can also be detected by analysis for silicon using optical emission spectroscopy[6] or atomic absorption spectrophotometry.[7] Smith[8] has published a reference book for silicone analysis.

TABLE 1. Physicochemical Properties of Phenyl Trimethicone

Property	*Value*	*Reference*
Structural formula	$(CH_3)_3SiO[(CH_3)_3SiOSi(C_6H_5)O]_nSi(CH_3)_3$	2
Boiling point at 760 mm Hg (°C)	265	6
Flash point, minutes (°F)	250	6
Specific gravity 25°: 25°C	0.970	6
Refractive index at 25°C	1.459	1
Total acid number	0.25 maximum	1
Methyl:phenyl ratio	5.00–7.14	1
Kinematic viscosity	5–30 centistokes	1
UV absorbance	Weak absorbance at 327 nm	5

Method of Manufacture

Silicones may be considered to be organic derivatives of silica, SiO_2, with organic groups replacing some of the oxygens in the polymeric silica molecule. One industrial process first converts silica to tetraethoxysilane. The ethoxy groups are replaced with the desired organic group by the Grignard reaction. The resulting organosilanes are hydrolyzable to organo-substituted silicic acids, called "silanols," which rapidly condense with each other to produce the silicon–oxygen–silicon framework of the silicone polymers. In these silicone structures, the organic radicals are firmly bonded to the silicon through a carbon–silicon linkage. Each silicon atom is linked to neighboring silicon atoms through an oxygen atom.[9]

COSMETIC USE

Phenyl Trimethicone is used in cosmetics intended for human skin contact. Some of its cosmetic uses are as a lubricant, water-repellent, and vehicle.[10–12] The types of products in which this ingredient is used, as well as the concentrations used, are presented in Table 2. The information in the table was obtained from FDA's computerized information file containing product formulation data submitted to FDA in 1981 by companies participating in the voluntary cosmetic registration program.[13,14]

Phenyl Trimethicone was reported as an ingredient in 113 cosmetic formulations at concentrations of ≤0.1% (27 products), >0.1–1% (53 products), >1–5% (32 products), and >5–10% (1 product). The maximum reported use was in aerosol hair sprays (25 products). The greatest concentration of use was in an outdoor tanning preparation (5–10%).[13] Voluntary filing of product formulation data with 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. Since certain cosmetic ingredients are supplied by the manufacturer at less than 100% concentration, the concentration reported by the cosmetic formulator may not necessarily reflect the actual concentration found in the finished product; the actual concentration in such a case would be a fraction of that reported to the FDA. The fact that data are only submitted within the framework of preset concentration ranges also provides 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 two- to ten-fold error in the assumed ingredient concentration.

Cosmetic products containing Phenyl Trimethicone may contact all external body surfaces, hair, and lungs, as well as conjunctivae and vaginal and other mucous membranes (Table 2). These products may be used daily or occasionally over a period of up to several years. The frequency and duration of application could result in continuous exposure.

TABLE 2. Product Formulation Data on Phenyl Trimethicone[13]

Product category	Total no. of formulations in category	Total no. containing ingredient	No. of product formulations within each concentration range (%)			
			>5–10	>1–5	>0.1–1	≤0.1
Baby products	15	1	–	–	1	–
Bath oils, tablets, and salts	237	1	–	–	1	–
Other bath preparations	132	2	–	2	–	–
Eye shadow	2582	1	–	1	–	1
Mascara	397	1	–	–	1	–
Other eye makeup preparations	230	1	–	–	1	–
Hair conditioners	478	10	–	1	7	2
Hair sprays (aerosol fixatives)	265	25	–	–	7	18
Hair straighteners	64	1	–	1	–	–
Hair rinses (noncoloring)	158	1	–	–	1	–
Tonics, dressings, and other hair grooming aids	290	9	–	2	6	1
Wave sets	180	2	–	1	1	–
Other hair preparations (noncoloring)	177	1	–	–	1	–
Blushers (all types)	819	11	–	11	–	–
Face powders	555	2	–	–	2	–
Makeup foundations	740	2	–	2	–	–
Lipstick	3319	2	–	2	–	–
Makeup bases	831	2	–	1	–	1
Nail polish and enamel	767	7	–	–	7	–
Preshave lotions (all types)	29	6	–	3	3	–
Face, body, and hand skin care preparations (excluding shaving preparations)	832	8	–	–	6	2
Moisturizing skin care preparations	747	7	–	1	4	2
Night skin care preparations	219	1	–	–	–	1
Other skin care preparations	349	1	–	1	–	–
Suntan gels, creams, and liquids	164	6	–	2	4	–
Indoor tanning preparations	15	1	1	–	–	–
Other suntan preparations	28	1	–	1	–	–
1981 TOTALS		113	1	32	53	27

BIOLOGY

Structure and Activity

Bennet et al.,[15] Hayden and Barlow,[16] Hobbs et al.,[6] LeFevre et al.,[17] LeVier and Jankowiak,[18] and Palazzolo et al.[19] have studied the relative activities and structure–activity relationships of various silicones and silanes.* Certain phenyl-substituted silicones have been shown to be active androgen depressants.[15] Those studies pertinent to Phenyl Trimethicone are presented in the following sections. They indicate that this ingredient does not affect the function of either male or female sex organs in rats.

ANIMAL TOXICOLOGY

A general review of silicone toxicity has been published by Rowe et al.[9]

Oral Studies

Acute Oral Toxicity

The acute oral toxicity of Phenyl Trimethicone was evaluated in Spraque-Dawley albino rats.[20] Single doses of undiluted Phenyl Trimethicone ranging from 10.2 to 34.6 g/kg were administered by intubation to groups of four rats (two male, two female). The animals were observed for 14 days and then necropsied. One rat receiving 34.6 g/kg Phenyl Trimethicone died; the others at this dose had hypoactivity, muscular weakness, diarrhea, diuresis, ruffed fur, and weight loss. There were no significant gross lesions in the tissues and organs examined. Phenyl Trimethicone was considered nontoxic (Table 3).

Samples taken from 54 production lots of Phenyl Trimethicone were administered to male Sprague-Dawley rats. Phenyl Trimethicone was administered at 3.3 mg/kg per day orally for 7 days to groups of 10 fasted rats. Doses were calculated on the basis of initial body weight and administered by gavage without an oil vehicle. Control groups were treated with saline solution. No significant effects were observed with reference to mortality, body weight changes, behavioral changes, or gross pathological alterations[6] (Table 3).

Phenyl Trimethicone and a series of low molecular weight organosiloxanes were assayed for uterine weight changes using immature female Wistar rats weighing 30–40 g. The rats were bilaterally ovariectomized and allowed 3 days to recover before treatment. On the fourth day, the animals were randomly distributed into treatment groups of six animals each. The test material was administered by oral intubation in a sesame oil vehicle. Doses of 10.0, 1.0, 0.1, and 0.01 mg/kg were administered in a final oil volume of 2 g/kg. Animals were dosed once daily for 3 days. Controls received the oil vehicle only. Animals were nec-

*In this series of publications in *Toxicology and Applied Pharmacology*, Volume 21, 1972, Dow Corning® 556 fluid was designated as the monomer, but, in fact, the product tested in the reported studies was the mixed oligomers.[4]

TABLE 3. Oral Toxicity of Phenyl Trimethicone

Ingredient	*Test*	*Dose*	*Animal*	*Comments*	*Reference*
Phenyl Trimethicone 100%	Acute	10.2–34.6 g/kg (single dose)	8 male rats 8 female rats	One rat at the high dose died; considered non-toxic; hypoactivity, muscular weakness, diarrhea, diuresis, ruffed fur, and weight loss noted at high dose	20
Phenyl Trimethicone 100%	Acute	3.3 mg/kg per day for 7 days	540 male rats	No significant effects	6
Phenyl Trimethicone in sesame oil	Assay for uterine weight change	0.01, 0.1, 1.0, and 10 mg/kg per day for 3 days	6 female rats per group	No significant uterine effects	16
Phenyl Trimethicone 10% in a product	Acute	Single dose of 10 ml/kg	10 mice	No deaths	21
Phenyl Trimethicone 10% in a product	Acute	Single dose of 10 ml/kg	10 mice	No deaths	22
Phenyl Trimethicone 10% in a product	Acute	Single dose of 10 ml/kg	10 mice	No deaths	23
Phenyl Trimethicone 5% in a foundation cream	Acute	Single 5.0 ml/kg dose	10 rats	No deaths	24

ropsied 24 h after the final dose. No toxic effects were observed in Phenyl Trimethicone-treated animals. Statistically significant increases were observed in the uterine weights of some animals treated with other phenyl-substituted organosiloxanes[16] (Table 3).

The acute toxicity of three cosmetic products containing 10% Phenyl Trimethicone was determined for male CD-1 albino mice. Treatment groups of 10 mice each were dosed by gavage once with 10 ml/kg of the products. No deaths were reported during the 14-day observation period[21-23] (Table 3).

A foundation cream containing 5% Phenyl Trimethicone was administered to five male and five female Sprague-Dawley rats. The selected dose was the same as the dose (per kilogram body weight) that would be received by a 10 kg child ingesting the entire contents of the largest marketed container. A single 5.0 ml/kg dose resulted in leg weakness, transient vasodilation of the ears, and hypoactivity. These signs disappeared within 6 h posttreatment, and no deaths were reported during the 2-week study[24] (Table 3).

Dermal Studies

Acute Dermal Toxicity

The acute dermal toxicity of Phenyl Trimethicone was evaluated in 10 albino rabbits. The trunk of each animal was clipped before application, and the skin of half of the rabbits was abraded. Single 24-h doses of 2.0 g/kg Phenyl Trimethicone were applied by means of an occlusive sleeve. No deaths or behavioral reactions were observed during 14 days postexposure. Phenyl Trimethicone was considered nontoxic[20] (Table 4).

Subchronic Dermal Toxicity

Phenyl Trimethicone was assayed for dermal toxicity in 10 adult male New Zealand rabbits. The exposure sites on the back, approximately 10% of the body surface, were shaved 24 h before application of the test material. A 200 mg/kg dose of Phenyl Trimethicone was distributed, without rubbing, over the entire clipped site. Applications were made daily for 28 days. Each animal was caged individually and fitted with a collar to prevent licking of the test site. Observations were made daily, and necropsy was performed at the end of the test period. No significant adverse effects were noted in any of the control or test animals with reference to body weight, mortality, behavioral reactions, testicular histology, and spermatogenic activity. Phenyl-substituted cyclosiloxanes were positive for testicular atrophy in similar studies[6] (Table 4).

Samples taken from five production lots of Phenyl Trimethicone were tested for biological activity. Treatment groups of four rabbits received dermal applications of 50 ml/kg per day for 20 days. No adverse effects were observed[6] (Table 4).

Phenyl Trimethicone was evaluated for dermal toxicity in three groups of 10 New Zealand albino rabbits (5 males and 5 females). The rabbits were dosed daily for 20 consecutive days with doses of 2, 6, and 20 mg/kg Phenyl Trimethicone. Solutions in polypropylene glycol-2-methyl ether corresponding to 1.0, 3.0, and 10.0% (w/v), respectively, were used to maintain a constant volume of test solution (0.2 ml/kg per day) in the three dose groups. Treated (with polypro-

TABLE 4. Dermal Toxicity of Phenyl Trimethicone

Ingredient	*Test*	*Dose*	*Animal*	*Comments*	*Reference*
Phenyl Trimethicone 100%	Acute	2.0 g/kg	10 rabbits	Nontoxic	20
Phenyl Trimethicone 100%	Subchronic	200 mg/kg per day for 28 days	10 rabbits	No significant adverse effects	6
Phenyl Trimethicone 100%	Subchronic	50 mg/kg per day for 20 days	20 rabbits	No significant adverse effects	6
Phenyl Trimethicone in polypropylene glycol-2-methyl ether	Subchronic	2, 6, and 20 mg/kg for 20 days (actual dose)	30 rabbits	No significant adverse effects	25
Phenyl Trimethicone 2.5% in a moisturizer	Subchronic	5.5 and 8.4 mg/cm²/ 8.4% body surface area	20 rabbits	Some irriation and inflammation at application site; no other adverse effects	26

pylene glycol-2-methyl ether) and untreated control groups were also used. Test sites of all rabbits were shaved weekly, and in two males and two females of each group the skin was abraded before compound application. The solutions of Phenyl Trimethicone were applied gently without rubbing, and the rabbits were fitted with collars to prevent ingestion of the test material. The rabbits were observed daily during the application period and for 14 days thereafter. No deaths or unusual behavioral reactions were noted. Local skin reactions were characterized by slight desquamation at the application site among rabbits of all test groups as well as the treated controls. No toxic effects were noted in body weight, hematological values, blood chemistry, urine analyses, and gross or microscopic pathological findings of the test or control groups[25] (Table 4).

A 3-month toxicity study was conducted in rabbits to investigate the effects of daily dermal exposure to a skin moisturizer containing 2.5% Phenyl Trimethicone. Two treatment groups and one control group each consisted of 10 New Zealand White rabbits. Two doses, 5.5 and 8.4 mg/cm^2 per 8.4% body surface area, were administered to the clipped back of the animals. Collars were fitted to prevent ingestion of the test material. These doses represented multiples of 7.5 and 12 of the anticipated human exposure of 2.2 mg/cm^2 per 2.8% body surface area. The moisturizer caused persistent erythema, slight edema, and slight desquamation; these changes appeared slightly more severe at the higher dose during the first month of exposure, but no differences between dose groups were observed by the second month. Signs of irritation were nearly maximum in the first week of exposure, declined slightly and remained unchanged for 2 months. The dermal irritation increased gradually in severity in the last month of exposure. No adverse hematological or clinical chemistry findings were reported. There were no significant differences between the organ weights (testes but not seminal vesicles were examined) of treated and control animals. At histopathological examination, no treatment-related changes other than inflammation were observed at the application sites[26] (Table 4).

Skin Irritation

Phenyl Trimethicone was evaluated for primary skin irritation in six albino rabbits. The rabbits were clipped free of hair, and the skin of three was abraded. A 0.5 ml sample of undiluted Phenyl Trimethicone was applied for 24 h to each animal using an occlusive patch. Sites were scored upon patch removal and 48 h later. Phenyl Trimethicone had a Primary Irritation Index (PII) of 0.7 (max = 8) and was considered nonirritating[20] (Table 5).

A foundation cream containing 5% Phenyl Trimethicone was applied to six rabbits for 14 days. A 0.5 ml dose was applied to the clipped back of the animal for 18 h on 14 consecutive days. The rabbits were fitted with collars to prevent licking of the test material. Slight erythema, slight edema, and desquamation were observed. The cream had a PII of 1.9 (max = 8) and was considered mildly irritating[24] (Table 5).

Primary irritation tests of three cosmetic products containing 10% Phenyl Trimethicone were conducted with groups of six male New Zealand white rabbits. Using single insult patch procedures, 0.5 ml of the test product was applied via an occlusive patch to the clipped back of each rabbit. Patches remained in

TABLE 5. Irritation and Sensitization of Phenyl Trimethicone

Ingredient	*Test*	*Dose*	*Animal*	*Comments*	*Reference*
Phenyl Trimethicone 100%	Single insult occlusive patch	0.5 ml/24 h	6 rabbits 3 intact 3 abraded	PII[a] = 0.7; nonirritating	20
Phenyl Trimethicone Induction 5% Booster 20% Challenge 10, 20%	Magnusson-Kligman Maximization Test	See text	20 guinea pigs	No sensitization	31
Phenyl Trimethicone 5% in a foundation cream	Irritation	0.5 ml/18 h for 14 consecutive days	6 rabbits	PII = 1.9; mildly irritating	24
Phenyl Trimethicone 10% in a product	Single insult occlusive patch	0.5 ml/24 h	6 rabbits	PII = 0.58; slightly irritating	27
Phenyl Trimethicone 10% in a product	Single insult occlusive patch	0.5 ml/24 h	6 rabbits	PII = 0.71; slightly irritating	28
Phenyl Trimethicone 10% in a product	Single insult occlusive patch	0.5 ml/24 h	6 rabbits	PII = 0.37; slightly irritating	29

[a]PII, Primary Irritation Index (max = 8).

place for 24 h, and sites were scored at 24 and 72 h. The products had group PIIs (max = 8) of 0.585,[27] 0.71,[28] and 0.375[29] and were considered slightly irritating (Table 5).

Skin Sensitization

The contact sensitization potential of Phenyl Trimethicone was assessed using the Magnusson-Kligman Maximization Test.[30] In the induction phase of the test, 10 female guinea pigs received 0.05 ml intradermal injections each of 50% aqueous Freund's Complete Adjuvant, 5% Phenyl Trimethicone in propylene glycol, and 5% Phenyl Trimethicone in 50% Freund's Complete Adjuvant. One week after induction injections, a topical booster of 20% Phenyl Trimethicone in petrolatum was applied to the induction site. (A 5% solution of sodium lauryl sulfate in petrolatum had been applied 24 h earlier to produce minor irritation.) The sites were then placed under occlusive patches for 48 h. Two weeks after the topical booster, the animals were challenged with topical applications of 10 and 20% Phenyl Trimethicone in petrolatum to the shaved sides of the guinea pigs, and application sites were covered by occlusive patches for 24 h. The challenge sites were scored 48 and 72 h after challenge application. No sensitization was observed in any of the Phenyl Trimethicone-treated animals, and the investigators concluded that Phenyl Trimethicone did not produce an allergic response in guinea pigs[31] (Table 5).

Ocular Studies

Phenyl Trimethicone was evaluated for ocular irritation in six albino rabbits. A 0.1 ml sample of undiluted Phenyl Trimethicone was instilled into one eye of each rabbit; the other eye served as the untreated control. Reactions were scored according to Draize at 24, 48, and 72 h. The total score was 21 (max = 110) at 24 h and 0 thereafter. Phenyl Trimethicone was not considered an eye irritant[29] (Table 6).

Eye irritation studies were conducted with three cosmetic products containing 10% Phenyl Trimethicone. Six adult, male albino rabbits were used for each test material, and a 0.10 ml dose was instilled into one eye; the other eye served as control. The eyes were graded according to the standard Draize eye irritation scale.[32] There were no positive reactions; the products were not considered eye irritants[33–35] (Table 6).

Six albino rabbits were given instillations (into the conjunctival sac) of 0.10 ml of a foundation cream containing 5% Phenyl Trimethicone. Slight conjunctivitis occurred. There was no evidence of corneal dullness or iritis[24] (Table 6).

Inhalation Studies

An aerosol formulation containing 3% Phenyl Trimethicone in propellants was evaluated for inhalation toxicity in five male and five female rats. An aerosol without Phenyl Trimethicone was used as the control. A single exposure consisted of a 30-second burst followed by a 15-minute exposure within a 350 L inhalation chamber. This exposure was repeated twice daily, 5 days per week, for 4 weeks (40 exposures). The animals were observed for deaths, behavioral reac-

TABLE 6. Ocular Irritation of Phenyl Trimethicone

Ingredient	*Test*	*Dose*	*Animal*	*Comments*	*Reference*
Phenyl Trimethicone 100%	Draize	0.1 ml	6 rabbits	Score of 21 (max = 110) at 24 h, score of 0 thereafter; not an eye irritant	20
Phenyl Trimethicone 10% in a cosmetic product	Draize	0.1 ml	6 male rabbits	No positive reactions; not an eye irritant	33
Phenyl Trimethicone 10% in a cosmetic product	Draize	0.1 ml	6 male rabbits	No positive reactions; not an eye irritant	34
Phenyl Trimethicone 10% in a cosmetic product	Draize	0.1 ml	6 male rabbits	No positive reactions; not an eye irritant	35
Phenyl Trimethicone 5% in a foundation cream	--	0.1 ml	6 rabbits	Slight conjunctivitis; no evidence of corneal dullness or iritis	24

tions, and body weight changes. Hematological and blood chemistry as well as urine analyses were conducted. The animals exposed to the Phenyl Trimethicone areosol gained slightly less weight than the controls; no other toxic effects were noted.[36]

Mutagenicity

Phenyl Trimethicone was evaluated for mutagenicity in the Ames bacterial assay using *Salmonella* strains both with and without metabolic activation. Phenyl Trimethicone was not mutagenic when tested either with or without activation.[36]

Teratogenicity/Reproductive Effects

Phenyl Trimethicone was evaluated for teratogenicity in three groups of 26 rats each and three groups of 15 rabbits each. Doses of 50 and 500 mg/kg body weight (0.05 and 0.5 ml/kg) were applied topically to two groups of the rats and rabbits on Days 6–16 and 6–18 of gestation, respectively. The third group of each species served as the untreated control. Doses were applied by syringe onto the shaved dorsal area of each animal. The rats and rabbits were killed on Day 20 and 30, respectively, and the fetuses were removed by cesarean section. Approximately one half of the fetuses were examined microscopically, and the remaining fetuses were examined for skeletal abnormalities.[37]

The mean number of implantation sites and the mean number of live fetuses derived from rats of the control and test groups were comparable and within

normal limits. No gross lesions were found in any group. All fetuses had the normal number of ribs, but 10 and 3 fetuses from the low and high test group, respectively, had incompletely developed sternebrae. A greater number of fetuses derived from the test groups had bipartite sternebrae and lack of closure of the coronal suture.[37]

Of the rabbits on test, one died from the control and two from the low-dose groups died. The control group had a greater mean number of implantation sites than the test groups, although the mean number of live fetuses from all three groups was comparable. None of the dead fetuses delivered from the control (8), low (9), and high (2) dose groups were abnormal; most showed signs of immaturity. All live pups had fully developed sternebrae and normal ribs. No abnormalities were found in soft tissues. The investigators concluded that Phenyl Trimethicone had no adverse effects on resorptions, in utero mortality, or gross fetal development in rats and rabbits. The delayed ossification found in both test groups of rats was not seen in rabbits and was considered a species variation.[37]

Phenyl Trimethicone was evaluated for teratogenicity in two studies using New Zealand albino rabbits. In both studies, 200 mg/kg of the test material was applied to the shaved back of each animal on Days 6–18 of gestation. The rabbits were killed on Day 29, and the fetuses were removed by cesarean section. All fetuses were examined for viability, abnormalities, and skeletal deformities.[38,39]

One study was conducted with three groups of 10 rabbits each: the first group received Phenyl Trimethicone suspended in corn oil, the second received an equal volume of corn oil, and the third served as an untreated control. No deaths, unusual behavioral reactions, or adverse effects on maternal body weight were noted. A slight but significant increase in the number of resorption sites and a decreased viability of the Phenyl Trimethicone-exposed fetuses were observed. The investigators concluded that Phenyl Trimethicone, at a dose of 200 mg/kg, was not teratogenic[38] (Table 7).

The other study was conducted 1 year later with three groups of 15 rabbits each: the first group received Phenyl Trimethicone, the second received an equal volume of sesame oil, and the third served as an untreated control. No deaths or unusual reactions were observed. No adverse effects were noted on maternal body weight, external or internal development of 84/85 fetuses, or on viability.

An increase in the number of resorption sites was noted in the Phenyl Trimethicone test group (21.3% compared to 7.5 and 6.0% in the treated and untreated control groups, respectively). No skeletal abnormalities were found. The investigators concluded that Phenyl Trimethicone, at a dose of 200 mg/kg, was not teratogenic[39] (Table 7).

CLINICAL ASSESSMENT OF SAFETY

Dermal Absorption

Dermal absorption of Phenyl Trimethicone was evaluated in a panel of five male volunteers. During a 25-day pretest period, silicon baseline analysis of 24-h urine samples was conducted. Samples of home drinking water and various brands of beer consumed during the test were analyzed for silicon content. Dur-

TABLE 7. Teratogenicity Studies on Phenyl Trimethicone

Ingredient	*Method*	*Dose*	*Animal*	*Comments*	*Reference*
Phenyl Trimethicone 100%	Dermal application to shaved skin on Days 6–16 of gestation	0,50, and 500 mg/kg per day	3 groups of 26 rats	No adverse effects on resorptions, in utero mortality, or gross fetal development; not teratogenic	37
Phenyl Trimethicone 100%	Dermal application to shaved skin on Days 6–18 of gestation	0, 50, and 500 mg/kg per day	3 groups of 15 rabbits	No adverse effects on resorptions, in utero mortality, or gross fetal development; not teratogenic	37
Phenyl Trimethicone suspended in corn oil	Dermal application to shaved skin on Days 6–18 of gestation	200 mg/kg per day	3 groups of 10 rabbits (including treated and untreated controls)	Slight but significant increase in number of resorptions and decreased viability—approaching fetotoxic dose; not teratogenic	38
Phenyl Trimethicone 100%	Dermal application to shaved skin on Days 6–18 of gestation	200 mg/kg per day	3 groups of 15 rabbits (including treated and untreated controls)	Increase in number of resorptions indicating approaching fetotoxic dose; no other adverse effects; not teratogenic	39

ing the 10-day test period, 50 mg/kg Phenyl Trimethicone was applied once daily over the entire surface of the back. The test material remained in contact with the back for a period of 20 h, after which time any excess material was removed by washing. No special covering other than clothing was used. Blood and urine samples were taken for analysis on Days 1, 3, 6, 8, and 10.[6]

Blood and urine silicon concentrations were determined using optical emission spectroscopy. The procedure is applicable to determination of silicon in the 5 to 100 μg/ml range, with a detectability of 5 μg/ml. There were no statistically significant increases in blood or urinary silicon concentrations[6] (Table 8).

Irritation and Sensitization

A Repeated Insult Patch Test (RIPT) evaluated the irritation and sensitization of Phenyl Trimethicone using a panel of 50 subjects (36 males and 14 females). The induction phase consisted of nine occlusive patches applied for 24 h on alternate days. The patches were coated with Phenyl Trimethicone and always applied to the same skin site. Two weeks after the last induction patch, a challenge

TABLE 8. Clinical Assessment of Safety

Ingredient	*Test*	*No. of panelists*	*Results*	*Reference*
Phenyl Trimethicone 100%	Dermal absorption	5 males	No detectable concentration in blood and urine	6
Phenyl Trimethicone 100%	RIPT[a]	50 (36 males, 14 females)	No irritation or sensitization	40
Phenyl Trimethicone 10% in each of 17 products	RIPT (modified 4 applications on consecutive days)	8 per group (80 total)	Highest total score of 5.0 (max = 256) and highest individual score of 1.0 (max = 8); minimally irritating	41–50
Phenyl Trimethicone 5% in a foundation	RIPT	189	No irritation or sensitization	51
Phenyl Trimethicone 2.5% in a moisturizer	RIPT	239	No irritation or sensitization	52
Phenyl Trimethicone 2.5% in a moisturizer	Cumulative Irritation test	9	Cumulative irritation score of 13 (max = 630); classified as a mild material (essentially no experimental irritation)	54

[a]RIPT, Repeated Insult Patch Test.

patch was applied to an adjacent site. All sites, both induction and challenge, were scored upon patch removal. No signs of erythema or edema were observed; all scores were 0. It was concluded that Phenyl Trimethicone was not irritating, fatiguing, or sensitizing[40] (Table 8).

RIPTs were conducted to evaluate the irritancy of 17 cosmetic products, each containing 10% Phenyl Trimethicone. For each product, four overnight patches were applied on 4 consecutive days to eight panelists. Sites were scored upon patch removal. The products were at most minimally irritating, as the highest total score was 5.0 (max = 256) and the highest individual score was 1.0 (max = 8)[41–50] (Table 8).

Two modified Draize-Shelanski RIPTs were conducted to evaluate the irritation and sensitization of a cosmetic foundation product and a moisturizer containing 5 and 2.5% Phenyl Trimethicone, respectively. The panels consisted of 189 and 239 individuals for the 5 and 2.5% products, respectively. Ten 24-h patches were applied during the 23-day induction period. Following a 2-week nontreatment period, a 48-h challenge patch was applied to a previously untreated site. No irritation or sensitization was observed in any of the subjects[51,52] (Table 8).

A moisturizer containing 2.5% Phenyl Trimethicone was tested for cumulative irritation by the methods of Phillips et al.[53] Using an occlusive patch, 0.3 ml of the product was applied to the back of nine panelists for 23 h on 21 consecutive days. Applications were made to the same site for the duration of the test. The cumulative irritation score was 13 (max = 630), and the product was classified as a mild material (essentially no experimental irritation)[54] (Table 8).

One case of allergic contact dermatitis to a sunscreen preparation containing Phenyl Trimethicone has been reported. A 64-year-old woman developed contact dermatitis 4 weeks after she had begun using a sunscreen on a regular basis. After patch testing with individual active and vehicular ingredients of the sunscreen, the patient reacted (at 72 h) to 2% Phenyl Trimethicone in petrolatum. Five control subjects patch tested with this mixture had no reactions.[10]

SUMMARY

Phenyl Trimethicone is a fluid, water white, almost odorless silicone polymer used in a variety of cosmetic products. It is generally used at a concentration of <5%.

In acute oral studies, Phenyl Trimethicone was relatively nontoxic for rats. Cosmetic products containing up to 10% Phenyl Trimethicone when administered orally were also relatively nontoxic for mice and rats.

Phenyl Trimethicone was nontoxic for rabbits in acute and subchronic dermal toxicity studies. Doses of up to 200 mg/kg applied once daily for up to 28 days caused no adverse effects. Topical application for 3 months of a moisturizer containing 2.5% Phenyl Trimethicone produced no treatment-related changes in rabbits other than inflammation at the application site.

Phenyl Trimethicone was nonirritating to the intact and abraded skin of rabbits. A cosmetic product containing 5% Phenyl Trimethicone was mildly irritating to rabbits when applied for 14 consecutive days, and cosmetic products

containing 10% Phenyl Trimethicone were slightly irritating to rabbits after a single application of the product.

Phenyl Trimethicone evaluated with the Magnusson-Kligman Maximization Test was not a sensitizer in guinea pigs.

Phenyl Trimethicone evaluated by the Draize Ocular Irritation Test was not irritating. Cosmetic products containing up to 10% Phenyl Trimethicone were also essentially nonirritating to eyes of rabbits.

An aerosol formulation containing 3% Phenyl Trimethicone tested by inhalation produced no significant adverse effects in rats.

Phenyl Trimethicone evaluated by the Ames assay was nonmutagenic both with and without metabolic activation.

Phenyl Trimethicone applied dermally at doses of up to 500 mg/kg per day was not teratogenic in rats and rabbits. An increase in the number of resorptions was noted in two studies (statistically significant in only one) at a dose of 200 mg/kg per day.

A clinical trial of Phenyl Trimethicone dermal absorption in five panelists was negative. A 50 mg/kg dose was applied once daily for 10 days. Using a spectroscopic method with a detection limit of 5 μg of silicone per ml, detectable amounts of silicone were not found in the blood and, compared to controls, only insignificant changes were seen in the urine.

Phenyl Trimethicone evaluated by RIPT using a panel of 50 subjects produced no irritation or sensitization. In clinical studies, cosmetic products containing Phenyl Trimethicone produced essentially no cumulative irritation (2.5% Phenyl Trimethicone) over 21 days and minimal irritation at most when applied for 4 consecutive days (10% Phenyl Trimethicone). In RIPTs, cosmetic products containing 5 and 2.5% Phenyl Trimethicone produced no irritation or sensitization in the 189 and 239 people, respectively. One case of allergic contact dermatitis to Phenyl Trimethicone in a sunscreen has been reported.

DISCUSSION

No photosensitization data were available on Phenyl Trimethicone. These were not considered essential for the evaluation of the safety of Phenyl Trimethicone in cosmetic products as the UV spectrum indicated only weak absorbance at 327 nm. It was considered unnecessary to request clinical photosensitization data. An increase in the number of resorption sites was noted in two of three teratogenicity/reproductive studies, but the results were statistically significant in only one study. The doses tested in these studies were comparatively greater than the concentrations used in cosmetics, and the Panel did not believe that additional data were required for evaluation of the safety of Phenyl Trimethicone in cosmetics.

CONCLUSION

Based on the data from animal and human studies included in this report, the CIR Expert Panel concludes that Phenyl Trimethicone is safe as a cosmetic ingredient in the present practices of use and concentration.

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