Safety Assessment of Phenyl-Substituted Methicones as Used in Cosmetics

Status:	Draft Report for Panel Review
Release Date:	September 1, 2022
Panel Meeting Date:	September 26-27, 2022

The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; David E. Cohen, M.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; Allan E. Rettie, Ph.D.; David Ross, Ph.D.; Thomas J. Slaga, Ph.D.; Paul W. Snyder, D.V.M., Ph.D.; and Susan C. Tilton, Ph.D. The Cosmetic Ingredient Review (CIR) Executive Director is Bart Heldreth, Ph.D. This safety assessment was prepared by Preethi Raj, Senior Scientific Analyst/Writer, CIR.

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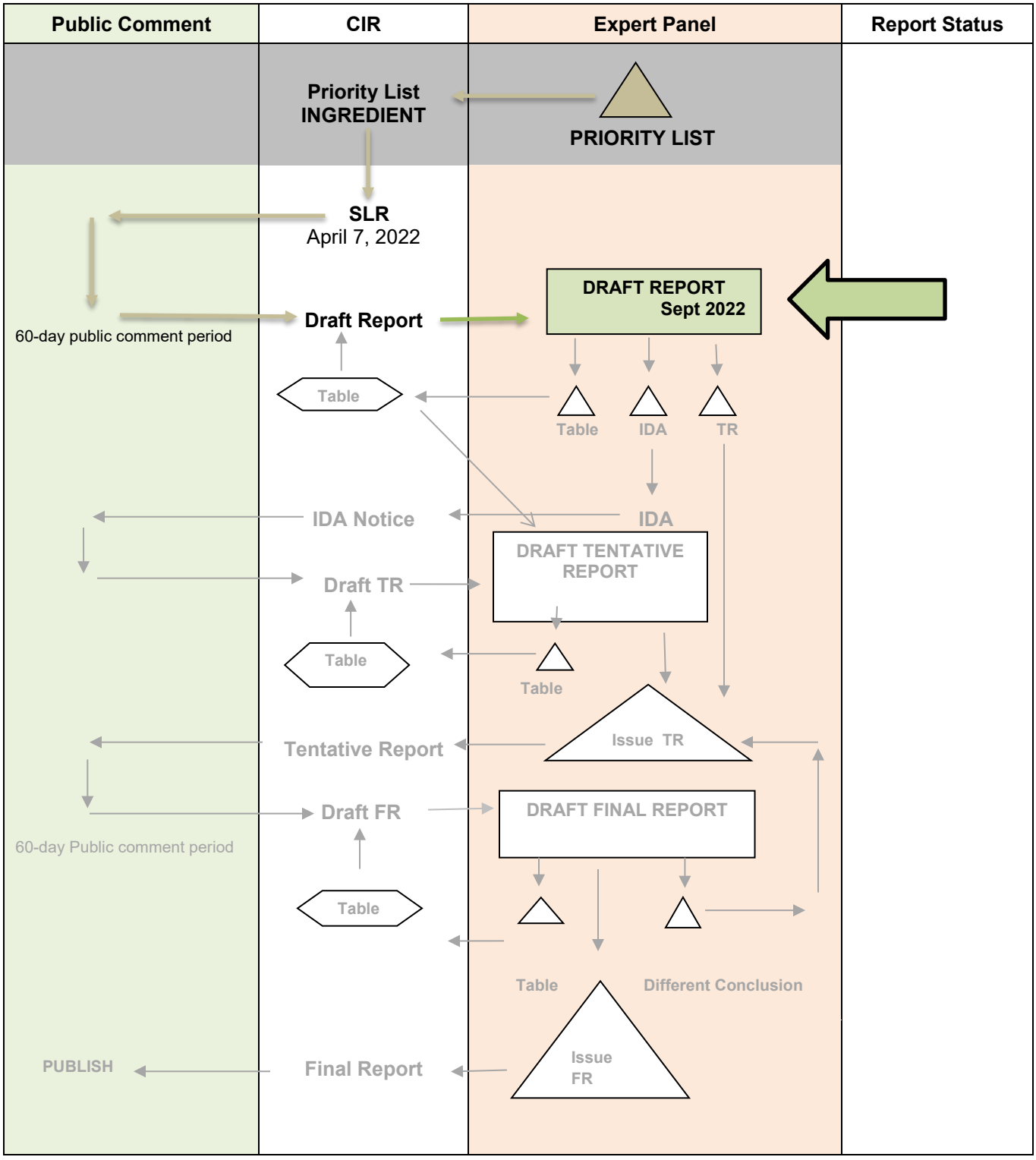
SAFETY ASSESSMENT FLOW CHART

INGREDIENT/FAMILY Phenyl-Substituted Methicones

MEETING September 2022



Cosmetic Ingredient Review

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Preethi S. Raj, M.Sc.
Senior Scientific Analyst/Writer, CIR
Date: September 1, 2022
Subject: Safety Assessment of Phenyl-Substituted Methicones as Used in Cosmetics

Enclosed is the Draft Report of the Safety Assessment of Phenyl-Substituted Methicones as Used in Cosmetics (identified as *report_PhenylSubMethicones_092022* in the pdf). This is the first time the Expert Panel for Cosmetic Ingredient Safety (Panel) is seeing a safety assessment of this group of 7 cosmetic ingredients. A Scientific Literature Review (SLR) was announced on April 7, 2022.

The Panel has previously reviewed the safety of Phenyl Trimethicone in 1986, with the conclusion that Phenyl Trimethicone is safe as a cosmetic ingredient in the practices of use and concentration described in the safety assessment. The Panel reaffirmed this conclusion in 2006. Since this ingredient is now included in this report, these previous reports are included in this package for your review (*originalreport_PhenylSubMethicones_092022*; *rereview2006_PhenylSubMethicones_092022* respectively). The associated meeting minutes are also included for your review (*originaltranscripts_PhenylSubMethicones_092022*).

Following the announcement of the SLR, the data listed below were received. Please note that due to file size restrictions, all materials for this report build have been divided into 3 separate books, a main book, which includes *data1 – data4* in the primary pdf (i.e., the Phenyl-Substituted Methicones pdf), and two additional files, one containing *data5* (pdf named Phenyl-Substituted Methicones_S1) and the other, *data6* (pdf named Phenyl-Substituted Methicones_S2).

data1_PhenylSubMethicones_092022

- 2021 concentration of use data (all except Phenyl Trimethicone)

data2_PhenylSubMethicones_092022

- 2022 concentration of use data for Phenyl Trimethicone

data3_PhenylSubMethicones_092022

- Acute oral toxicity – Limits Test (78-82% Phenyl Trimethicone, 18-22% Polysilicone-11); AMA Laboratories 1995
- Primary skin irritation (78-82% Phenyl Trimethicone, 18-22% Polysilicone-11); AMA Laboratories 1995
- Primary ocular irritation (78-82% Phenyl Trimethicone, 18-22% Polysilicone-11); AMA Laboratories 1995
- Repeated insult patch test (100% Trimethylsiloxyphenyl Dimethicone); Consumer Product Testing Co. 2002

data4_PhenylSubMethicones_092022

- Toxicity and hazardousness information of cosmetic silicone ingredients: Diphenyl Dimethicone 100%; ShinEtsu 2022
- Toxicity and hazardousness information of cosmetic silicone ingredients: Diphenylsiloxy Phenyl Trimethicone 100%; Shin Etsu 2022

data5_PhenylSubMethicones_092022

- Human patch test (shine gloss containing 5% Trimethylsiloxyphenyl Dimethicone); Anonymous 2005
- Determination of the irritating propensities of serum (containing 2% Trimethylsiloxyphenyl Dimethicone) on human skin; Anonymous 2012
- Repeated insult patch test (cream containing 3% Trimethylsiloxyphenyl Dimethicone); Anonymous 2009
- Determination of the photo-allergic potential of serum (containing 2% Trimethylsiloxyphenyl Dimethicone): In humans; Anonymous 2012

- Human patch test (late night ampoules containing 0.5% Diphenylsiloxy Phenyl Trimethicone); Anonymous 2019
- Repeated insult patch test (product containing 0.5% Diphenylsiloxy Phenyl Trimethicone); Anonymous 2019
- Human patch test (eye primer containing 10% Phenyl Trimethicone); Anonymous 2009
- A 14-day cumulative irritation assay (SPF cream containing 3.2363% Phenyl Trimethicone); Anonymous 2010
- An evaluation of the contact sensitization potential of topically-coded products in human skin by means of the human maximization assay (concealer containing 26.18% Phenyl Trimethicone); Anonymous 2014
- An assessment of the photosensitization potential of three topical coded test products using a human photocontact allergenicity assay (lotion 2 contains 7.5% Phenyl Trimethicone); Anonymous 2012
- Human patch test (lip color containing 9.06% Diphenyl Dimethiicone); Anonymous 2008

data6_PhenylSubMethicones_092022

- 13-week toxicity study by oral route (gavage) in rats (mixture containing 15% Diphenyl Dimethicone); Anonymous 2004
- Clinical study for the verification of the absence of sensitizing potential and of the good cutaneous compatibility of a cosmetic test article, by repeated cutaneous applications under occlusive patch on 112 (or 111) healthy adult subjects (product contains 2% Diphenyl Dimethicone); Anonymous 2006
- Evaluation of skin sensitization potential in mice using the local lymph node assay (LLNA) (test material contains 15% Diphenyl Dimethicone); Anonymous 2003
- Repeated insult patch test (Marzulli and Maibach Method) (test material contains 0.2% Phenyl Methicone); Anonymous 2009
- Repeated insult patch test (test material contains 28.67% Phenyl Trimethicone); Anonymous 2009
- Repeated insult patch test (test material containing 38.006% Trimethylsiloxyphenyl Dimethicone); Anonymous 2011

The following are also included in the primary pdf, for your review: a flow chart (*flow_PhenylSubMethicones_092022*), literature search strategy (*search_PhenylSubMethicones_092022*), data profile (*dataprofile_PhenylSubMethicones_092022*), ingredient history (*history_PhenylSubMethicones_092022*), and 2022 FDA VCRP data (*VCRP_PhenylSubMethicones_092022*).

Comments on the SLR (*PCPCcomments_PhenylSubMethicones_092022*) that were received from the Council have been addressed, and follow this memo. A comments response checklist is also included (*response-PCPCcomments_PhenylSubMethicones_092022*).

After reviewing these documents, if the available data are deemed sufficient to make a determination of safety, the Panel should issue a Tentative Report with a safe as used, safe with qualifications, split, or unsafe conclusion, and Discussion items should be identified. If the available data are insufficient, the Panel should issue an Insufficient Data Announcement (IDA), specifying the data needs therein.

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: April 13, 2022

SUBJECT: Scientific Literature Review: Safety Assessment of Phenyl-Substituted Methicones as Used in Cosmetics (release date: March 29, 2022)

The Personal Care Products Council has no suppliers listed for Diphenylsiloxy Phenyl/Propyl Trimethicone.

The Personal Care Products Council respectfully submits the following comments on the scientific literature review, Safety Assessment of Phenyl-Substituted Methicones as Used in Cosmetics.

Key Issue
The Australian assessment of Diphenylsiloxy Phenyl Trimethicone (reference 6) includes some chemical properties information that has not yet been added to the CIR report. In addition, reference 6 cites an ECHA dossier on this material that is not included in the reference section.

Additional Considerations
Cosmetic Use; Table 2 – The Cosmetic Use information from the original CIR review and the re-review of Phenyl Trimethicone should be mentioned in the Cosmetic Use section and in Table 2.

Dermal Absorption; Summary – As in the Summary, the Dermal Absorption section should indicate that the estimate of dermal absorption was based physicochemical properties. The 10% value is really a default value for an ingredient thought to have low absorption (rather than a predicted value).

Acute, Inhalation; Summary; Table 3 – Please revise the description of the inhalation study. The rats were exposed for 1 hour, not for 5-minute intervals. What happened at 5-minute intervals was that Diphenyl Dimethicone was placed on a hot plate to vaporize it. It should be stated that the exposure concentrations were calculated (not measured values) based on the volume of the chamber and the amount of Diphenyl Dimethicone that was vaporized. Please state if there were any effects observed at the two lowest concentrations.

Genotoxicity, In Vitro, Diphenylsiloxy Phenyl Trimethicone; Summary – Please correct "≤ 0.15 µl/ml" to "≥0.15 µl/ml"

Ocular Irritation – Please correct: "7 d of after exposure" (delete "of")

Risk Assessment; Summary – As presented in the SLR, the information in this section is a description of an exposure assessment. Therefore, if the text in this section is not changed, the title of the section should be changed to "Exposure Assessment". If the section is changed to add that the exposure estimate (7.68 mg/kg/day) was compared to the >1000 mg/kg/day NOAEL from the 28-day oral rat study, and was not considered an unreasonable risk for humans, the title of the section should remain as "Risk Assessment".

Summary – Please call the sensitization test in mice an LLNA in the Summary.

Summary – In the description of the Australian exposure assessment, please state the assumed product concentrations of Diphenylsiloxy Phenyl Trimethicone.

Phenyl-Substituted Methicones - September 26-27, 2022 Panel Meeting – Preethi Raj			
Comment Submitter: Personal Care Products Council **Date of Submission: April 13, 2022 (comments received on SLR after April 7, 2022 posting)**			
#	**Report section/Comment**	**Response/Action**	**Needs Panel Input**
1	Key Issue – suggestion to add chemical properties for Diphenylsiloxy Phenyl Trimethicone in AICIS ref -Cite ECHA dossier which includes same info in AICIS	- most properties in AICIS and ECHA were measured/calculated; unsure of the nature of the polymer (not added) - Have cited ECHA dossier	
2	Cosmetic Use; Table 2—conc use info from original CIR review and re-rereview of Phenyl Trimethicone should be included	- Added use info from 2006 re-review	
3	Dermal absorption; Summary – indicate that estimated dermal absorption is based on physicochemical properties	- Have indicated	
4	Acute, Inhalation; Summary; Table 3 – revise/correct description of inhalation study	- Have revised	
5	Genotoxicity, In Vitro, Diphenylsiloxy Phenyl Trimethicone; Summary – Please correct ≤ 0.15 µl/ml to ≥ 0.15 µl/ml	- Have corrected	
6	Ocular Irritation – delete of in phrase '7 d of after'	- Have deleted	
7	Risk Assessment; Summary – Do Either: -keep same text; section title 'Exposure Assessment' -mention exposure estimate (7.68 mg/kg/d) was compared to > 1000 mg/kg/d NOAEL from the 28-d oral tox study in rats; section title 'Risk Assessment	- Kept same text and changed title to Exposure Assessment	
8	Summary – call sensitization in mice an LLNA	- Have revised	
9	Summary – state the assumed product concentrations in the AICIS exposure assessment description	- Have included	

CIR History of:

Phenyl-Substituted Methicones

July 2021; January 2022

-Concentration of use data submitted by Council

January 2022

-FDA frequency of use data obtained

April 2022

- SLR posted on the CIR website; received SLR comments

Data received, by date:

April 12, 2022:

78-82% Phenyl Trimethicone, 18-22% Polysilicone-11

- Acute oral toxicity study of rats
- Primary skin irritation test of rabbits
- Primary ocular irritation test of rabbits

100% Trimethylsiloxyphenyl Dimethicone; HRIPT in 51 subjects

April, 2022:

- 3 SIOPTs
  - 0.06% Diphenyl Dimethicone in a lip color (20 subjects)
  - 0.5% Diphenylsiloxy Phenyl Trimethicone in an ampoule (20 subjects)
  - 10% Phenyl Trimethicone in a mousse foundation (21 subjects)
- 2 cumulative irritation assays
  - 3.2363% Phenyl Trimethicone in a SPF cream (25 subjects)
  - 2% Trimethylsiloxyphenylphenyl Dimethicone in a serum (28 subjects)
- 3 HRIPTs
  - 0.5% Diphenylsiloxy Phenyl Trimethicone in an ampoule (112 subjects)
  - 3% Trimethylsiloxyphenyl Dimethicone in a cream (103 subjects)
  - 5% Trimethylsiloxyphenyl Dimethicone in a shine gloss (18 subjects)
- 7.5% Phenyl Trimethicone; Photocontact allergenicity assay of a lotion (27 subjects)
- 26.18% Phenyl Trimethicone; Maximization assay of a concealer (26 subjects)
- 2% Trimethylsiloxyphenyl Dimethicone; Photo-allergenicity test of a serum (26 subjects)

May 18, 2022:

- 15% Diphenyl Dimethicone; LLNA in CBA mice
- 15% Diphenyl Dimethicone; 13-wk, repeated dose oral toxicity study in rats
- 4 HRIPTs:
  - 2% Diphenyl Dimethicone; Modified Marzulli-Maibach (111 subjects)
  - 0.2% Phenyl Methicone; Marzulli-Maibach (107 subjects)
  - 28.67% Phenyl Trimethicone (203 subjects)
  - 38.006% Trimethylsiloxyphenyl Dimethicone (205 subjects)

May 20, 2022:

- 100% Diphenyl Dimethicone: Buehler test in guinea pigs; 24-h primary dermal irritation test in rabbits

- 100% Diphenylsiloxy Phenyl Trimethicone ; LLNA in mice; primary dermal irritation test in rabbits

September 2022

-A Draft Report is being presented to the Panel.

Phenyl-Substituted Methicones Data Profile* – September 26-27, 2022 – Writer, Preethi Raj

				Toxicokinetics			Acute Tox			Repeated Dose Tox			DART		Genotox		Carci		Dermal Irritation			Dermal Sensitization				Ocular Irritation		Clinical Studies	
	Reported Use	Method of Mfg	Impurities	log P/log K_{ow}	Dermal Absorption	ADME	Dermal	Oral	Inhalation	Dermal	Oral	Inhalation	Dermal	Oral	In Vitro	In Vivo	Dermal	Oral	In Vitro	Animal	Human	In Vitro	Animal	Human	Phototoxicity	In Vitro	Animal	Retrospective/ Multicenter	Case Reports
Diphenyl Dimethicone	X							X	X		X									X	X		X	X			X		
Diphenylsiloxy Phenyl Trimethicone	X				X		X	X			X			X	X					X	X		X	X			X		
Diphenylsiloxy Phenyl/Propyl Trimethicone	X																												
Phenyl Dimethicone	X																												
Phenyl Methicone	X											X									X			X			X		
Phenyl Trimethicone	X	O			O	X	O	OX		O		O	O	OX	O					OX	OX		OX	OX	X		OX		
Trimethylsiloxyphenyl Dimethicone	X																				X			X	X				

* "X" indicates that data were available in a category for the ingredient; "O" indicates that data from the original assessment were available

[Phenyl-Substituted Methicones – 7 ingredients]

Ingredient	CAS #	PubMed	FDA	HPVIS	NIOSH	NTIS	NTP	FEMA	EU	ECHA	ECETOC	SIDS	SCCS	AICIS	FAO	WHO	Web
Diphenyl Dimethicone	68083-14-7	NR	NR	NR	NR	✓*	NR	NR	✓*	✓*	NR	NR	NR	NR	NR	NR	✓*
Diphenylsiloxy Phenyl/Propyl Trimethicone	NR	NR	NR	NR	NR	NR	NR	NR	✓*	NR	NR	NR	NR	NR	NR	NR	✓*
Diphenylsiloxy Phenyl Trimethicone	352230-22-9	NR	NR	NR	NR	NR	NR	NR	✓*	✓	NR	NR	NR	✓	NR	NR	✓*
Phenyl Dimethicone	9005-12-3	NR	NR	NR	NR	✓*	NR	NR	✓*	NR	NR	NR	NR	NR	NR	NR	✓*
Phenyl Methicone	31230-04-03 63148-58-3	✓*	NR	NR	NR	✓*	NR	NR	✓*	NR	NR	NR	NR	NR	NR	NR	✓*
Phenyl Trimethicone	NR	NR	NR	NR	NR	NR	✓*	NR	NR	✓*	✓	NR	NR	NR	NR	NR	✓*
Trimethylsiloxyphenyl Dimethicone	73138-88-2	✓*	NR	NR	NR	NR	NR	NR	✓*	NR	NR	NR	NR	NR	NR	NR	✓*

✓ - relevant data available; ✓* - data available, but not relevant; NR- not reported

Search Strategy

[*total # of hits / # hits that were useful*]

Pubmed

((((((((((((((diphenyl dimethicone) OR (68083-14-7)) OR (diphenylsiloxy phenyl/propyl trimethicone)) OR (diphenylsiloxy phenyl trimethicone)) OR (352230-22-9)) OR (Hydrogen Diphenyl Dimethicone)) OR (68037-60-5)) OR (Phenyl Dimethicone)) OR (9005-12-3)) OR (Phenyl Methicone)) OR (31230-04-03)) OR (63148-58-3)) OR (Phenyl Trimethicone)) OR (Triphenyl Trimethicone)) OR (Trimethylsiloxyphenyl Dimethicone)) OR (73138-88-2) – 251/0

((diphenyl dimethicone) OR (68083-14-7)) AND (toxicity) – 0/0
diphenylsiloxy phenyl/propyl trimethicone AND toxicity – 0/0
((diphenylsiloxy phenyl trimethicone) OR (352230-22-9)) AND (toxicity)- 0/0
((Hydrogen Diphenyl Dimethicone) OR (68037-60-5)) AND (toxicity) -0/0
((Phenyl Dimethicone) OR (9005-12-3)) AND (toxicity) – 0/0
((Phenyl Methicone) OR (31230-04-03)) AND (toxicity) – 40/0
(phenyl trimethicone) AND (toxicity) -0/0
(triphenyl trimethicone) AND (toxicity)- 0/0
((73138-88-2) OR (Trimethylsiloxyphenyl Dimethicone)) AND (toxicity) – 19/0

Google Search
diphenyl dimethicone acute oral toxicity – 13/0
diphenyl dimethicone short term oral toxicity – 46/2
diphenyl dimethicone subchronic oral toxicity – 55/0
diphenyl dimethicone chronic oral toxicity – 62/0
diphenyl dimethicone dermal toxicity – 37/0
diphenyl dimethicone acute dermal toxicity – 55/0
diphenyl dimethicone short term dermal toxicity- 45/0
diphenyl dimethicone subchronic dermal toxicity- 27/0
diphenyl dimethicone chronic dermal toxicity – 38/0
diphenyl dimethicone inhalation toxicity – 43/0
diphenyl dimethicone acute inhalation toxicity- 25/0
diphenyl dimethicone short term inhalation toxicity – 37/0
diphenyl dimethicone subchronic inhalation toxicity – 45/0
diphenyl dimethicone chronic inhalation toxicity- 11/0
diphenyl dimethicone developmental toxicity- 48/0
diphenyl dimethicone reproductive toxicity – 38/0
diphenyl dimethicone dermal sensitization – 33/0
diphenyl dimethicone genotoxicity -80/1
diphenyl dimethicone mutagenicity – 99/0
diphenyl dimethicone carcinogenicity- 112/0

diphenylsiloxy phenyl trimethicone acute oral toxicity – 12/0
diphenylsiloxy phenyl trimethicone short term oral toxicity – 29/0
diphenylsiloxy phenyl trimethicone subchronic oral toxicity – 10/0
diphenylsiloxy phenyl trimethicone chronic oral toxicity – 28/2
diphenylsiloxy phenyl trimethicone dermal toxicity – 37/0
diphenylsiloxy phenyl trimethicone acute dermal toxicity – 15/0
diphenylsiloxy phenyl trimethicone short term dermal toxicity- 26/0
diphenylsiloxy phenyl trimethicone subchronic toxicity- 10/0
diphenylsiloxy phenyl trimethicone chronic dermal toxicity – 27/0
diphenylsiloxy phenyl trimethicone inhalation toxicity – 30/0
diphenylsiloxy phenyl trimethicone acute inhalation toxicity- 13/0
diphenylsiloxy phenyl trimethicone short term inhalation toxicity – 11/0
diphenylsiloxy phenyl trimethicone subchronic inhalation toxicity – 12/0
diphenylsiloxy phenyl trimethicone chronic inhalation toxicity- 14/0
diphenylsiloxy phenyl trimethicone developmental toxicity- 53/0
diphenylsiloxy phenyl trimethicone reproductive toxicity – 24/0
diphenylsiloxy phenyl trimethicone dermal sensitization – 48/0
diphenylsiloxy phenyl trimethicone genotoxicity - 15/0
diphenylsiloxy phenyl trimethicone mutagenicity – 30/0
diphenylsiloxy phenyl trimethicone carcinogenicity- 19/0

Phenyl trimethicone acute oral toxicity-34/0
Phenyl trimethicone shortterm oral toxicity – 72/0
Phenyl trimethicone subchronic oral toxicity – 33/0
Phenyl trimethicone chronic oral toxicity – 54/0
phenyl trimethicone dermal toxicity – 148/0
phenyl trimethicone acute dermal toxicity – 45/0
phenyl trimethicone shortterm dermal toxicity- 109/0
phenyl trimethicone subchronic toxicity- 27/0
phenyl trimethicone chronic dermal toxicity – 51/0
phenyl trimethicone inhalation toxicity – 80/0
phenyl trimethicone acute inhalation toxicity- 37/0
phenyl trimethicone short term inhalation toxicity – 74/0
phenyl trimethicone subchronic inhalation toxicity – 42/0
phenyl trimethicone chronic inhalation toxicity- 78/0
phenyl trimethicone developmental toxicity- 133/0
phenyl trimethicone reproductive toxicity – 100/0
phenyl trimethicone dermal sensitization – 103/0
phenyl trimethicone genotoxicity -112/1

phenyl trimethicone mutagenicity – 105/0
phenyl trimethicone carcinogenicity- 137/0
phenyl trimethcone comedogenic – 159/0
phenyl trimethicone depigmentation – 167/0
phenyl trimethicone phototoxicity – 101/0

Polymethylphenylsiloxane toxicity – 13,200/2
Methyl phenyl polysiloxane toxicity – 622,000/2
Polyphenylmethylsiloxane toxicity – 7,910/0

LINKS

Search Engines

- Pubmed - http://www.ncbi.nlm.nih.gov/pubmed
  - appropriate qualifiers are used as necessary
  - search results are reviewed to identify relevant documents
- Connected Papers - https://www.connectedpapers.com/

Pertinent Websites

- wINCI - http://webdictionary.personalcarecouncil.org
- FDA databases http://www.ecfr.gov/cgi-bin/ECFR?page=browse
- FDA search databases: http://www.fda.gov/ForIndustry/FDABasicsforIndustry/ucm234631.htm;,
- Substances Added to Food (formerly, EAFUS): https://www.fda.gov/food/food-additives-petitions/substances-added-food-formerly-eafus
- GRAS listing: http://www.fda.gov/food/ingredientspackaginglabeling/gras/default.htm
- SCOGS database: http://www.fda.gov/food/ingredientspackaginglabeling/gras/scogs/ucm2006852.htm
- Indirect Food Additives: http://www.accessdata.fda.gov/scripts/fdcc/?set=IndirectAdditives
- Drug Approvals and Database: http://www.fda.gov/Drugs/InformationOnDrugs/default.htm
- FDA Orange Book: https://www.fda.gov/Drugs/InformationOnDrugs/ucm129662.htm
- (inactive ingredients approved for drugs: http://www.accessdata.fda.gov/scripts/cder/iig/
- HPVIS (EPA High-Production Volume Info Systems) - https://iaspub.epa.gov/oppthpv/public_search.html_page
- NIOSH (National Institute for Occupational Safety and Health) - http://www.cdc.gov/niosh/
- NTIS (National Technical Information Service) - http://www.ntis.gov/
  - technical reports search page: https://ntrl.ntis.gov/NTRL/
- NTP (National Toxicology Program) - http://ntp.niehs.nih.gov/
- Office of Dietary Supplements https://ods.od.nih.gov/
- FEMA (Flavor & Extract Manufacturers Association) GRAS: https://www.femaflavor.org/fema-gras
- EU CosIng database: http://ec.europa.eu/growth/tools-databases/cosing/
- ECHA (European Chemicals Agency – REACH dossiers) – http://echa.europa.eu/information-on-chemicals;jsessionid=A978100B4E4CC39C78C93A851EB3E3C7.live1
- ECETOC (European Centre for Ecotoxicology and Toxicology of Chemicals) - http://www.ecetoc.org
- European Medicines Agency (EMA) - http://www.ema.europa.eu/ema/
- OECD SIDS (Organisation for Economic Co-operation and Development Screening Info Data Sets)- http://webnet.oecd.org/hpv/ui/Search.aspx
- SCCS (Scientific Committee for Consumer Safety) opinions: http://ec.europa.eu/health/scientific_committees/consumer_safety/opinions/index_en.htm
- AICIS (Australian Industrial Chemicals Introduction Scheme)- https://www.industrialchemicals.gov.au/
- International Programme on Chemical Safety http://www.inchem.org/
- FAO (Food and Agriculture Organization of the United Nations) - http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/jecfa-additives/en/
- WHO (World Health Organization) technical reports - http://www.who.int/biologicals/technical_report_series/en/
- www.google.com - a general Google search should be performed for additional background information, to identify references that are available, and for other general information

Safety Assessment of Phenyl-Substituted Methicones as Used in Cosmetics

Status: Draft Report for Panel Review
Release Date: September 1, 2022
Panel Meeting Date: September 26-27, 2022

The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; David E. Cohen, M.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; Allan E. Rettie, Ph.D.; David Ross, Ph.D.; Thomas J. Slaga, Ph.D.; Paul W. Snyder, D.V.M., Ph.D.; and Susan C. Tilton, Ph.D. The Cosmetic Ingredient Review (CIR) Executive Director is Bart Heldreth, Ph.D. This safety assessment was prepared by Preethi Raj, Senior Scientific Analyst/Writer, CIR.

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ABBREVIATIONS

AICIS	Australian Industrial Chemicals Introduction Scheme
CAS	Chemical Abstracts Service
CII	cumulative irritation index
CIR	Cosmetic Ingredient Review
Council	Personal Care Products Council
CPSC	Consumer Product Safety Commission
cSt	centistokes
Dictionary	*International Cosmetic Ingredient Dictionary and Handbook*
DPM	disintegrations per minute
ECHA	European Chemicals Agency
FDA	Food and Drug Administration
GHS	Globally Harmonized System
HRIPT	human repeat insult patch test
LC	lethal concentration
LD	lethal dose
LLNA	local lymph node assay
MED	minimal erythema dose
MII	mean irritation index
MMTS	maximum mean total score
MW	molecular weight
NOAEL	no-observed-adverse-effect-level
N/A	not applicable
NR	not reported/none reported
NS	not specified
NTP	National Toxicology Program
OECD	Organisation for Economic Co-operation and Development
Panel	Expert Panel for Cosmetic Ingredient Safety
PII	primary irritation index
SI	stimulation index
SIOPT	single insult occlusive patch test
SLS	sodium lauryl sulfate
SPF	sun protection factor
TG	test guideline
US	United States
UV	ultraviolet
UVA/UVB	ultraviolet radiation A/ ultraviolet radiation B
VCRP	Voluntary Cosmetic Registration Program

INTRODUCTION

This assessment reviews the safety of the following 7 phenyl-substituted methicones as used in cosmetic formulations:

Diphenyl Dimethicone
Diphenylsiloxy Phenyl Trimethicone
Diphenylsiloxy Phenyl/Propyl Trimethicone
Phenyl Dimethicone
Phenyl Methicone
Phenyl Trimethicone
Trimethylsiloxyphenyl Dimethicone

According to the web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI; *Dictionary*), the majority of the ingredients included in this assessment are reported to function in cosmetics as anti-foaming agents and skin and/or hair conditioning agents (Table 1).[1]

The rationale for this grouping of ingredients stems from the fact that these ingredients are structurally-related as phenyl-substituted methicones (i.e. polymers of methicone and dimethicone). In 2022, the Expert Panel for Cosmetic Ingredient Safety (Panel) issued a final amended report on 30 dimethicone, methicone, and methicone-substituted polymers, with the conclusion that these ingredients are safe in cosmetics in the present practices of use and concentration described in the safety assessment when formulated to be non-irritating, with the exception that the available data are insufficient to make a determination of safety for use of these ingredients in products that may be incidentally inhaled when applied using airbrush devices.[2]

In 1986, the Panel published a final report on the safety of Phenyl Trimethicone, with the conclusion that Phenyl Trimethicone is safe as a cosmetic ingredient in the practices of use and concentration described in the safety assessment.[3] The Panel reaffirmed this conclusion in 2006.[4] Excerpts of summarized data from the original 1986 safety assessment of Phenyl Trimethicone are included throughout the text of this document, as appropriate, and are identified by *italicized text*. (This information is not included in the tables or Summary section.) For complete and detailed information, the original report can be accessed on the Cosmetic Ingredient Review (CIR) website (https://www.cir-safety.org/ingredients).

This safety assessment includes relevant published and unpublished data that are available for each endpoint that is evaluated. Published data are identified by conducting an exhaustive search of the world's literature. A listing of the search engines and websites that are used and the sources that are typically explored, as well as the endpoints that the Panel typically evaluates, is provided on the CIR website (https://www.cir-safety.org/supplementaldoc/preliminary-search-engines-and-websites; https://www.cir-safety.org/supplementaldoc/cir-report-format-outline). Unpublished data are provided by the cosmetics industry, as well as by other interested parties.

Much of the data included in this safety assessment was found on the European Chemicals Agency (ECHA)[5,6] and Australian Industrial Chemicals Introduction Scheme (AICIS)[7] websites. Please note that these sources provide summaries of information generated by industry, and it is those summary data that are reported in this safety assessment when these sources are cited.

CHEMISTRY

Definition and Structure

The definitions and structures of the phenyl-substituted methicones included in this review are provided in Table 1. The ingredients in this group are all phenyl-substituted methicones (siloxane polymers). Generically, ingredients are organic derivatives of silica, SiO_2, with organic groups replacing some of the oxygens in the polymeric silica molecule.[3] These polymers comprise an alternating framework of silicon with other molecules. The interspersed molecules are covalently bonded to the silicon through a carbon-silicon linkage.

For example, Diphenylsiloxy Phenyl Trimethicone (CAS No. 352230-22-9) is a siloxane polymer that conforms to the idealized structure depicted in Figure 1.

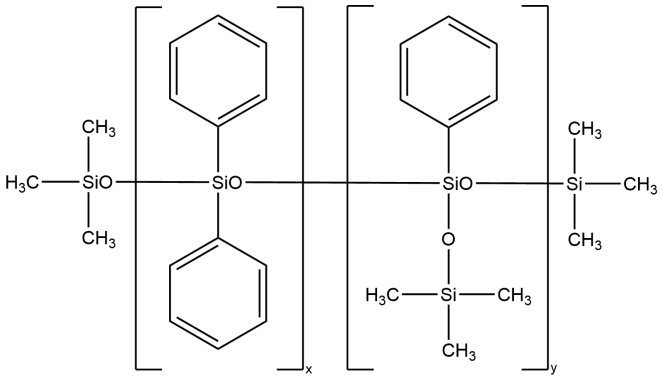


Figure 1. Diphenylsiloxy Phenyl Trimethicone (x and y are undefined)

Chemical Properties

Phenyl Trimethicone is a water white, almost odorless, fluid silicone polymer.[3] Physicochemical properties of Phenyl Trimethicone include a boiling point of 265 °C (at 760 mm Hg), specific gravity of 0.970 (at 25 °C), kinematic viscosity between 5 - 30 centistokes [cSt], a refractive index of 1.459, and a total acid number of 0.25 (maximum). The ultraviolet spectrum for Phenyl Trimethicone indicates weak absorbance centered at approximately 327 nm.

No additional chemical properties data were found in the published literature, and unpublished data were not submitted.

Method of Manufacture

In one industrial process, silica is first converted to tetraethoxysilane, and the ethoxy groups are replaced with the desired chemical 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.

No additional methods of manufacture data were found in the published literature, and unpublished data were not submitted.

Impurities

Impurities data were not found in the published literature, and unpublished data were not submitted.

USE

Cosmetic

The safety of the cosmetic ingredients addressed in this assessment is evaluated based on data received from the US Food and Drug Administration (FDA) and the cosmetics industry on the expected use of these ingredients in cosmetics, and does not cover their use in airbrush delivery systems. Data are submitted by the cosmetic industry via the FDA's Voluntary Cosmetic Registration Program (VCRP) database (frequency of use) and in response to a survey conducted by the Personal Care Products Council (Council) (maximum use concentrations). The data are provided by cosmetic product categories, based on 21CFR Part 720. For most cosmetic product categories, 21CFR Part 720 does not indicate type of application and, therefore, airbrush application is not considered. Airbrush delivery systems are within the purview of the US Consumer Product Safety Commission (CPSC), while ingredients, as used in airbrush delivery systems, are within the jurisdiction of the FDA. Airbrush delivery system use for cosmetic application has not been evaluated by the CPSC, nor has the use of cosmetic ingredients in airbrush technology been evaluated by the FDA. Moreover, no consumer habits and practices data or particle size data are publicly available to evaluate the exposure associated with this use type, thereby preempting the ability to evaluate risk or safety.

According to 2022 VCRP survey data, Phenyl Trimethicone has the greatest reported frequency of use; it is reported to be used in 781 formulations, 722 of which are leave-on products (Table 2).[8] Diphenylsiloxy Phenyl Trimethicone is reported to be used in 269 formulations, and Diphenyl Dimethicone is reported to be used in 145 formulations (Table 3). The results from concentration of use surveys conducted by the Council in 2021 and 2022 indicate that Phenyl Trimethicone has the highest reported maximum concentration of use, at 59.5% in non-coloring shampoos; it also has the highest reported maximum concentration of use in leave-on formulations, at up to 24.8% (in other makeup preparations).[9,10] Use concentration data were reported for Diphenylsiloxy Phenyl/Propyl Trimethicone in makeup bases at 5.3%, but no uses were received in the VCRP; it should be presumed there is at least one use in this category.

Since its last review in 2006, the reported frequency and concentrations of use have increased for Phenyl Trimethicone. Notably, reported uses in non-coloring hair products have increased from 69 to 216 and the maximum reported concentrations

of use for this category have also increased from 18% to 59.5%.[4,8,10] Recent and historical frequency and concentration of use data for Phenyl Trimethicone are provided in Table 2.

Several of the ingredients are reported to be used in products applied near the eye (e.g., Diphenylsiloxy Phenyl Trimethicone is used at up to 19.9% in eyeliners), and in products that can result in incidental ingestion (e.g., Diphenyl Dimethicone is used at up to 24.1% in lipsticks). Phenyl Trimethicone is reported to be used in baby products at up to 6.5%.

Some of these ingredients are used in formulations that could possibly be inhaled; for example, Phenyl Trimethicone is reported to be used at up to 7.5% in aerosol hair sprays, at up to 15.6% in face powders, and at up to 2.2% in deodorants. In practice, as stated in the Panel's respiratory exposure resource document (https://www.cir-safety.org/cir-findings), most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and tracheobronchial regions and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount. There is some evidence indicating that deodorant spray products can release substantially larger fractions of particulates having aerodynamic equivalent diameters in the range considered to be respirable. However, the information is not sufficient to determine whether significantly greater lung exposures result from the use of deodorant sprays, compared to other cosmetic sprays. Conservative estimates of inhalation exposures to respirable particles during the use of loose powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace.

Although products containing some of these ingredients may be marketed for use with airbrush delivery systems, this information is not available from the VCRP or the Council survey. Without information regarding the frequency and concentrations of use of these ingredients, and without consumer habits and practices data or particle size data related to this use technology, the data are insufficient to evaluate the exposure resulting from cosmetics applied via airbrush delivery systems.

The phenyl-substituted methicone ingredients named in the report are not restricted from use in any way under the rules governing cosmetic products in the European Union.[11]

Non-Cosmetic

Phenyl Methicone and Phenyl Trimethicone are both approved as indirect food additives, and are used as adhesives in the components of articles intended for use in the packaging, transporting, or holding of food [21CFR § 175.105]. Additionally, Phenyl Trimethicone is an approved indirect food additive used as a polymeric coating for food-contact surfaces of articles intended for use in food processing, manufacture, and packaging [21CFR § 175.300]; furthermore, Phenyl Trimethicone is required to contain no more than 2%, by weight, of cyclosiloxanes, having up to and including 4 siloxy units, for this use.

TOXICOKINETIC STUDIES

Dermal Absorption

The dermal absorption of Phenyl Trimethicone was evaluated in 5 male subjects.[3] During a 25-d pretest period, baseline analysis of 24-h silicon urine levels was conducted. Phenyl Trimethicone (50 mg/kg) was applied once daily over the entire back surface of the 5 subjects for 10 d; the test material remained on the skin for 20 h, before the excess was removed by washing. Blood and urine silicon concentrations obtained on day 1, 3, 6, 8, and 10 of treatment did not show any significant increases in blood or urinary silicon concentrations.

Diphenylsiloxy Phenyl Trimethicone

Based on its physicochemical properties, Diphenylsiloxy Phenyl Trimethicone has an estimated dermal absorption value of 10%.[7]

Absorption, Distribution, Metabolism, and Excretion (ADME)

Phenyl Trimethicone

Seven rats were fed Phenyl Trimethicone (4% in the diet; between 944 – 1071 mg), with olive oil and rat cake powder (16% and 80% of the diet, respectively) for 8 d.[12] Tissues, feces, and urine were examined for test article presence. No silicon was found in the lipids of the gastrointestinal tract, feces, liver, kidney, or fat depots of control animals which were only fed rat cake powder and olive oil. For animals treated with Phenyl Trimethicone, almost all of the siloxane was recovered as silicon in the feces or gastrointestinal tract, indicating no siloxane absorption (mean % siloxane fluid recovery of 96.0 ± 1.0).

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

An acute, 24-h, dermal application of Phenyl Trimethicone was considered non-toxic to 10 albino rats when administered at 2000 mg/kg via an occlusive sleeve.[3] In 3 separate experiments, no deaths occurred in groups of 10 male albino mice which received a single oral dose of 10 ml/kg of a cosmetic product, containing 10% Phenyl Trimethicone. Single doses of Phenyl Trimethicone, ranging from 10,200 - 34,600 mg/kg were orally administered to groups of 8 male and 8 female Sprague-Dawley rats, and the animals were observed for 14 d before necropsy. One rat in the 34,600 mg/kg group died; others at the

highest dose exhibited hypoactivity, muscular weakness, diarrhea, diuresis, ruffled fur, and weight loss. No significant gross lesions were found in the tissues and organs; the test material was deemed non-toxic. No mortality, body weight changes, behavioral changes, or gross pathological changes occurred in 540 male rats administered an oral dose of 3.3 mg/kg Phenyl Trimethicone for 7 d. An acute, oral, 5 ml/kg dose of a product containing 5% Phenyl Trimethicone resulted in leg weakness, transient vasodilation of the ears, and hypoactivity in 5 male and 5 female Sprague-Dawley rats; these effects resolved within 6 h post-treatment and no deaths occurred.

The acute dermal, oral, and inhalation toxicity studies summarized below are described in Table 4.

The acute dermal LD_{50} of Diphenylsiloxy Phenyl Trimethicone, when applied under semi-occlusion to male and female Wistar rats, was determined to be > 2000 mg/kg.[6,7] The acute oral LD_{50} of Diphenyl Dimethicone, administered via a stomach tube at doses of 8190, 16,380, 32,770, or 65,540 mg/kg in rats, was determined to be > 65,540 mg/kg bw.[13] One rat from each of the 3 highest dose groups died 3 or more days after dosing, exhibiting diffuse pulmonary and hepatic hemorrhage; no other gross abnormalities were found upon necropsy. In other acute oral toxicity studies, the LD_{50} value for Diphenylsiloxy Phenyl Trimethicone was > 2000 mg/kg in female Wistar Han rats,[6,7] and the LD_{50} values for Phenyl Trimethicone were ≥ 2000 mg/kg in female Wistar rats and > 5000 mg/kg in male and female rats.[5] The acute oral LD_{50} value for a test material comprising 78-82% Phenyl Trimethicone and 18-22% Polysilicone-11 was determined to be > 5000 mg/kg in male and female Wistar-derived albino rats.[14]

In an acute inhalation toxicity study of Diphenyl Dimethicone, groups of 5 male and 5 female albino rats were exposed to the test article (whole body) at concentrations of 5, 10, 23, 24, 42, 90, 101, 168, or 214 mg/l for 1 h.[13] One animal from the 42 mg/l and one from the 101 mg/l group died during the exposure period. Within 24 h of exposure, 3 animals each from the 10 mg/l and 168 mg/l groups, 6 animals each from the 23 mg/l and 42 mg/l groups, 7 animals each from the 24 mg/l and 101 mg/l groups, 8 animals from the 90 mg/l group, and 1 animal from the 214 mg/l group, died. At higher volumes of dispensation (≥ 101 mg/l), residues accumulated on the hot plate. The lower conductivity of these concentrations was suspected to modify temperature and vaporization, thus, resulting in lower mortality than at intervening dose levels. Granular livers were observed in ~30% of the animals exposed to ≥ 24 mg/l, and enlarged and hyperemic lymph nodes were noted in several rats in each dosage group. (No further details were provided.) Severe and diffuse pulmonary hemorrhages accounted for most of the deaths and pulmonary consolidation was found in surviving animals. The LC_{50} was determined to be 18 mg/l.

Short-Term Toxicity Studies

Dermal

No adverse effects were observed in 4 rabbits which received daily dermal applications of 50 ml/kg Phenyl Trimethicone for 20 d.[3] Groups of 10 New Zealand albino rabbits were dermally treated with 2, 6, or 20 mg/kg Phenyl Trimethicone, in polypropylene glycol (control), for 20 d. Local skin reactions were characterized by slight desquamation at the application site of both test and control animals. No toxic effects were noted in body weight, hematological values, blood chemistry, urine analysis, and gross or microscopic pathological findings of the test or control groups. Ten male New Zealand rabbits were dosed for 28 d with 200 mg/kg Phenyl Trimethicone to evaluate dermal toxicity. No significant adverse effects were noted with reference to body weight, mortality, behavioral reactions, testicular histology, and spermatogenic activity.

Oral

Diphenylsiloxy Phenyl Trimethicone

In a short-term oral toxicity study, performed in accordance to the Organisation for Economic Development (OECD) test guideline (TG) 407, groups of Wistar Han rats (5/sex) were given 0, 200, 600, or 1000 mg/kg bw Diphenylsiloxy Phenyl Trimethicone, in corn oil, via gavage, for 28 d.[6,7] A statistically significant, 18 - 19% reduction in body weight gain was observed in male rats from the 1000 mg/kg group (when compared to controls) on day 8 and day 15 of observation. Significant reduction in body weight gain (48%, compared to controls) also occurred in female rats from the 600 and 1000 mg/kg groups on day 8. There were no reported treatment-related changes to food consumption in test animals. No treatment-related changes in hematology, clinical chemistry, urinalysis, or deaths occurred. Compared to controls, relative liver weights increased by 12%, 22%, and 18% for low-, mid-, and, high-dose groups for the male rats, respectively, while relative liver weights increased by 23%, 29%, and 43% for low-, mid-, and high-dose groups for the female rats, respectively. Treatment-related microscopic liver changes, such as the following, were observed: hepatocellular hypertrophy (ranging from minimal to moderate degrees) in all test animals, increased incidence or severity of change in fatty tissue deposition in the livers of males from the high dose group and in all of the test females, and the increased incidence of bile duct production in males from the mid dose group and females from the low and mid dose groups. Minimal hypertrophic changes in the follicular epithelium of the thyroid gland were observed in 2 males from the low-dose group, 1 male from the mid-dose group, and 4 males from the high-dose group. The authors considered the hepatic hypertrophy adaptive, and the thyroid changes as secondary, and a result of the metabolic turnover of thyroid hormones. The no-observed-adverse-effect level (NOAEL) was determined to be > 1000 mg/kg.

Inhalation

Five male and 5 female rats were exposed (whole body) to an aerosol containing 3% Phenyl Trimethicone, twice daily, 5 d/wk, for 4 wk.[3] A single exposure consisted of a 30-sec burst, followed by a 15-min exposure to the test material within a 350

l inhalation chamber. The animals exposed to the Phenyl Trimethicone aerosol gained slightly less weight than the controls; no other toxic effects were observed.

Phenyl Methicone

Phenyl Methicone (9.2 cSt, at 25 °C) was aspirated into a mist at a rate of 67.4 mg/min, and administered in a chamber at a concentration of 0.52 mg/l, whole body, to 1 cat, 2 guinea pigs, 2 rabbits, and 4 rats for 7 h/d, over 10 d.[15] None of the animals died during and after exposure. Histopathological examination did reveal moderate degenerative changes in the livers of cats and guinea pigs. However, in the absence of control data, moderate degenerative changes in livers of the cats and guinea pigs were considered only circumstantially associated with siloxane exposure.

Subchronic Toxicity Studies

Dermal

The dermal toxicity of a skin moisturizer containing 2.5% Phenyl Trimethicone was evaluated for 90 d in groups of 10 New Zealand white rabbits.[3] Two treatment groups were administered 5.5 or 8.4 mg/cm^2 per 8.4% body surface area of the test article, and compared to a control group. Erythema, slight edema, and slight desquamation were observed in both groups throughout the experiment. These effects appeared slightly more severe at the 8.4 mg/cm^2 dose during the first month of exposure; no differences between dose groups were observed by the second month. Signs of dermal irritation were nearly maximal in the first week and increased gradually in severity during the last month of exposure. No treatment-related effects in hematology, clinical chemistry, organ weights, or histopathology were observed.

Oral

Diphenyl Dimethicone

Groups of 10 male and 10 female Sprague-Dawley rats were dosed with 0, 5, 20, or 80 mg/kg/d of a mixture containing 15% Diphenyl Dimethicone (in a vehicle solution of 10% polyethylene glycol 660 hydroxystearate, in purified water), via gavage, for 90 d.[16] The animals were observed daily for mortality and clinical abnormalities; body weights and food consumption were recorded weekly. Animals were killed at the end of treatment; post-mortem evaluation of animal organs and hematological parameters, including glucose, triglycerides, white blood cell counts, and prothrombin time, as well as urinalysis, were performed. No deaths related to treatment with the test article occurred and no changes were observed in body weight and food consumption. Higher absolute and relative liver weights in animals given 80 mg/kg were considered to be treatment-related and were correlated with slight hepatocellular hypertrophy seen in 8 males and 10 females in the 80 mg/kg group; both effects were considered toxicologically-significant. Liver enlargement was noted in 3 males from the 80 mg/kg group, which was attributed to treatment with the test article. Higher liver weight was noted in females from the 5 and 20 mg/kg/d groups, but these effects were not related to relevant microscopic findings and were therefore not considered toxicologically-significant. Other statistically-significant differences (including higher prothrombin time in males given 80 mg/kg and lower mean leukocyte counts in all the test group females) were not considered toxicologically-significant, as they were minimal, without a dose-response relationship, did not exhibit any trend between the sexes, and individual values were within the expected historical range. The NOAEL for the test item containing 15% Diphenyl Dimethicone was determined to be 20 mg/kg/d.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY STUDIES

Dermal

Phenyl Trimethicone was tested in several dermal developmental and reproductive toxicity studies.[3] In one study using 3 groups of 26 rats and 3 groups of 15 rabbits, 50 or 500 mg/kg Phenyl Trimethicone was applied topically to 2 groups of each species on days 6-16 or 6-18 of gestation, respectively. Untreated animals served as controls. Rats were killed on day 20 and rabbits were killed on day 30, while untreated animals served as controls. Fetuses were removed by cesarean section, and one half were examined microscopically, while the other half were examined for skeletal abnormalities. In the rats, the mean number of implantation sites and mean number of live fetuses derived from control and test group dams were comparable; however, 10 fetuses from the low-dose group and 3 fetuses from the high-dose group had incompletely developed sternebrae. A greater number of rat fetuses derived from the test groups had bipartite sternebrae and lack of closure of the coronal suture, compared to controls. Of the rabbits tested, one dam died in the control group and two animals died from the low-dose group. The control rabbit group had a greater mean number of implantation sites than the test groups, although the mean number of live fetuses from all 3 groups was comparable. None of the dead rabbit fetuses delivered from the control (8), low-dose (9), or high-dose (2) groups were abnormal, besides showing signs of immaturity. All live pups had fully developed sternebrae and normal ribs with no abnormalities in the soft tissues; the delayed ossification found in both test groups of rats was therefore considered a species variation. Two separate studies evaluated the teratogenicity of Phenyl Trimethicone, in groups of 10 or 15 rabbits; 200 mg/kg of the test material was applied on days 6-18 of gestation in both studies. Rabbits in the first study received either 200 mg/kg Phenyl Trimethicone in corn oil, corn oil, or were untreated. A slight but significant increase in the number of resorption sites and decreased viability of the Phenyl Trimethicone-treated fetuses was observed. Rabbits in the second study received either 200 mg/kg Phenyl Trimethicone (undiluted), sesame oil, or were untreated. No deaths, unusual

reactions, or adverse effects on maternal body weight, or the viability and external/internal development of the fetuses was observed. Consequently, Phenyl Trimethicone was not considered teratogenic in either study.

Oral

Phenyl Trimethicone was assayed for effects upon uterine weights in groups of 6 immature female Wistar rats which were bilaterally ovariectomized 3 d prior to treatment.[3] On the fourth day, groups of 6 rats received 0.01, 0.1, 1, or 10 mg/kg Phenyl Trimethicone in sesame oil, via gavage; animals received a daily dose for 3 d and were necropsied after the final dose. Controls received the oil vehicle. No toxic effects or changes in uterine weights were observed in treated animals.

Diphenylsiloxy Phenyl Trimethicone

The effect of maternal (and paternal) consumption of Diphenylsiloxy Phenyl Trimethicone upon reproductive and developmental toxicity was evaluated, in accordance with OECD TG 422.[6] Groups of Sprague-Dawley rats (10/sex/group) were administered 0, 100, 500, or 1000 mg/kg bw/d, in corn oil, via gavage; both males and females were treated with the test substance 2 wk prior to, and during, mating. One group which received no treatment served as negative controls. Males were treated for 92 d and were killed at the end of the treatment period, while dams were treated up until postpartum day 3. Males, pups, and dams which delivered were killed on day 4 postpartum; mated females which did not deliver were killed on day 25 or 26 of gestation. No statistically significant changes in body weight, food consumption, or organ weights were observed. (Statistically-significant changes in body weight for females during week 2 of gestation were not toxicologically significant.) No treatment-related effects were apparent for reproductive endpoints in the parents, including testis weight, epididymis weight, mean gestation length, mean number of corpora lutea, mean number of implantation sites, mean mating and fertility indices, nor were there effects observed in the offspring for gross pathology, mean litter size, mean litter weight, or mean ration live births/litter size. Thus, under the conditions of this study, the NOAEL for reproductive (male and female) and developmental toxicity was determined to be ≥ 1000 mg/kg bw/d.

Phenyl Trimethicone

Groups of 20 male Wistar rats were given Phenyl Trimethicone, in oil, via gavage, at doses of 100, 300, or 1000 mg/kg bw, 5 d/wk, for 4 wk.[5] The main purpose of this study was to observe if testicle weight reduction occurred with repeated doses of the test article. No visible changes, body weight fluctuations, or deaths occurred during the course of the study. Animals were killed 24 h after the final dose, and testicles were weighed and examined microscopically. No effects on testicle weight or histology were observed. The NOAEL for effects on body weight, testicle weight, and histology was determined to be > 1000 mg/kg.

GENOTOXICITY STUDIES

In Vitro

Phenyl Trimethicone was not mutagenic in an Ames test using Salmonella strains, both with and without metabolic activation.[3] (Test concentrations were not stated.)

Diphenylsiloxy Phenyl Trimethicone

An Ames test was performed, in accordance with OECD TG 471, using *Salmonella typhimurium* strains TA 98, TA100, TA1535, TA1537 and *Escherichia coli* WP2 to determine the mutagenicity of Diphenylsiloxy Phenyl Trimethicone, with or without metabolic activation.[6,7] The test article, dissolved in ethanol, was administered at concentrations up to 5000 µg/plate, and appropriate positive and negative controls were used. The test article did not produce any mutagenic effects.

In a mammalian chromosomal aberration study performed in accordance with OECD TG 473, the genotoxic potential of Diphenylsiloxy Phenyl Trimethicone (in ethanol) was tested in the Chinese hamster lung (V79) cell line, with and without metabolic activation.[6,7] Cell lines were treated with 0.025 – 0.3 µl/ml of the test article for 4 h, 0.006 – 0.2 µl/ml for 18 h, or 0.013 – 0.1 µl/ml for 28 h, without metabolic activation; cells treated with metabolic activation were treated with either 0.003 – 0.2 µl/ml or 0.040 – 5 µl/ml of the test substance for 4 h. Appropriate positive and negative controls were used. Cells were treated prior to harvest with a metaphase-arresting substance, stained, and analyzed microscopically for induced cytotoxicity or the presence of chromatid-type and chromosome-type aberrations in cells undergoing metaphase. Cell numbers below 50% of the controls or poor metaphase quality were observed in cells treated with ≥ 0.15 µl/ml of the test substance in the absence of metabolic activation for 18 h. No statistically significant increase in the frequency of cells with chromosome aberrations was induced in either the absence or presence of metabolic activation. The test article was considered non-clastogenic to Chinese hamster lung cell lines.

CARCINOGENICITY STUDIES

No carcinogenicity studies were found in the published literature, and unpublished data were not submitted.

DERMAL IRRITATION AND SENSITIZATION STUDIES

An undiluted, 24-h dose of 0.5 ml Phenyl Trimethicone was non-irritating to the skin of 6 albino rabbits.[3] A foundation cream containing 5% Phenyl Trimethicone was applied at 0.5 ml to 6 rabbits, for 14 d; slight erythema, slight edema, and desquamation were observed. The cream had a primary irritation index of 1.9 (max =8) and was considered mildly irritating. Three separate products, each containing 10% Phenyl Trimethicone, were found to be slightly irritating to groups of 6 male New Zealand white rabbits when tested at 0.5 ml in single insult occlusive patch tests. Phenyl Trimethicone (tested at 5% in propylene glycol during induction, and at 10 and 20% in petrolatum during challenge) was not irritating or sensitizing to 10 female guinea pigs in a maximization test.[3]

In clinical testing, the cumulative irritation score of a moisturizer containing 2.5% Phenyl Trimethicone was found to be 13 (max=630) in 9 subjects.[3] The product was classified as a mild material (essentially no experimental irritation). Undiluted Phenyl Trimethicone was not found to be irritating or sensitizing in a human repeated insult patch test (HRIPT) of 50 subjects.[3] In an HRIPT using groups of 8 subjects, the highest total irritancy score of 17 cosmetic products, each containing 10% Phenyl Trimethicone, was 5 (max = 256) and the highest individual score was 1 (max = 8); overall, the products were considered minimally irritating. No irritation or sensitization was observed in 2 separate modified Draize-Shelanski HRIPTs of a cosmetic foundation containing 5% Phenyl Trimethicone (189 subjects) and a moisturizer containing 2.5% Phenyl Trimethicone (239 subjects).

The dermal irritation and sensitization studies summarized below are described in Table 5.

The sensitization potential of a product containing 15% Diphenyl Dimethicone (tested at concentrations of 2.5, 5, 10, 25, or 50%, in acetone: olive oil (4:1 v/v)) was evaluated using groups of 4 female CBA mice in a local lymph node assay (LLNA).[17] Two of 4 of the animals in the 10% group died on day 3 and 1 of the animals in the 50% group died on day 6; these deaths were not attributed to the test article. No positive lymphoproliferative responses were noted at any of the concentrations and the test article was deemed non-sensitizing. Diphenyl Dimethicone (100% pure and applied neat) was neither irritating when applied to 6 New Zealand white rabbits (0.5 ml) in a primary dermal irritation test, nor sensitizing in a Buehler test using 6 male and 6 female Hartley albino guinea pigs.[18] In a primary skin irritation test, performed in accordance OECD TG 404, a semi-occlusive application of 0.5 ml, 100 % pure Diphenylsiloxy Phenyl Trimethicone was not irritating when applied neat to the skin of 3 New Zealand white rabbits.[19] In a similar study, Diphenylsiloxy Phenyl Trimethicone was deemed slightly irritating (or non-irritating, in another description) to 1 male and 2 female New Zealand white rabbits; very slight to well-defined erythema was noted in all animals 1 h after patch removal and mean erythema/eschar scores were 0.33 for animal 1 and 2, and 0.67 for animal 3.[6,7] Very slight erythema persisted in all animals until the 24-h reading and in 1 animal at the 48-h reading; all effects were reversible within 72 h. Groups of 4 female mice were tested with Diphenylsiloxy Phenyl Trimethicone (tested at concentrations 25, 50, or 100% w/w in acetone: olive oil (4:1 v/v)) in two separate LLNAs.[6,7,19] All mice in the 100% group exhibited slight ear swelling on both ear lobes on day 2 and 3, and similar results were seen for all mice in the 50% group on day 3; these results persisted throughout the observation period; the test materials were not considered sensitizing. The one-time application of a mixture comprising 72-82% Phenyl Trimethicone and 18-22% Polysilicone-11 (0.5 ml) was not irritating to 6 New Zealand white rabbit skin in an acute skin irritation test.[20]

A 24-h single insult occlusive patch test (SIOPT) of a lip color formulation containing 9.06% Diphenyl Dimethicone and a modified Marzulli-Maibach human repeated insult patch test (HRIPT) of a formulation containing 2% Diphenyl Dimethicone were completed in 20 subjects and 111 subjects, respectively; the test materials were neither irritating nor sensitizing.[21,22] Two separate ampoule formulations containing 0.5 % Diphenylsiloxy Phenyl Trimethicone were not irritating in an occlusive, 24-h SIOPT performed in 20 subjects, and not sensitizing in an occlusive HRIPT performed in 112 subjects, respectively.[23,24] A sun protection factor (SPF) cream formulation containing 3.2363% Phenyl Trimethicone was not irritating in a 14-d cumulative irritation test performed in 25 subjects, and an eye primer formulation containing 10% Phenyl Trimethicone was not irritating in a 24-h SIOPT performed in 21 subjects.[25,26] A Marzulli-Maibach HRIPT of a formulation containing 0.2% Phenyl Methicone and a semi-occlusive HRIPT of a product containing 28.67% Phenyl Trimethicone were performed in 107 and 203 subjects, respectively; the test materials were neither irritating or sensitizing.[27,28] Similarly, a concealer formulation containing 26.18% Phenyl Trimethicone was not sensitizing to 26 subjects in a maximization assay.[29] A shine gloss formulation containing 5% Trimethylsiloxyphenyl Dimethicone and a serum formulation containing 2% Trimethylsiloxyphenyl Dimethicone did not cause irritation in a 24-h SIOPT of 18 subjects and in a 15-d cumulative irritation test of 28 subjects, respectively.[30,31] HRIPTs performed using a cream formulation containing 3% Trimethylsiloxyphenyl Dimethicone (103 subjects), a product containing 38.006% Trimethylsiloxyphenyl Dimethicone (205 subjects), and 100% pure Trimethylsiloxyphenyl Dimethicone (51 subjects) yielded negative results.[32-34]

Photosensitization/Photoallergy

Phenyl Trimethicone

The photosensitization potential of a lotion containing 7.5% Phenyl Trimethicone, and 2 other products, was assessed in a photocontact allergenicity assay of 27 subjects.[35] During the pre-testing phase, the minimal erythema dose (MED) of each subject was determined by exposing one side of the midback to a series of radiation exposures from a xenon arc solar simulator (290-400 nm; ultraviolet A radiation (UVA) = 75 mW/cm^2). During the induction phase the following procedure was

performed twice a wk, over 3 wk (total of 6 exposures): 24-h occlusive patch applications of 40 mg of the test materials were wiped dry, exposed to 2 MED doses, left open for 48 h, and exposed to a subsequent 24-h occlusive application, made to the same test site. After a 10-14 d rest period, during the challenge phase, the test materials were applied as done during the induction phase, in duplicate, to previously untreated sites; one set of patches were wiped dry and irradiated with 0.5 MED of solar simulated radiation plus 4 J/cm^2 of UVA. The second set of patches were not radiated and served as control treated sites. All test sites were examined for reactions at 48 and 72 h following UV radiation exposure. No reactions were observed at either timepoint. The test material was not considered to be a potential photosensitizer.

Trimethylsiloxyphenyl Dimethicone

The photo-allergic potential of a serum containing 2% Trimethylsiloxyphenyl Dimethicone was assessed in a similar manner to the study described above in 26 subjects (minor differences: 40 µl patch applications, UVA/UVB radiation during induction, one additional blank control was irradiated during challenge).[36] No reactions were observed, and the repeated dermal application of the test material was not contraindicated with sunlight exposure.

OCULAR IRRITATION STUDIES

Phenyl Trimethicone, tested undiluted (in 6 rabbits) and at 10% in 3 cosmetic products (in groups of 6 rabbits), was not considered irritating to rabbit eyes in several Draize tests.[3] Slight conjunctivitis occurred from instilling 0.10 ml of a foundation cream, containing 5% Phenyl Trimethicone in 6 albino rabbit eyes; no evidence of corneal dullness or iritis was observed.

The ocular irritation studies summarized below are described in Table 6.

Groups of 3 albino rabbits had Diphenyl Dimethicone instilled, undiluted (0.1 ml) into one eye.[13] In the first group eyes remained unwashed, while eyes were washed after 2 s or 4 s after exposure in a second and third group; eyes were observed for irritation for up to 7 d. A maximum score of 8 (out of 110), which indicated slight irritation was observed within 4 h for 1 animal in the second group. By day 3 all eyes appeared normal, regardless of rinsing status; the test article was considered slightly, and transiently irritating, to eyes of rabbits. According to the Globally Harmonized System (GHS) classification, Diphenylsiloxy Phenyl Trimethicone was not irritating to 1 male and 2 female New Zealand white rabbit eyes in an acute, 72-h ocular irritation study, performed in accordance with OECD TG 405.[6,7] When evaluated using Kay and Calandra criteria (same test), the test article was deemed slightly irritating; mild ocular changes, including reddening of the conjunctivae and sclerae, discharge, and chemosis were observed 1 h after instillation, but resolved within 24 h. Directly instilled Phenyl Methicone (unspecified amount) was determined to be non-irritating to rabbit eyes (number and strain not specified) in a 48-h ocular irritation test; slight irritation observed 4 and 8 h after exposure subsequently subsided.[15] A mixture of 78-82% Phenyl Trimethicone and 18-22% Polysilicone-11 produced a maximum mean total score (MMTS) of 0 when tested for ocular irritancy potential in 6 New Zealand white rabbits; the test article was deemed non-irritating.[37]

EXPOSURE ASSESSMENT

Total daily systemic exposure to Diphenylsiloxy Phenyl Trimethicone, from concurrent use of cosmetic products applied via various routes, was calculated using concentration of 30% in all cosmetic products, except in aerosol products (in which a maximum concentration of 3% was used).[7] Dermal exposure use patterns were assumed to be similar to those in Europe, and were calculated using 10% dermal absorption; exposure from aerosol products was calculated assuming an adult inhalation rate of 20 m^3/d, in a two-zone approach. Based on these daily systemic exposure calculations, assuming maximum aggregate exposures from simultaneous use of all possible cosmetic products, the combined internal dose of Diphenylsiloxy Phenyl Trimethicone was estimated to be 7.68 mg/kg bw/d.

SUMMARY

According to the *Dictionary*, the phenyl-substituted methicone ingredients included in this safety assessment are reported to function in cosmetics as antifoaming agents and skin and/or hair conditioning agents. This group of phenyl-substituted methicones are either siloxane polymers or compounds of silicone molecules attached to phenyl or propyl groups. Data from the 2022 VCRP and Council survey indicate that Phenyl Trimethicone has the highest reported use in 781 leave-on products, as well as the highest reported concentration of use, at up to 59.5% in non-coloring shampoos. Phenyl Trimethicone is also reported to be used in leave-on formulations at up to 24.8%.

Based on its physicochemical properties, Diphenylsiloxy Phenyl Trimethicone is estimated to have a dermal absorption value of 10%. Phenyl Trimethicone fed to rats at 4% in the diet for 8 d was mostly recovered as silicon (mean % recovery: 96 ± 1.0) in the feces or gastrointestinal tract, indicating no siloxane absorption.

In an acute dermal toxicity study, the LD_{50} of Diphenylsiloxy Phenyl Trimethicone, when applied under semi-occlusion to Wistar rats, was determined to be > 2000 mg/kg. The acute oral toxicity of Diphenyl Dimethicone was evaluated in rats administered a single oral dose of 8190, 16,380, 32,770, or 65,540 mg/kg Diphenyl Dimethicone, via gavage. One rat from

each of the 3 highest dose groups died 3 or more days after dosing, and exhibited diffuse pulmonary and hepatic hemorrhage; the acute oral LD_{50} was determined to be > 65,500 mg/kg. The oral LD_{50} value for Diphenylsiloxy Phenyl Trimethicone in Wistar Han rats was determined to be > 2000 mg/kg. The acute oral LD_{50} values for Phenyl Trimethicone were determined to be > 2000 mg/kg in female Wistar rats and > 5000 mg/kg in male and female rats. The acute oral LD_{50} value for a test material comprising 78-82% Phenyl Trimethicone and 18-22% Polysilicone-11 was determined to > 5000 mg/kg in male and female Wistar-derived albino rats.

In an acute inhalation study, albino rats were exposed (whole-body) to undiluted, vaporized Diphenyl Dimethicone at concentrations of 5, 10, 23, 24, 42, 90, 101, 168, or 214 mg/l for over an hour. One animal each from the 42 mg/l and 101 mg/l group died during the exposure period, while 6 animals each from the 23 mg/l and 42 mg/l groups, 7 animals each from the 24 mg/l and 101 mg/l groups, 8 animals from the 90 mg/l group, and 1 animal from the 214 mg/l group died within 24 h of exposure. Granular livers were seen in ~30% of the animals exposed to ≥ 24 mg/ l. Severe and diffuse pulmonary hemorrhages accounted for most of the deaths and pulmonary consolidation was found in surviving animals; the LC_{50} was determined to be 18 mg/l.

No treatment related changes or deaths occurred during a short-term oral toxicity study in which Wistar Han rats were dosed with 0, 200, 600, or 1000 mg/kg Diphenylsiloxy Phenyl Trimethicone in corn oil, via gavage, for 28 d. Statistically significant reductions in the body weight gain of male rats (18-19%) in the 1000 mg/kg group and females (48%) in the 600 and 1000 mg/kg groups were observed, when compared to controls. In the liver, hepatocellular hypertrophy was seen in all test animals, and changes in hepatic fatty tissue deposition were seen in males from the high dose group and all of the test females. Increased incidence of bile duct production was seen in males from the mid dose group and in females from the low and mid dose groups. Minimal hypertrophic changes in the follicular epithelium of the thyroid gland were observed in 4 males from the high dose group, 2 males from the low dose group, and 1 male from the mid dose group The NOAEL was determined to be > 1000 mg/kg. In an inhalation study, no mortality occurred in 1 cat, 2 guinea pigs, 2 rabbits, and 4 rats exposed, whole body, to a mist of Phenyl Methicone (67.4 mg/min) contained in a chamber, at a concentration of 0.52 mg/l, for 7 h/d, over 10 d. In the absence of control data, moderate degenerative changes in the livers of the cats and guinea pigs were considered only circumstantially associated with siloxane exposure.

Groups of 10 male and 10 female Sprague Dawley rats were orally dosed with 0, 5, 20, or 80 mg/kg/d of a mixture containing 15% Diphenyl Dimethicone, via gavage, for 90 d. Higher absolute and relative liver weights, liver enlargement, and slight hepatocellular hypertrophy in animals from the 80 mg/kg group were considered to be treatment-related and toxicologically significant. The NOAEL for the test article was determined to be 20 mg/kg/d.

Groups of Sprague-Dawley rats (10/sex/group) received 0, 100, 500, or 1000 mg/kg bw/d Dipenylsiloxy Phenyl Trimethicone, in corn oil, via gavage 2 wk prior to mating, and until 4 d postpartum, in a reproductive and developmental toxicity study. No treatment-related effects on reproductive endpoints in the parents, including testis weight, epididymis weight, mean gestation length, mean number of corpora lutea, mean number of implantation sites, mean mating and fertility indices, nor changes in gross pathology, mean litter size, mean litter weight, or mean ration live births/litter size of the pups were observed. The NOAEL for reproductive (male and female) and developmental toxicity was determined to by ≥ 1000 mg/kg bw/d. In a 4-wk study of the effects of Phenyl Trimethicone on testicular histology and weight, male Wistar rats were dosed with up to 1000 mg/kg Phenyl Trimethicone 5d/wk, via gavage. No visible changes, body weight fluctuations, deaths, or changes in testicle histology or weight were observed. The NOAEL for effects on body weight, testicle weight, and histology was determined to be > 1000 mg/kg.

In an Ames test, Diphenylsiloxy Phenyl Trimethicone was tested at concentrations up to 5000 µg/plate, using *S. typhimurium* strains TA98, TA100, TA1535, TA1537 and *E.coli* WP2. No increase in revertant colonies was observed in the presence or absence of metabolic activation. The genotoxic potential of Diphenylsiloxy Phenyl Trimethicone, tested at up to 5 µl/ml for 4, 18, or 28 h, with and without metabolic activation, was evaluated in a mammalian chromosomal aberration test, using the Chinese hamster lung cell line. Cell numbers below 50% of the controls or poor metaphase quality were observed in cells treated in the absence of metabolic activation with ≥ 0.15 µl/ml of the test substance for 18 h. No statistically significant increase in the frequency of cells with chromosome aberrations was induced in either the absence or presence of metabolic activation.

A product containing 15% Diphenyl Dimethicone (tested at concentrations of 2.5, 5, 10, 25, or 50% in acetone:olive oil (4:1 v/v)) was not sensitizing in a LLNA in groups of 4 female CBA mice; 2 of the animals from the 10% group died on day 3 and 1 of the animals in the 50% group died on day 6, but these deaths were not attributed to the test article. Diphenyl Dimethicone (100% pure and applied neat) was neither irritating to New Zealand white rabbit skin in a primary dermal irritation test nor sensitizing to female Hartley albino guinea pig skin in a Buehler test. Diphenylsiloxy Phenyl Trimethicone was considered not irritating, and slightly irritating or non-irritating, in 2 separate, 4-h, semi occlusive patch tests made to New Zealand white rabbit skin, when tested neat; in the second test, very slight erythema persisted in all animals until 24 h after patch removal, and in 1 animal at the 48-h reading; all effects were reversible within 72 h. In two LLNAs using female CBA mice, the topical application of 25, 50, or 100 % w/w Diphenylsiloxy Phenyl Trimethicone in acetone and olive oil (4:1 v/v) was not considered sensitizing. A mixture of 72-82% Phenyl Trimethicone and 18-22% Polysilicone-11 was not irritating to New Zealand white rabbit skin in an acute skin irritation test. A lip color formulation containing 9.06% Diphenyl Dimethicone

and a formulation containing 2% Diphenyl Dimethicone were neither irritating nor sensitizing in a 24-h SIOPT (20 subjects) and a Marzulli- Maibach HRIPT (111 subjects), respectively. Similarly, two separate ampoule formulations containing 0.5% Diphenylsiloxy Phenyl Trimethicone were not irritating in a 24-h SIOPT performed in 20 subjects, nor sensitizing in a HRIPT performed in 112 subjects. A SPF cream formulation containing 3.2363% Phenyl Trimethicone and an eye primer formulation containing 10% Phenyl Trimethicone were not irritating in a 14-d cumulative irritation test (25 subjects) and a 24-h SIOPT (21 subjects), respectively. A Marzulli-Maibach HRIPT of a formulation containing 0.2% Phenyl Methicone (107 subjects), a semi-occlusive HRIPT of a product containing 28.67% Phenyl Trimethicone (203 subjects), a maximization assay of a concealer formulation containing 26.18% Phenyl Trimethicone (26 subjects), a 24-h SIOPT of a shine gloss formulation containing 5% Trimethylsiloxyphenyl Dimethicone (18 subjects), a 15-d cumulative irritation test of a serum formulation containing 2% Trimethylsiloxyphenyl Dimethicone (28 subjects), and 3 separate HRIPTs of a cream formulation containing 3% Trimethylsiloxyphenyl Dimethicone (103 subjects), a product containing 38.006% Trimethysiloxyphenyl Dimethicone (205 subjects), and 100% pure Trimethylsiloxyphenyl Dimethicone (51 subjects) all yielded negative results.

A lotion containing 7.5% Phenyl Trimethicone was not considered to be a potential photosensitizer in a photocontact allergenicity assay of 27 subjects. The repeated dermal application of a serum containing 2% Trimethylsiloxyphenyl Dimethicone was not contraindicated with sunlight exposure in a test of photoallergic potential in 26 subjects.

The ocular irritation potential of Diphenyl Dimethicone was tested in albino rabbits eyes; the maximal irritation score (8 of out of 110) was observed within 4 h in 1 animal from the group with eyes washed after 2 s; any signs of irritation resolved by the second or third day. Under these conditions, the test article was considered slightly, and transiently irritating to rabbit eyes. In an acute ocular irritation study, rabbit eyes were treated with undiluted Diphenylsiloxy Phenyl Trimethicone for 72 h; the test article was deemed slightly irritating to rabbit eyes based on Kay and Calandra criteria, but was not deemed irritating according to the Globally Harmonized System of classification. Phenyl Methicone was slightly irritating at 4 and 8 h after being instilled in rabbit eyes; subsequently, the irritation subsided. A mixture of 78-82% Phenyl Trimethicone and 18-22% Polysilicone-11 produced an MMTS of 0 when tested for acute irritancy in the eyes of New Zealand white rabbits; the test article was deemed a non-irritant.

Total daily systemic exposure to Diphenylsiloxy Phenyl Trimethicone was evaluated in an Australian exposure assessment. The simultaneous use of cosmetic products applied via varied routes of exposure was estimated to be 7.68 mg/kg bw/d, assuming 30% concentration in all cosmetic products, with the exception of aerosols (in which a maximum concentration of 3% was used).

DISCUSSION

To be developed.

CONCLUSION

To be determined.

TABLES

Table 1. Definitions, idealized structures, and reported functions[1, CIR Staff]

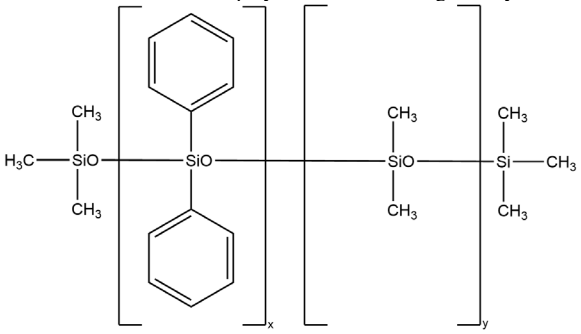
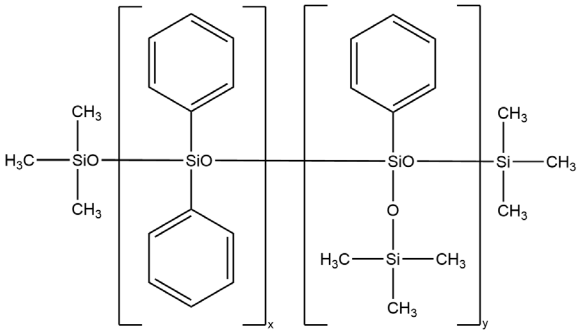
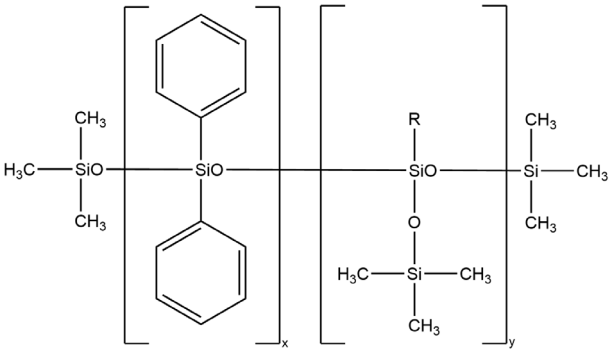
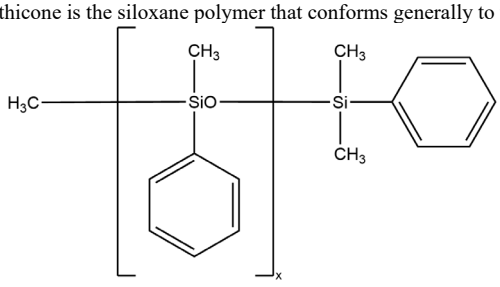
Ingredient/CAS No.	Definition	Function(s)
Diphenyl Dimethicone 68083-14-7	Diphenyl Dimethicone is a siloxane polymer that conforms generally to the structure: 	Antifoaming agents; Skin-conditioning agents - occlusive
Diphenylsiloxy Phenyl Trimethicone 352230-22-9	Diphenylsiloxy Phenyl Trimethicone is the silicone compound that conforms to the structure: 	Antifoaming agents; Hair conditioning agents; Skin-conditioning agents-miscellaneous
Diphenylsiloxy Phenyl/Propyl Trimethicone	Diphenylsiloxy Phenyl/Propyl Trimethicone is the silicone compound that conforms to the structure:  wherein R represents either a phenyl or propyl group.	Hair conditioning agents; Skin conditioning agents - emollient
Phenyl Dimethicone 9005-12-3	Phenyl Dimethicone is the siloxane polymer that conforms generally to the structure: 	Antifoaming agents; Skin-conditioning agents - occlusive

Table 1. Definitions, idealized structures, and reported functions[1, CIR Staff]

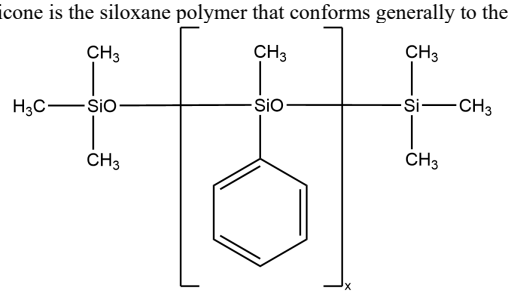
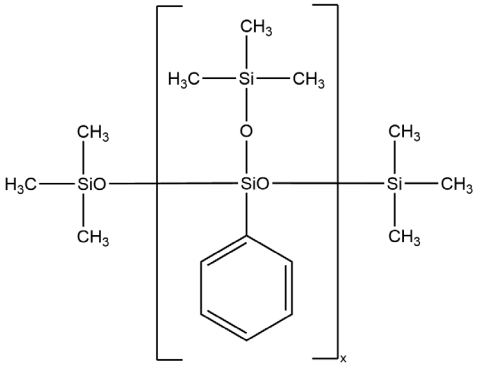
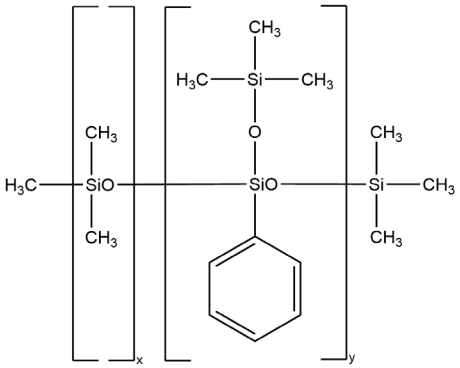
Ingredient/CAS No.	Definition	Function(s)
Phenyl Methicone 31230-04-3 63148-58-3	Phenyl Methicone is the siloxane polymer that conforms generally to the structure: 	Skin-conditioning agents - emollient
Phenyl Trimethicone 18758-91-3 18876-34-1 195868-36-1 2116-84-9 70131-69-0 73559-47-4	Phenyl Trimethicone is the siloxane polymer that conforms generally to the structure: 	Antifoaming agents; Hair conditioning agents; Skin-conditioning agents - occlusive
Trimethylsiloxyphenyl Dimethicone 73138-88-2	Trimethylsiloxyphenyl Dimethicone is the siloxane polymer that conforms generally to the structure: 	Hair conditioning agents

Table 2. Recent and historical frequency and concentration of use data for Phenyl Trimethicone

	# of Uses		*Max Conc of Use (%)*	
	2022[8]	**2002[4]**	**2022[10]**	**2004[4]**
Totals*	**781**	**279**	**0.1 – 59.5**	**0.0075-36**
Duration of Use				
Leave-On	722	*264*	*0.1 – 24.8*	*0.0075 - 36*
Rinse-Off	59	*14*	*0.75 – 59.5*	*0.3 - 4*
Diluted for (Bath) Use	NR	*1*	*NR*	*NR*
Exposure Type				
Eye Area	137	83	0.75 - 17	0.008 - 15
Incidental Ingestion	88	34	1 - 13.8	0.08 - 36
Incidental Inhalation-Spray	60; 144[a]; 47[b]	24; 56[a]; 7[b]	0.1 -7.5; 6[a]	0.1 – 18; 0.2 – 11[a]; 0.2 -18[b]
Incidental Inhalation-Powder	32; 47[b]; 3[c]	10; 7[b]	1.2 – 15.6; 1.7 – 13[c]	0.1 – 8; 0.2 -18[b]
Dermal Contact	466	175	0.1 – 24.8	0.0075 - 22
Deodorant (underarm)	1[a]	1[a]	spray: 2.2 not spray: 1.8 – 10.2	NR
Hair - Non-Coloring	216	69	0.5 – 59.5	0.1 - 18
Hair-Coloring	10	NR	NR	NR
Nail	1	NR	3	0.5
Mucous Membrane	88	36	1 – 13.8	0.08 - 36
Baby Products	3	NR	6.5	NR

*Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.
[a] It is possible these products are sprays, but it is not specified whether the reported uses are sprays.
[b] Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories
[c] It is possible these products are powders, but it is not specified whether the reported uses are powders
NR- none reported

Table 3. Frequency (2022)[8] and concentration (2021)[9] of use according to duration and exposure

	# of Uses	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*
	Diphenyl Dimethicone		**Diphenylsiloxy Phenyl Trimethicone**		**Diphenylsiloxy Phenyl/Propyl Trimethicone**	
Totals*	**145**	**0.1 – 24.1**	**269**	**0.3 – 19.9**	**NR**	**5.3**
Duration of Use						
Leave-On	*143*	*0.1 – 24.1*	*262*	*0.3 – 19.9*	NR	*5.3*
Rinse-Off	*2*	*NR*	*7*	*1 – 8.8*	NR	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	NR	*NR*
Exposure Type						
Eye Area	32	NR	47	4.4 – 19.9	NR	NR
Incidental Ingestion	64	1.9 - 24.1	75	9.4 – 15.2	NR	NR
Incidental Inhalation-Spray	1; 6[a]; 3[b]	0.1 - 1	33[a]; 14[b]	0.3 – 5; 3.5[a]	NR	NR
Incidental Inhalation-Powder	3[b]	0.42[c]	12; 14[b]	5.7; 0.4 – 0.5[c]	NR	NR
Dermal Contact	79	0.42 – 1.3	194	0.4 – 19.9	NR	5.3
Deodorant (underarm)	NR	NR	NR	spray: 0.5 not spray: 0.5	NR	NR
Hair - Non-Coloring	2	0.9 - 1	NR	1.2 – 3.5	NR	NR
Hair-Coloring	NR	0.1	NR	0.3 – 8.8	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous Membrane	64	1.9 – 24.1	75	9.4 – 15.2	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR
	Phenyl Dimethicone		**Phenyl Methicone**		**Trimethylsiloxyphenyl Dimethicone**	
Totals*	**8**	**0.0096 – 19.5**	**10**	**0.28**	**47**	**0.2 - 23**
Duration of Use						
Leave-On	*8*	*0.0096 – 19.5*	10	*0.28*	*46*	*0.2 - 23*
Rinse Off	*NR*	*NR*	NR	*NR*	*1*	*0.5*
Diluted for (Bath) Use	*NR*	*NR*	NR	*NR*	*NR*	*NR*
Exposure Type						
Eye Area	NR	2.1	1	NR	2	14
Incidental Ingestion	1	19.5	NR	NR	29	18 - 23
Incidental Inhalation-Spray	2; 3[a]	NR	4[a]	NR	1[b]	5[a]
Incidental Inhalation-Powder	NR	NR	NR	0.28[c]	1[b]	3.5
Dermal Contact	3	2.1	7	0.28	17	3.5 - 20
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	4	NR	NR	NR	1	0.5 - 5
Hair-Coloring	NR	NR	NR	NR	NR	NR
Nail	NR	0.0096	3	NR	NR	0.2
Mucous Membrane	1	19.5	NR	NR	29	18 – 23
Baby Products	NR	NR	NR	NR	NR	NR

*Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.
[a] It is possible these products are sprays, but it is not specified whether the reported uses are sprays.
[b] Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories
[c] It is possible these products are powders, but it is not specified whether the reported uses are powders
NR- none reported

Table 4. Acute toxicity studies

Ingredient	Animals	No./Group	Vehicle	Concentration/Dose/Protocol	LD_{50}/LC_{50}/Results	Reference
DERMAL						
Diphenylsiloxy Phenyl Trimethicone	Wistar Han rats	5/sex	none	OECD TG 402. Semi-occlusive application of 2000 mg/kg bw for 24 h.	LD_{50} >2000 mg/kg. Slight crust formation in 1 female rat on the fourteenth and fifteenth day of observation. There were no signs of systemic or clinical toxicity.	6,7
ORAL						
Diphenyl Dimethicone	Rats	3/sex	none	Rats were administered 8190, 16,380, 32,770, or 65,540 mg/kg bw of the test article, intragastrically. Animals were observed for 14 d before necropsy.	LD_{50} > 65,550 mg/kg bw, computed via the Miller and Taint method. Abdominal pain was observed after administration, followed by excessive laxation and urinary incontinence. One rat/group from the three highest dose groups died (3 or more days after dosing) and diffuse pulmonary hemorrhage and petechial hepatic hemorrhage was observed. No gross abnormalities were found at necropsy.	13
Diphenylsiloxy Phenyl Trimethicone	Female Wistar Han rats	3/group	corn oil	OECD TG 423. The animals were given 2000 mg/kg bw of the test article, via gavage.	LD_{50} > 2000 mg/kg. Slightly ruffled fur was observed in 1 male and 1 female for up to 3 h after administration. No mortality or other abnormalities occurred.	6,7
Phenyl Trimethicone	Female Wistar rats	3/group	corn oil	OECD TG 423. Two groups were administered 2000 mg/kg bw (no control group), via gavage and were observed for 14 d prior to necropsy.	$LD_{50} \geq$ 2000 mg/kg. No mortality or clinical abnormalities were observed.	5
Phenyl Trimethicone	Rats (strain NS)	NR (both males and females)	NS	OECD TG 401. Animals were administered 1000, 2500, or 5000 mg/kg bw of the test article, via gavage and observed for 7 d (necropsy not performed).	LD_{50} > 5000 mg/kg. No mortality or clinical abnormalities were observed.	5
78- 82% Phenyl Trimethicone and 18-22% Polysilicone-11	Wistar-derived albino rats	5/sex	none	The animals were given 5000 mg/kg bw of the test article, via gavage.	LD > 5000 mg/kg. No mortality or clinical abnormalities were observed.	14
INHALATION						
Diphenyl Dimethicone	Albino rats	5/sex/group	none	The test article was vaporized during 5-min intervals, at 370 °C on an electric hot plate, housed within a bell jar (maintained at 25 - 30 °C) connected to an animal exposure chamber. Fresh air mixed with the heated vapors entered the exposure chamber at an airflow rate of 5 lb/in^2. Animals were exposed to either 5, 10, 23, 24, 42, 90, 101, 168, or 214 mg/l of the vaporized test article for 1 h. Exposure concentrations were calculated based on the volume of the chamber and the amount of Diphenyl Dimethicone being vaporized. Animals were observed for 14 d after exposure.	LC_{50}: 18 mg/l (estimated). Little or no respiratory distress was observed during the exposure period. One animal each from the 42 mg/l and 101 mg/l group died during the exposure period. Within 24 h after exposure, the following deaths occurred: 5 mg/l: none 10 mg/1: 3 animals 23 mg/l: 6 animals 24 mg/l: 7 animals 42 mg/l: 6 animals 90 mg/l: 8 animals 101 mg/l: 7 animals 168 mg/l: 3 animals 214 mg/l: 1 animal At higher volumes of dispensation (≥101 mg/l), residues accumulated on the hot plate. The lower conductivity of these concentrations was suspected to modify temperature and vaporization, thus, resulting in lower mortality than at intervening dose levels. Granular livers were seen in ~30% of the animals exposed to ≥ 24 mg/ l. Severe and diffuse pulmonary hemorrhages accounted for most of the deaths. Pulmonary consolidation, varying from pinkish orange petechia to major involvement, was found in surviving animals.	13

N/A – not applicable; NR- none reported; NS – not specified

Table 5. Dermal irritation and sensitization studies

Test Article	Vehicle	Concentration/Dose	Test Population	Procedure	Results	Reference
			ANIMAL			
Product containing 15% Diphenyl Dimethicone	acetone: olive oil (4:1 v/v)	25 ml; 2.5, 5, 10, 25, or 50%	Groups of 4 female CBA mice	OECD TG 429; LLNA. The test article was topically applied on days 1, 2, and 3 to one ear, while acetone:olive oil (vehicle control) was applied to the other ear. One group which received 25% α-hexylcinnamaldehyde in the acetone:olive oil mixture served as positive controls. Animals were observed for clinical and gross abnormalities for up to 6 d before being killed. Stimulation indices (SI) were calculated.	Not sensitizing. Two of 4 of animals in the 10% group died on day 3 and 1 of the animals in the 50% group died on day 6. These deaths were not attributed to the test article. No positive lymphoproliferative response (SI > 3) were noted at any tested concentration.	[17]
Diphenyl Dimethicone, 100% pure	N/A	0.5 ml, applied neat	6 New Zealand white rabbits	Primary dermal irritation test. The test article was simultaneously applied to an abraded and unabraded test site, under occlusion, for 24 h. Mean scores from 24 and 72 h after application were used to determine the PII. Under study conditions, the test article was not considered to be a primary dermal irritant.	Not irritating; PII = 0.28	[18]
Diphenyl Dimethicone, 100% pure	N/A	NS, applied neat	6 male and 6 female Hartley albino guinea pigs	Buehler test. Animals received 3 topical, occluded applications of the test article over the 3-wk induction period. Five males and 5 females served as the control group (which received no treatment during induction). After 2 wk, a challenge application of the test article was made to an untreated site on both the test and control animals. Reactions were scored 7 and 24 h after each induction and challenge application, and also at 48 h following the challenge application. The test article was deemed a non-sensitizer.	Not sensitizing	[18]
Diphenylsiloxy Phenyl Trimethicone, 100% pure	N/A	0.5 ml, applied neat	3 New Zealand white rabbits	OECD TG 404; primary skin irritation test. A semi-occlusive patch application of the test article was made for 4 h, and test sites were scored at 1, 24, 48, and 72 h after patch removal.	Not irritating	[19]
Diphenylsiloxy Phenyl Trimethicone	N/A	NS, applied neat	1 male and 2 female New Zealand white rabbits	OECD TG 404; dermal irritation study. A semi-occlusive patch application of the test article was made for 4 h, and test sites were scored at 24, 48, and 72 h after patch removal. Mean scores for erythema/eschar and edema were calculated for each animal from scores taken at the 3 time points.	Slightly irritating; non-irritating in another description. Very slight to well-defined erythema was noted in all 3 animals 1 h after patch removal. Mean erythema/eschar scores were 0.33 for both animal 1 and 2, and 0.67 for animal 3; no edema was observed. Very slight erythema persisted in all animals until the 24-h reading, and was still present in 1 animal at the 48-h reading. The noted effects were reversible and no longer evident at the 72 h. In another description of the same study, GHS criteria were not met, and the test article was deemed non-irritating.	[6,7]

Table 5. Dermal irritation and sensitization studies

Test Article	Vehicle	Concentration/Dose	Test Population	Procedure	Results	Reference
Diphenylsiloxy Phenyl Trimethicone, 100% pure	acetone: olive oil (4:1 v/v)	25, 50, or 100% w/w	Groups of 4 female mice	LLNA. The test article was applied topically to the back of both left and right ear lobes for 3 consecutive days. A control group was treated only with the acetone:olive oil mixture. Five days after the first topical application the mice were intravenously injected with radio-labelled thymidine. The animals and were killed and lymph nodes were excised for evaluation approximately 5 h after injection.	25% group SI = 1 50% group SI = 2 100% group SI = 2.4 (An SI < 3 is non-sensitizing) No deaths occurred during the study period, and no clinical signs were observed in controls or animals in the 25% group. All mice in the 100% group exhibited slight ear swelling at both ear lobes on day 2, which persisted for 4 d. All mice in the 50% and 100% groups exhibited such results on the day 3, which persisted for 3 d.	[19]
Diphenylsiloxy Phenyl Trimethicone	acetone: olive oil (4:1 v/v)	25, 50, or 100% w/w	Groups of 4 female CBA mice	OECD TG 429; LLNA. The test item was topically administered for an unspecified duration. Vehicle controls received the acetone:olive oil mixture, while animals treated previously with α-hexylcinnamide served as positive controls. Lymphocyte proliferative responses (measured as DPM/lymph node) and SIs (test/control ratio) were calculated for each group.	No evidence of induction of a lymphocyte proliferative response indicative of skin sensitization to the test substance was observed. Slight ear swelling was observed in test animals exposed to 100% of the test article on the second day of application. Animals exposed to 50% and 100% of the test article also exhibited slight erythema of the ear on the third day of application, which persisted until the end of the study.	[6,7]
72-82% Phenyl Trimethicone 18-22% Polysilicone-11	N/A	0.5 ml, applied neat	6 New Zealand white rabbits	In an acute skin irritation test, an occlusive application of the test material was made to intact and abraded skin on the shaved trunk (approximately 6 cm^2) for 24 h. Upon removal of the patch, test sites were gently wiped, and were scored for erythema and edema at 24 and 72 h after application.	Not irritating; PII = 0	[20]
			HUMAN			
Lip color containing 9.06% Diphenyl Dimethicone	N/A	NS, applied neat	20 subjects	24-h, SIOPT. Irritation scores were made on a scale of 0 -4 and PIIs were calculated. A liquid lip color was tested in tandem.	Not irritating; PII = 0	[21]
Product containing 2% Diphenyl Dimethicone	N/A	0.02 ml, applied neat	111 subjects	Modified Marzulli-Maibach HRIPT. Nine occlusive applications were made to a 50 mm^2 area of the back using Finn chambers over a 3-wk period for 48- or 72-h. After a 13-d non-treatment period, a single 48-h challenge application was made to the induction site and a previous untreated site. Reactions were scored on a 0-4 irritation scale between 15 and 30 min of patch removal during both the induction and challenge phases; challenge phase reactions were additionally evaluated 48 h after application. An MII was calculated by dividing the sum of the quotations of the 9 induction readings by the number of subjects and readings performed. The test article did not demonstrate potential to produce irritation or cutaneous sensitization.	Not irritating or sensitizing; MII = 0.01	[22]
Ampoule containing 0.5% Diphenylsiloxy Phenyl Trimethicone	N/A	NS, applied neat	20 subjects	24-h, SIOPT. Irritation scores were made on a scale of 0 -4 and PIIs were calculated. A serum was tested in tandem.	Not irritating; PII = 0.03	[23]

Table 5. Dermal irritation and sensitization studies

Test Article	Vehicle	Concentration/Dose	Test Population	Procedure	Results	Reference
Ampoule containing 0.5% Diphenylsiloxy Phenyl Trimethicone	N/A	0.2 g, applied neat	112 subjects	HRIPT. Nine occlusive, 24-h applications of the test material were made over 3 wk. After a 2-wk non-treatment period, a 24-h challenge application was made to a previously untreated site in the same manner as the induction applications, and reactions were scored 24, 48, 72, and 96 h after application.	Not sensitizing Two subjects exhibited low level reactions during induction and 2 other subjects exhibited low level reactions during challenge.	[24]
Product containing 0.2% Phenyl Methicone	N/A	NS, applied neat	107 subjects	Marzulli-Maibach HRIPT. Nine occlusive, 48-h induction applications were made using 8 mm Finn chambers to the same site over a 3-wk period. Induction sites were evaluated for dermal reactions immediately prior to application of the next patch. After a 2-wk non-treatment period, challenge applications were made to the original test site and a previously untreated site in the same manner as the induction applications. Challenge sites were scored 48, 72, and 96 h after application.	Not irritating or sensitizing	[27]
SPF cream containing 3.2363% Phenyl Trimethicone	N/A	0.05 ml, applied neat	25 subjects	14 -d cumulative irritation test. Occlusive, 15 mm^2 applications of the test material were made to a site on the upper arm or back for 14 d. Positive and negative control sites comprised 0.05 ml of 0.25% SLS or plain cotton, respectively. Test sites were graded daily after patch removal on a scale of 0 -5.	Not irritating. Cumulative score and CII = 0. Control results were as expected.	[25]
Eye primer containing 10% Phenyl Trimethicone	N/A	NS, applied neat	21 subjects	24-h, SIOPT. Performed as described previously. A mousse foundation was tested in tandem.	Not irritating; PII = 0	[26]
Concealer containing 26.18% Phenyl Trimethicone	N/A	0.05 ml, applied neat	26 subjects	Maximization assay. Five, occlusive induction applications were made. Prior to each induction application, a 24-h application of 0.05 ml of 0.25% aqueous SLS was made. After removal of the SLS-pre-treatment patch, 0.5 ml of the test material was applied for 48-72 h using an occlusive patch. After a 10-d non-treatment period, subjects were pre-treated with 0.05 ml of 1 % aqueous SLS for 1 h on a novel site, prior to a 48-h challenge application, in the same manner as the induction applications. Challenge reactions were scored immediately after patch removal and 24 h later	Not sensitizing No instances of contact allergy or irritation were observed.	[29]
Product containing 28.67% Phenyl Trimethicone	N/A	0.2 g, applied neat	203 subjects	HRIPT. The test material was applied to the skin using a 2 cm^2 absorbent pad for semi-occlusive, 24-h induction and challenge applications. Challenge reactions were scored 48 and 72 h after application.	Not sensitizing	[28]
Shine gloss containing 5% Trimethylsiloxy-phenyl Dimethicone	N/A	NS, applied neat	18 subjects	24-h, SIOPT. Performed as described previously. A frizz shine spray was tested in tandem.	Not irritating; PII = 0	[30]
Serum containing 2% Trimethylsiloxy-phenyl Dimethicone	N/A	200 µl, applied neat	28 subjects	15-d cumulative irritation test. Occlusive, 24-h applications of the test material (2 cm^2) were made to the back for 15 d. Positive and negative control sites comprised 200 µl of 0.25% SLS or plain cotton, respectively. Test sites were graded daily after patch removal on a scale of 0 - 4.	Not irritating. No reactions were observed in 27 subjects. Grade 1 reactions (mild redness) occurred twice in one participant, yielding a CII = 0.002 (negligible/non-significant irritation). Control results were as expected.	[31]
Cream containing 3% Trimethylsiloxy-phenyl Dimethicone	N/A	0.2 g, applied neat	103 subjects	HRIPT. The test material was applied using a 0.75 in^2 absorbent pad for the occlusive, 24-h induction and challenge applications. Challenge reactions were scored 24 and 72 h after application. The test material did not demonstrate a potential for eliciting dermal irritation or allergic contact sensitization.	Not irritating or sensitizing	[32]

Table 5. Dermal irritation and sensitization studies

Test Article	Vehicle	Concentration/Dose	Test Population	Procedure	Results	Reference
Product containing 38.006% Trimethylsiloxyphenyl Dimethicone	N/A	0.2 g, applied neat	205 subjects	HRIPT. The test material was applied using a 2 cm^2 absorbent pad for 24-h occlusive induction and challenge applications. Challenge reactions were scored 48 and 72 h after application.	Not sensitizing	[33]
Trimethylsiloxyphenyl Dimethicone, 100% pure	N/A	0.2 ml, applied neat	51 subjects	HRIPT. The test material was applied using a 0.75 in^2 absorbent pad for the 24 -h induction and challenge applications. Challenge reactions were scored 24 and 72 h after application. The test material did not demonstrate a potential for eliciting dermal irritation or allergic contact sensitization.	Not irritating or sensitizing	[34]

Abbreviations: CII- cumulative irritation index; DPM- disintegrations per minute; GHS- Globally Harmonized System of classification; HRIPT- human repeat insult patch test; LLNA – local lymph node assay; MII – mean irritation index; N/A- not applicable; NS – not specified; PII- primary irritation index; SI- stimulation index; SIOPT- single insult occlusive patch test; SLS – sodium lauryl sulfate

Table 6. Ocular irritation studies

Test Article	Vehicle	Concentration/Dose	Test Population	Procedure	Results	Reference
ANIMAL						
Diphenyl Dimethicone	N/A	0.1 ml, undiluted	Groups of 3 albino rabbits	Ocular irritation test. Each animal had the test material instilled in the conjunctival sac of one eye. Treated eyes remained unwashed in the first group, were washed 2 s after exposure with 20 ml water in the second group, and were washed 4 s after exposure with 20 ml water in the third group. The eyes were examined and irritation was scored 4 h, and 1, 2, 4, and 7 d after exposure.	Slightly, but transiently, irritating. A maximum score of 8 (out of the potential maximum of 110), indicating slight irritation, was observed only within 4 h in 1 animal from the second group. By the second or third day the eyes appeared normal, regardless of rinsing status.	[13]
Diphenylsiloxy Phenyl Trimethicone	N/A	0.1 ml, undiluted	1 male and 2 female New Zealand white rabbits	OECD TG 405; Acute ocular irritation study. Rabbit eyes were treated with the undiluted test article for 72 h.	Not irritating (according to GHS classification); slightly irritating according to Kay and Calandra criteria. Mild ocular changes, including reddening of the conjunctivae and sclerae, discharge, and chemosis were observed 1 h after instillation, but resolved within 24 h.	[6,7]
Phenyl Methicone	N/A	NS	Rabbits (strain and number NS)	Ocular irritation test. The test article (35 and 75 cSt viscous) was directly instilled into rabbit eyes and the eyes were observed for irritation from application for up to 48 h.	Not irritating Slight irritation, observed 4 and 8 h after exposure, subsequently subsided.	[15]
78-82% Phenyl Trimethicone 18-22% Polysilicone-11	N/A	0.1 ml, undiluted	6 New Zealand white rabbits	Ocular irritation test. The test material was instilled on the everted lower lid of one eye, and the upper and lower eye lids were gently held together for 1 s before releasing. The contralateral, untreated eye served as control. The cornea, iris, and conjunctivae were evaluated according to the Draize method at 24 and 72 h post-instillation. A 2% fluorescein sodium solution, followed by saline solution wash was utilized as necessary.	Not irritating; MMTS = 0	[37]

Abbreviations: cSt – centistoke; GHS – Globally Harmonized System of classification; MMTS- maximum mean total score; NS – not specified; OECD- Organisation for Economic Cooperation and Development; TG- test guideline

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4

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.

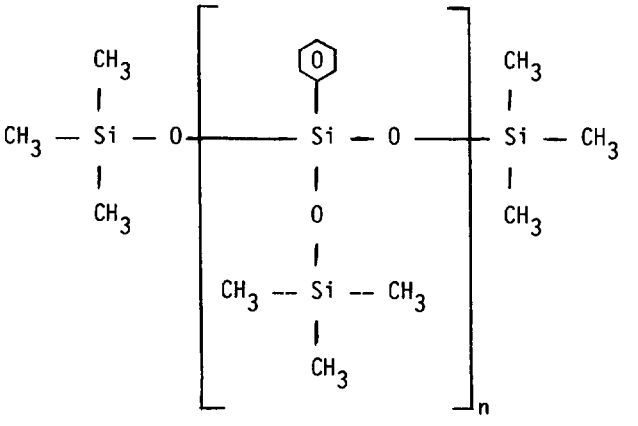
Phenyl Trimethicone is neither an irritant nor a sensitizer to humans. No photosensitization data are available on Phenyl Trimethicone; however, the UV absorption spectrum indicated only weak absorbance at 327 nm.

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/cm^2/ 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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PHENYL TRIMETHICONE

In 1986, the CIR Expert Panel found that Phenyl Trimethicone is safe as a cosmetic ingredient in the present practices of use and concentration (Elder 1986). A review of the recent literature uncovered no new studies regarding Phenyl Trimethicone,

but the Panel did consider updated information regarding uses and use concentrations. The Panel determined to not reopen the safety assessment.

Phenyl Trimethicone uses have increased from 169 in 1981 to 279 in 2002, based on industry voluntary reports provided to FDA (Elder 1986; FDA 2002). An industry survey in 2003 indicated that use concentrations range from 0.0075% to 36% (CTFA 2004). The maximum value in that range is higher than the maximum use concentration of 5% reported in 1981 (Elder 1986). Table 17 presents the available use and concentration information for Phenyltrimethicone. The most recent information now represents the present practice of use and concentration.

The Panel considered the increased use concentrations in the context of the reproductive and developmental toxicity data in the original safety assessment. Phenyl Trimethicone was not teratogenic at 500 mg/kg/day in rats and rabbits. For a 70-kg person, this dose corresponds to 35 g/day. At the current maximum use in lipsticks and the amount of lipstick used in a typical day, a dose of Phenyl Trimethicone was estimated to be 10 mg/day. This dose was 3500× lower than the observable effect level.

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PROPYLENE CARBONATE

A safety assessment of Propylene Carbonate was published in 1987 with the conclusion that it is safe as a cosmetic ingredient in the present practices of use and concentration (Elder 1987). Studies published since the last assessment were reviewed along with updated information concerning frequency of use and use concentrations. The CIR Expert Panel determined to not reopen the safety assessment.

Based on voluntary reports provided by industry to FDA, there were 295 reported uses in 1981 (Elder 1987) and 178 reported uses in 2002 (FDA 2002). Use concentrations from an industry survey (CTFA 2003) ranged from 0.003% to 6%, not very different from the use concentration range reported in 1981 of ≤0.1% to >5% (Elder 1987).

Table 18 presents the available use and concentration information for Propylene Carbonate. The most recent information constitutes present practices of use and concentration.

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POLYVINYLPYRROLIDONE/VINYL ACETATE COPOLYMER

In 1983, the CIR Expert Panel concluded that this ingredient is safe as a cosmetic ingredient under the present practices of product and concentration use (Elder 1983). New studies available since that review have been considered by the Expert Panel,

[18] Available for review: Director, Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 412, Washington, DC 20036-4702, USA.

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TABLE 17
Historical and current cosmetic product uses and concentrations for Phenyl Trimethicone

Product category	1981 uses (Elder 1986)	2002 uses (FDA 2002)	1986 concentrations (Elder 1986) %	2003 concentrations (CTFA 2004) %
Baby Care	1*	—	>0.1–1*	—
Bath				
Oils, tablets, and salts	1	1	>0.1–1	—
Other bath	2	—	>1–5	—
Eye Makeup				
Eyeliners	—	1	—	2–6
Eye shadow	1	77	≤0.1–5	4–13
Eye lotions	—	—	—	0.008–1
Mascara	1	1	>0.1–1	0.1–0.4
Other eye makeup	1	4	>0.1–1	6–15
Fragrances				
Colognes and toilet waters	—	—	—	0.5
Perfumes	—	1	—	—
Powders	—	1	—	—
Other fragrances	—	—	—	0.5
Noncoloring hair care				
Conditioners	10	8	≤0.1–5	0.3–2
Sprays	25	23	≤0.1–1	0.1–18
Straighteners	1	—	>1–5	—
Rinses	1	—	>0.1–1	—
Shampoos	—	—	—	1
Tonics, dressings, etc.	9	31	≤0.1–5	5–11
Wave sets	2	—	>0.1–5	—
Other noncoloring hair care	1	7	>0.1–1	0.5–2
Makeup				
Blushers	11	1	>1–5	2–15
Face powders	2	9	>0.1–1	0.1–8
Foundations	2	17	>1–5	2–22
Leg and body paints	—	—	—	2
Lipsticks	2	34	>1–5	0.08–36
Makeup bases	2	8	≤0.1–5	—
Rouges	—	2	—	—
Other makeup	—	13	—	0.0075–22
Nail care				
Creams and lotions	—	—	—	0.5
Polishes and enamels	7	—	>0.1–1	—
Personal hygiene				
Underarm deodorants	—	1	—	—
Other personal hygiene	—	1	—	—
Shaving				
Aftershave lotions	—	1	—	0.5–2
Preshave lotions	6	1	>0.1–5	2
Other shaving	—	—	—	0.5
Skin care				
Cleansing creams, lotions, etc.	—	4	—	2–4
Face and neck skin care	8**	3	≤0.1–1**	4–6
Body and hand skin care		4		0.2–18
Moisturizers	7	15	≤0.1–5	0.8–3
Night skin care	1		≤0.1	2
Other skin care	1		>1–5	2
Suntan				
Suntan gels, creams, liquids and sprays	6	2	—	0.5–9
Indoor tanning	1	8	—	0.2–5
Other suntan	1		>1–5	2
Total uses/ranges for Phenyl Trimethicone	**113**	**279**	**≤0.1–5**	**0.0075–36**

*Product categories within the group not given.

**These categories were combined originally, but are now separate.

JUNE 1985 PANEL MEETING – INITIAL REVIEW/DRAFT REPORT

The Schroeter team noted that it had taken some time to clean up the physical chemistry of this ingredient and that "n" was not defined. The UV spectrum had been provided showing minor absorption in the UVB range, negating the need for photosensitization data. An increase in the number of resorptions noted in the reproductive/teratogenicity studies was not considered significant.

Dr. Hoffmann reemphasized the need for a paragraph on impurity data, and if no such data exist, a statement to that effect.

Subject to minor revisions, the following Discussion and Conclusion were unanimously accepted and approved:

Discussion

No photosensitization data are available on Phenyl Trimethicone; however, as the UV spectrum indicates only weak absorbance at 327 nm, the Panel did not feel it was necessary to request clinical photosensitization data. An increase in the number of resorption sites was noted in two of three teratogenicity/reproductive studies although these results were statistically significant in only one study. However, as the doses tested in these studies are higher than those used in cosmetics, the Panel did not feel further data were required.

Conclusion

Based on the animal and human data 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.

The document will shortly be issued as a Tentative Report for a 90-day public comment period.

[Minutes of the meeting at which a Final Report was issued were not found]

JUNE 2004 MEETING – RE-REVIEW

Dr. Belsito said that, in 1986, CIR published a Final Report with a conclusion stating that Phenyl Trimethicone is safe as a cosmetic ingredient in the present practices of use and concentration. He noted that no new studies have been identified in the published literature since the Final Report was published; however, the uses of Phenyl Trimethicone in cosmetics have increased from 169 in 1986 to 279, currently. Additionally, the current use concentration range (0.0075% to 36%) is broader than it was in 1986.

Dr. Belsito noted that the data presented in the published Final Report cover the new use concentration range and product uses.

The Panel unanimously concluded that the Final Report on Phenyl Trimethicone should not be reopened.

Concerning current use concentration data, Dr. Andersen said that Phenyl Trimethicone is used in lipsticks at a reasonably high concentration (36%) and noted that a calculation was done at yesterday's Team meeting to evaluate this use concentration in light of the data included in the published report. The Final Report indicates that a dose of 200 mg/kg/day was a fetotoxic dose, and, thus, the Panel wanted to know whether it is remotely possible that the use of Phenyl Trimethicone in cosmetics could result in this level of exposure.

Dr. Andersen said that lipsticks at an average of 10 mg/day, for a 70 kg individual, produce a dose that is lower than the fetotoxic dose. He added that this calculation and the Panel's decision not to reopen the Final Report will be captured in the Annual Review that CIR produces. The Annual Review is published in the *International Journal of Toxicology*.

The Panel agreed that the calculation referred to above should be included in the Annual Review.

2022 Priorities

Concentration of Use by FDA Product Category – Diphenylsiloxy Phenyl Trimethicone and Related Ingredients*

Diphenylsiloxy Phenyl Trimethicone
Diphenyl Dimethicone
Diphenylsiloxy Phenyl/Propyl Trimethicone
Hydrogen Diphenyl Dimethicone
Phenyl Dimethicone
Phenyl Methicone
Trimethylsiloxyphenyl Dimethicone
Triphenyl Trimethicone

Ingredient	Product Category	Maximum Concentration of Use
Diphenylsiloxy Phenyl Trimethicone	Eyebrow pencils	4.4%
Diphenylsiloxy Phenyl Trimethicone	Eyeliners	19.9%
Diphenylsiloxy Phenyl Trimethicone	Eye shadows	15%
Diphenylsiloxy Phenyl Trimethicone	Hair conditioners	1.2%
Diphenylsiloxy Phenyl Trimethicone	Tonics, dressings, and other hair grooming aid	3.5%
Diphenylsiloxy Phenyl Trimethicone	Hair tints	8.8%
Diphenylsiloxy Phenyl Trimethicone	Hair rinses (coloring)	1%
Diphenylsiloxy Phenyl Trimethicone	Hair color sprays	0.3%
Diphenylsiloxy Phenyl Trimethicone	Blushers	4.7%
Diphenylsiloxy Phenyl Trimethicone	Face powders	5.7%
Diphenylsiloxy Phenyl Trimethicone	Foundations	3.3-7.5%
Diphenylsiloxy Phenyl Trimethicone	Lipstick	9.4-15.2%
Diphenylsiloxy Phenyl Trimethicone	Deodorants Aerosol Not spray	 0.5% 0.5%
Diphenylsiloxy Phenyl Trimethicone	Face and neck products Not spray	 0.4-0.5%
Diphenylsiloxy Phenyl Trimethicone	Body and hand products Spray	 5%
Diphenylsiloxy Phenyl Trimethicone	Moisturizing products Not spray	 1.7%
Diphenylsiloxy Phenyl Trimethicone	Other skin care preparations	2-9%
Diphenyl Dimethicone	Hair sprays Aerosol	 0.9-1%
Diphenyl Dimethicone	Hair color sprays	0.1%
Diphenyl Dimethicone	Foundations	0.6-1.3%
Diphenyl Dimethicone	Lipstick	1.9-24.1%
Diphenyl Dimethicone	Face and neck products Not spray	 0.42%
Diphenylsiloxy Phenyl/Propyl Trimethicone	Makeup bases	5.3%
Phenyl Dimethicone	Eye shadows	2.1%
Phenyl Dimethicone	Lipstick	19.5%

Phenyl Dimethicone	Nail polish and enamel	0.0096%
Phenyl Methicone	Face and neck products Not spray	0.28%
Trimethylsiloxyphenyl Dimethicone	Eye shadows	14%
Trimethylsiloxyphenyl Dimethicone	Hair conditioners	0.5%
Trimethylsiloxyphenyl Dimethicone	Tonics, dressings, and other hair grooming aids	5%
Trimethylsiloxyphenyl Dimethicone	Other hair preparations (noncoloring)	5%
Trimethylsiloxyphenyl Dimethicone	Face powders	3.5%
Trimethylsiloxyphenyl Dimethicone	Lipstick	18-23%
Trimethylsiloxyphenyl Dimethicone	Nail polish and enamel	0.2%
Trimethylsiloxyphenyl Dimethicone	Moisturizing products Not spray	20%

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

Information collected in 2021
Table prepared: July 6, 2021

Concentration of Use by FDA Product Category – Phenyl Trimethicone

Product Category	Maximum Concentration of Use
Other baby products	6.5%
Eyebrow pencils	8.8%
Eyeliners	3.4-16.5%
Eye shadows	2.4-17%
Other makeup preparations	0.75%
Perfumes	3%
Other fragrance preparations	0.5%
Hair conditioners	0.75-3%
Hair sprays	
Aerosol	0.5-7.5%
Shampoos (non-coloring)	59.5%
Tonic, dressings, and other hair grooming aids	
Not spray	0.51-9%
Pump spray	2%
Aerosol	7%
Other hair preparations (noncoloring)	3%
Blushers	5.2%
Face powders	1.2-15.6%
Foundations	7-12%
Lipstick	1-13.8%
Rouges	2-4.8%
Other makeup preparations	12.1-24.8%
Nail polish and enamel	3%
Deodorants	
Not spray	1.8-10.2%
Aerosol	2.2%
Preshave lotions	2.5%
Face and neck products	
Not spray	3.4-13%
Body and hand products	
Not spray	1.7%
Moisturizing products	
Not spray	0.8-22.7%
Other skin care preparations	0.5-4.9%
Suntan products	
Aerosol	0.1%
Pump spray	0.5%
Other suntan preparation	6%

Information collected in 2021

Table prepared: January 10, 2022

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Carol Eisenmann, Ph.D.
Personal Care Products Council

DATE: April 12, 2022

SUBJECT: Phenyl Trimethicone and Trimethylsiloxyphenyl Dimethicone

AMA Laboratories. 1995. Acute Oral Toxicity - Limits Test (78-82% Phenyl Trimethicone, 18-22% Polysilicone-11).

AMA Laboratories. 1995. Primary Skin Irritation (78-82% Phenyl Trimethicone, 18-22% Polysilicone-11).

AMA Laboratories. 1995. Primary Ocular Irritation (78-82% Phenyl Trimethicone, 18-22% Polysilicone-11).

Consumer Product Testing Co. 2002. Repeated Insult Patch Test (100% Trimethylsiloxyphenyl Dimethicone).

AMA LABORATORIES, INC.
216 Congers Road, Bldg. 1
New City, NY 10956 USA
(914) 634-4300
FAX: (914) 638-4872

ACUTE ORAL TOXICITY

AMA REF. NO.:

SPONSOR:

PRODUCT DESCRIPTION:

AMA LAB NO.: B-3227

DATE RECEIVED: January 20, 1995

DATE OF REPORT: February 27, 1995

Test material:
78-82% Phenyl Trimethicone
18-22% Polysilicone-11

REFERENCE: Acute Oral Toxicity - Limits Test. FHSLA, 16 CFR 1500.3.

SOP REFERENCE: 101.00

ANIMALS: Healthy, young adult Wistar derived albino rats weighing between 150 to 300 grams were obtained from ACE Animals, Inc., Boyertown, Pennsylvania. Five male and five female rats were selected for the dose level chosen for this study.

DIET: Purina Rat Chow. Feed and water were supplied ad-libitum. Animals are fasted 18-24 hours prior to dosing; feed and water are returned ad-libitum immediately thereafter. Records were kept of the food supplier, delivery date, feed identity, batch number (if available) and expiration date. No feed was used beyond its expiration date.

ENVIRONMENTAL CONDITIONS:

Prior to the test period the animals were each uniquely identified with sequentially numbered ear tags and individually housed in wire bottom cages in a temperature controlled room with a 12 hour light/dark cycle. Feed and water were provided ad-libitum after dosing. Litter is changed not less frequently than every third day and more if deemed necessary. Floors are broom

cleaned as necessary and mopped with disinfectant (Sparatan Sterigent Germicidal Cleanser or Pine Multi-Purpose Disinfectant) on each day of litter removal. Newly received animals are quarantined for a period of 24 hours or more if necessary to determine the health status, prior to assignment in the housing facility. The animals are then further conditioned for a period of not less than 4 additional days before testing commencement.

PROCEDURE:

Preparation of the Test Material: Not Applicable.

Dilutions: Not Applicable.

Diluent (Vehicle): Not Applicable.

Eighteen to twenty-four hours prior to dosing the rats were fasted. During the fast period water was allowed ad-libitum. After fasting rats were individually weighed. All body weights were recorded and individual doses calculated based on these weights. The test material was then delivered by gavage at a dose level of 5.0 g/kg body weight. The animals were individually and singly dosed by gavage using a 12-18 gauge stainless steel needle attached to an appropriately calibrated syringe. Once the material had been ingested completely, feed and water were provided ad-libitum. The rats were individually caged and observed for mortality or other signs of gross toxicity for 14 days. At the end of the test period, all surviving animals were weighed.

STATISTICAL METHOD: Not applicable.

ARCHIVING:

All original samples, raw data sheets, technicians notebooks, correspondence files and copies of final reports and remaining specimens are maintained on the premises of AMA Laboratories in limited access storage files marked "Archive". A duplicate disk copy of final reports is separately archived in a bank safe deposit vault.

OBSERVATIONS: Unremarkable.

RESULTS: See attached Table.

CONCLUSIONS: The above material , when tested as indicated herein may be regarded as **ORALLY NON-TOXIC** according to the reference. LD_{50} > 5 g/kg.

Shyla Cantor, Ph.D.
Study Director

Albert Lukin, B.S.
Animal Toxicologist

David R. Winne, B.S.
Quality Assurance Supervisor

2/27/95
Date

TABLE

ACUTE ORAL TOXICITY

RESULTS:

AMA Lab. No.:
Client No.: ---
DOSAGE: 5 g/kg
Dilution : Not Applicable.

Animal #	Sex	Body Weight Initial (g)	Body Weight Final (g)	Dosage (g)	Dose Delivered* (ml)	Mortality Day	Mortality Autopsy
3481	M	245	266	1.23	1.34	NA	NA
3482	M	264	284	1.32	1.44	NA	NA
3483	M	256	277	1.28	1.40	NA	NA
3484	M	248	264	1.24	1.35	NA	NA
3485	M	263	281	1.32	1.44	NA	NA
$\bar{x}$		255	274	1.28	1.39		
3440	F	240	252	1.20	1.31	NA	NA
3441	F	234	261	1.17	1.28	NA	NA
3442	F	237	255	1.19	1.30	NA	NA
3443	F	248	261	1.24	1.35	NA	NA
3444	F	236	253	1.18	1.29	NA	NA
$\bar{x}$		239	256	1.20	1.31		

* - 1 ml weighs 0.9159 g
NA - Not applicable

AMA LABORATORIES, INC.
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New City, NY 10956 USA
(914) 634-4300
FAX: (914) 638-4872

PRIMARY SKIN IRRITATION

AMA REF. NO.:

SPONSOR:

PRODUCT DESCRIPTION:

AMA LAB NO.:	B-3227
DATE RECEIVED:	January 20, 1995
DATE OF REPORT:	January 27, 1995
REFERENCE:	Primary Skin Irritation. FHSLA, 16 CFR 1500.41.
SOP REFERENCE:	201.00
ANIMALS:	Six healthy, Adult New Zealand White Albino Rabbits (2.0 - 3.0 kg) from Sgarlats Rabbitry, Harvey's Lake, Pennsylvania.
DIET:	Purina Rabbit Pellets. Feed and water were supplied ad-libitum prior to dosing and immediately thereafter. Records were kept of the food supplier, delivery date, feed identity, batch number (if available) and expiration date. No feed was used beyond its expiration date.

Test material:
78-82% Phenyl Trimethicone
18-22% Polysilicone-11

ENVIRONMENTAL CONDITIONS:

Prior to the test period the animals were each uniquely identified with sequentially numbered metal ear tags and individually housed in stainless steel wire bottomed cages in an environmentally controlled room with a 12 hour light/dark cycle. Feed and water were provided ad-libitum after dosing. Litter is changed not less frequently than every third day and more if deemed necessary. Floors are broom cleaned as necessary and mopped with disinfectant (Spartan Sterigent Germicidal Cleanser or Pine Multi-Purpose Disinfectant) on each day of litter removal. Newly received animals are quarantined for a period of 24 hours or more if necessary to determine the health status, prior to assignment in the housing facility. The animals are then further conditioned for a period of not less than 4 additional days before testing commencement.

PROCEDURE:

Preparation of the Test Material:

Dilutions: not applicable

Diluent (Vehicle): not applicable

Preparation of Animals: Six healthy and well adapted adult New Zealand White Albino rabbits weighing between 2.0 and 3.0 kg each were used. Approximately 24 hours before testing the rabbits were prepared by clipping the trunk free of hair. After shaving and just before testing, the skin of each animal was evaluated for any anomalies by grading according to the scale of "FHSLA, 16 CFR 1500.41". If any site scores greater than zero, that rabbit was rejected and replaced. Any newly grown fur is removed on the day of the test with care to avoid irritation to the skin.

Preparation of the Test Site and Application of the Test Substance: Five-tenths of a milliliter (0.5 ml) of the test material was applied to a small area (approximately 6 cm^2) of the previously cleared intact and abraded skin and covered with a occlusive gauze patch, which was held in place with non-irritating, non-sensitizing tape. The entire trunk of the animal was wrapped with a rubberized elastic bandage to retard evaporation and as an aid in maintaining the test patch in position.

Exposure Period: Animals were exposed to the test substance as indicated for a period of 24 hours after which, bandages were removed and all test sites were gently wiped with a cloth to remove any residual test material. Animals were examined for signs of erythema and edema and the responses were scored at 24 hours after application and then again at 72 hours. Scoring was conducted in accordance with the reference. Observations to fully evaluate the reversibility or irreversibility may be extended to a maximum of 14 days after application.

ARCHIVING:

All original samples, raw data sheets, technicians notebooks, correspondence files, and copies of final reports and remaining specimens are maintained on premises of AMA Laboratories in limited access storage files marked "Archive". A duplicate disk copy of final reports is separately archived in a bank safe deposit vault.

OBSERVATIONS: Unremarkable.

RESULTS: Please refer to attached Table.

CONCLUSIONS: The above material

when tested as indicated herein is considered to be a **NON-PRIMARY IRRITANT** to the skin according to the reference.

Skyla Cantor, Ph.D.
Study Director

Albert Lukin, B.S.
Animal Toxicologist

David R. Winne, B.S.
Quality Assurance Supervisor

1/27/95
Date

TABLE

ERYTHEMA & ESCHAR SCORES

AMA Lab. No.: B-3227
Client No.:
Amount Test Material Used: 0.5 ml
Dilution: not applicable Diluent: not applicable

Rabbit No:		2756	2757	2758	2764	2765	2766	
Sex:		M	M	M	F	F	F	
Induction Weight (Kg):		2.92	2.90	2.94	2.90	2.96	2.88	MEAN
SKIN SITES	REACTION							$\bar{x}$
		24 Hours						
INTACT (Left)	Erythema	0	0	0	0	0	0	0.00
	Edema	0	0	0	0	0	0	0.00
ABRADED (Right)	Erythema	0	0	0	0	0	0	0.00
	Edema	0	0	0	0	0	0	0.00
		72 Hours						
INTACT (Left)	Erythema	0	0	0	0	0	0	0.00
	Edema	0	0	0	0	0	0	0.00
ABRADED (Right)	Erythema	0	0	0	0	0	0	0.00
	Edema	0	0	0	0	0	0	0.00

Primary Irritation Index (PII) of 24 and 72 hour scores:

PII = 0.00

Primary Skin Irritation Score

0 - 0.5 - non-primary irritant
0.6 - 2.0 - mild primary irritant
2.1 - 5.0 - moderate primary irritant
5.1 - severe primary irritant

FHSLA PRIMARY SKIN IRRITATION

Evaluation of skin reactions:

Erythema and eschar formation	Value
No erythema	0
Very slight erythema (barely perceptible)	1
Well-defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth)	4

Edema formation	
No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well defined by definite raising)	2
Moderate edema (raised approximately 1 mm)	3
Extreme edema (raised more than 1 mm and extending beyond the area of exposure)	4

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PRIMARY OCULAR IRRITATION

AMA REF. NO.:

SPONSOR:

PRODUCT DESCRIPTION:

AMA LAB NO.:	B-3227
DATE RECEIVED:	January 20, 1995
DATE OF REPORT:	January 27, 1995
REFERENCE:	Primary Eye Irritation. FHSLA 16 CFR 1500.42.
SOP REFERENCE:	301.00
ANIMALS:	Six healthy, Adult New Zealand White Albino Rabbits (2.0 - 3.0 kg), from Sgarlats Rabbitry, Harvey's Lake, Pennsylvania.
DIET:	Purina Rabbit Pellets. Feed and water were supplied ad-libitum prior to dosing and immediately thereafter. Records were kept of the food supplier, delivery date, feed identity, batch number (if available) and expiration date. No feed was used beyond its expiration date.

Test material:
78-82% Phenyl Trimethicone
18-22% Polysilicon-11

ENVIRONMENTAL CONDITIONS:

Prior to the test period the animals were uniquely identified with metal ear tags and individually housed in wire bottom cages in an environmentally controlled room with a 12 hour light/dark cycle. Feed and water were provided ad-libitum after dosing. Litter is changed not less frequently than every third day and more frequently if deemed necessary. Floors are broom cleaned as necessary and mopped with disinfectant (Spartan Sterigent Germicidal Cleanser or Pine Multi-Purpose Disinfectant) on each day of litter removal. Newly received animals are quarantined in a separate area for a period of 24 hours or more if necessary to determine the health status, prior to assignment in the housing facility. The animals are then further conditioned for a period of not less than 4 additional days before testing commencement.

PROCEDURE:

Preparation of the Test Material:

Dilutions: Not Applicable.

Diluent (Vehicle): Not Applicable.

Six healthy, adult, albino rabbits exhibiting no ocular defects or corneal injury were selected for test. One-tenth of a milliliter (0.1 ml) of the test material was placed on the everted lower lid of one eye of each rabbit. The upper and lower lids were gently held together for one second before releasing, to prevent loss of the test material. The contralateral eye of each rabbit remained untreated and served as a control. Ocular lesions were evaluated by the method of Draize/1.

The Draize scores were then classified according to Kay and Calandra/2. Lesions were evaluated at 24 hours and 72 hours post instillation. A 2% fluorescein sodium solution, followed by wash with physiological saline solution, was utilized as necessary for ocular observations.

ARCHIVING:

All original samples, raw data sheets, technicians notebooks, correspondence files, and copies of final reports and remaining specimens are maintained on premises of AMA Laboratories in limited access storage files marked "Archive". A duplicate disk copy of final reports is separately archived in a bank safe deposit vault.

REFERENCE:

/1 Draize et al. J. Pharmacol. Exp. Ther. 83 : 377-390, 1944.
/2 Kay & Calandra, J. Soc. Cos. Chem. 13 : 281-289, 1962.

OBSERVATIONS: Unremarkable.

RESULTS: Please refer to attached Table.

CONCLUSIONS: The 24 hour MMTS of the test material is 0.00. The above material when tested as described herein is considered to be **NON-IRRITATING** to the eyes according to the reference.

Shyla Cantor, Ph.D.
Study Director

Albert Lukin, B.S.
Animal Toxicologist

David R. Winne, B.S.
Quality Assurance Supervisor

1/29/95
Date

TABLE

PRIMARY EYE IRRITATION

AMA LAB. NO.:
CLIENT NO.:
Amount Test Material Used: 0.1 ml
Dilutions: Not Applicable Diluent (Vehicle): Not Applicable

Rabbit No.:	2756			2757			2758			2764			2765			2766		
Sex:	M			M			M			F			F			F		
Induction Weight (Kg):	2.92			2.90			2.94			2.90			2.96			2.88		
Hours:	24	48	72	24	48	72	24	48	72	24	48	72	24	48	72	24	48	72
I. Cornea																		
A. Opacity	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B. Area	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
AxBx5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
II. Iris																		
A. Values	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Ax5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
III. Conjunctivae																		
A. Hyperemia	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
B. Chemosis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
C. Discharge	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
(A+B+C)x2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Total I+II+III	0			0			0			0			0			0		

Mean: 0.00

MMTS: Maximum Mean Total Score = 0.00

MMTS	Classification
0.0 - 0.5	Non-irritating
0.6 - 2.5	Practically non-irritating
2.6 - 15.0	Minimally irritating
15.0 - 25.0	Mildly irritating
25.1 - 50.0	Moderately irritating
50.1 - 80.0	Severely irritating
80.1 - 100.0	Extremely irritating
100.1 - 110.0	Maximally irritating

Scale for Scoring Ocular Lesions

(1) Corneas
(A) Opacity - degree of density (area most dense taken for reading)

No opacity..... 0
Scattered or diffused area, details of iris clearly visible..... 1
Easily discernible translucent areas, details of iris slightly obscured..... 2
Opalescent areas, no details of iris visible, size of pupil barely discernable..... 3
Opaque, iris invisible..... 4

(B) Area of cornea involved

One quarter or less, but not zero..... 1
Greater than one quarter, but less than half..... 2
Greater than half, but less than three quarters..... 3
Greater than three quarters, up to whole area..... 4

AxBx5 Total Maximum = 80

(2) Iris
(A) Values

Normal..... 0
Folds above normal, congestion, swelling, circumcorneal injection (any or all of these, or combination of any thereof) iris still reacting to light (sluggish reaction is positive)..... 1
No reaction to light, hemorrhage, gross destruction (any or all of these)..... 2

(3) Conjunctivae
(A) Redness (refers to palpebral and bulbar conjunctivae excluding cornea and iris)

Vessels normal..... 0
Vessels definitely injected above normal..... 1
More diffuse, deeper crimson red, individual vessels not easily discernable..... 2
Diffuse, beefy red..... 3

(B) Chemosis

No swelling..... 0
Any swelling above normal (included nictating membrane)..... 1
Obvious swelling with partial eversion of lids..... 2
Swelling with lids about half closed..... 3
Swelling with lids about half to completely closed.... 4

(C) Discharge

No discharge..... 0
Any amount different form normal (does not include small amounts observed in inner canthus of normal animals)..... 1
Discharge with moistening of the lids and hairs just adjacent to lids..... 2
Discharge with moistening of the lids and hairs and considerable area around the eye..... 3

Score (A+B+C)x2 Total maximum = 20

TOTAL MAXIMUM SCORE: 110 represents the sum of all scores obtained for the cornea, iris and conjunctivae.

Consumer Product Testing Co.

EST. 1975

FINAL REPORT

CLIENT:

ATTENTION:

TEST: Repeated Insult Patch Test
Protocol No.: 1.01

TEST MATERIAL:

Test material 100% Trimethylsiloxy phenyl Dimethicone

EXPERIMENT REFERENCE NUMBER: C02-0974.01

35-45 cps (viscosity)

1500 - 3000 Daltons

Richard R. Eisenberg, M.D.
Board Certified Dermatologist

R. W. Shanahan

Robert W. Shanahan, Ph.D.
Principal Investigator

Joy Frank

Joy Frank, R.N.
Study Director

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Consumer Product Testing Co.
EST 1975

QUALITY ASSURANCE UNIT STATEMENT

Study No.: C02-0974.01

The objective of the Quality Assurance Unit (QAU) is to monitor the conduct and reporting of clinical laboratory studies. These studies have been performed with adherence to ICH Guideline E6 for Good Clinical Practice and requirements provided for in 21 CFR parts 50 and 56 and in accordance to standard operating procedures and applicable protocols. The QAU maintains copies of study protocols and standard operating procedures and has inspected this study on the date(s) listed below. The findings of these inspections have been reported to management and the Study Director. All materials and data pertinent to this study will be stored in the Archive Facility at 70 New Dutch Lane, Fairfield, New Jersey, 07004, unless specified otherwise, in writing by the Sponsor.

Date(s) of inspection:
October 22, 2002
November 26, 2002
December 11, 2002
December 16, 2002

Senior personnel involved:

Laura A. Artiles, M.A. - Manager, Quality Assurance

Marie Terlizzese
Marie Terlizzese, M.S.
Quality Assurance Associate

The representative signature of the Quality Assurance Unit signifies that this study has been performed in accordance with standard operating procedures and study protocol as well as government regulations regarding such procedures and protocols.

Objective: To determine by repetitive epidermal contact the potential of a test material to induce primary or cumulative irritation and/or allergic contact sensitization.

Participants: Fifty-six (56) qualified subjects, male and female, ranging in age from 17 to 79 years, were selected for this evaluation. Fifty-one (51) subjects completed this study. The remaining subjects discontinued their participation for various reasons, none of which were related to the application of the test material.

Inclusion Criteria:

a. Male and female subjects, age 16[a] and over.
b. Absence of any visible skin disease which might be confused with a skin reaction from the test material.
c. Prohibition of use of topical or systemic steroids and/or antihistamines for at least seven days prior to study initiation.
d. Completion of a Medical History form and the understanding and signing of an Informed Consent form.
e. Considered reliable and capable of following directions.

Exclusion Criteria:

a. Ill health.
b. Under a doctor's care or taking medication(s) which could influence the outcome of the study.
c. Females who are pregnant or nursing.
d. A history of adverse reactions to cosmetics or other personal care products.

Test Material:

Study Schedule:

Panel #	Initiation Date	Proposed Completion Date	Actual Completion Date
20020513	October 23, 2002	December 5, 2002	December 6, 2002

[a]With parental or guardian consent

Methodology:

The upper back between the scapulae served as the treatment area. Approximately 0.2 ml of the test material, or an amount sufficient to cover the contact surface, was applied to the 3/4" x 3/4" absorbent pad portion of an adhesive dressing*. This was then applied to the appropriate treatment site to form an occluded patch.

Induction Phase:

Patches were applied three (3) times per week (e.g., Monday, Wednesday, and Friday) for a total of nine (9) applications. The site was marked to ensure the continuity of patch application. Following supervised removal and scoring of the first Induction patch, participants were instructed to remove all subsequent Induction patches at home, twenty-four hours after application. The evaluation of this site was made again just prior to re-application. If a participant was unable to report for an assigned test day, one (1) makeup day was permitted. This day was added to the Induction period.

With the exception of the first supervised Induction Patch reading, if any test site exhibited a moderate (2-level) reaction during the Induction Phase, application was moved to an adjacent area. Applications are discontinued for the remainder of this test phase, if a moderate (2-level) reaction was observed on this new test site. Applications would also be discontinued if marked (3-level) or severe (4-level) reactivity was noted.

Rest periods consisted of twenty-four hours following each Tuesday and Thursday removal, and forty-eight hours following each Saturday removal.

Challenge Phase:

Approximately two (2) weeks after the final Induction patch application, a Challenge patch was applied to a virgin test site adjacent to the original Induction patch site, following the same procedure described for Induction. The patch was removed and the site scored at the clinic twenty-four and seventy-two hours post-application.

It was noted that due to inclement weather, numerous subjects were unable to report as scheduled. They were instructed to remove the patch and report on the following test day.

*Manufactured by TruMed Technologies, Inc., Burnsville, MN

Evaluation Key:

0 = No visible skin reaction
+ = Barely perceptible or spotty erythema
1 = Mild erythema covering most of the test site
2 = Moderate erythema, possible presence of mild edema
3 = Marked erythema, possible edema
4 = Severe erythema, possible edema, vesiculation, bullae and/or ulceration

Results:

The results of each participant are appended (Table 1).

Observations remained within normal limits throughout the test interval.

Summary:

Under the conditions of this study, test material, did not indicate a potential for dermal irritation or allergic contact sensitization.

Table 1
Panel #20020513

Individual Results

Subject Number	24*hr	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site 24*hr	72 hr
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	1	+	+	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0[m]	0	0
8	0	0	0	0	DID NOT COMPLETE STUDY							
9	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0	0	0[W]
14	0	0	0	0	0	0	0	0	0	0	0	0[W]
15	0	0	0	0	0	0	0	0	DID NOT COMPLETE STUDY			
16	0	0	0	0	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0	0	0	0	0[W]
21	0	0	0	0	0	0	0	0	0	0	0	0[W]
22	0	0	0	0	0	0	0	0	0	0	0	0[W]
23	0	0	0	0	0	0	0	0	0	0	0	0[W]
24	0	0	0	0	0	0	0	0	0	0	0	0[W]
25	0	0	0	0	0	0	0	0	0	0	0	0[W]
26	0	0	0	0	0	0	0	0	0	0	0	0[W]
27	0	0	0	0	0	0	0	0	0	0	0	0[W]
28	0	0	0	0	0	0	0	0	0	0	0	0[W]
29	0	0	0	0	0	0	0	0	0	0	0	0

24* = Supervised removal of 1st Induction and Challenge Patch
m = Additional makeup day granted at the discretion of the clinic supervisor
W = Inclement weather. Subject unable to report as scheduled. Observation recorded 96 hours post challenge application.

Table 1
(continued)
Panel #20020513

Individual Results

Subject Number	Induction Phase 24*hr	1	2	3	4	5	6	7	8	9	Virgin Challenge Site 24*hr	72 hr
30	0	0	0	0	0	0	0	0	0	0	0	0
31	0	0	0	0	0	0	0	0	0	0	0	0 W
32	0	0	0	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0	0	0
34	0	0	0	0	0	0	0	0	0	0	0	0 W
35	0	0	0	0	0	0	0	0	0	0	0	0 W
36	0	0	0	0	0	0	0	0	0	0	0	0
37	0	0	0	0	0	0	0	0	0	0	0	0
38	0	0	0	0	0	0	0	0	0	0	0	0 W
39	0	0	0	0	0	0	0	0	0	0	0	0
40	0	0	0	0	0	0	0	0	0	0	0	0 W
41	0	0	0	0	0	0	0	0	0	0	0	0 W
42	0	0	0	0	0	0	0	0	0	0	0	0
43	0	0	0	0	0	0	0	0	0	0	0	0 W
44	0	0	0	0	0	0	0	0	0	0	0	0 W
45	0	0	0	0	0	0	0	0	0	0	0	0 W
46	0	0	0	0	0	0	0	0	0	0	----DNC---	
47	0	0	0	0	0	0	0	0	0	0	0	0
48	0	0	0	0	0	0	0	0	0	0	0	0 W
49	0	0	0	0	0	0	0	0	0	0	0	0 W
50	0	0	0	0	0	0	0	0	0	0	0	0 W
51	0	0	0	0	0	0	0	0	0	0	0	0
52	0	0	0	0	0	0	0	0	0	0	0	0
53	0	0	0	0	0	0	0	0	0	0	0	0 W
54	0	0	0	0	0	0	0	0	0	0	0	0
55	0	0	0	0	0	0	0	0	0	0	0	DNC
56	0	0	0	0	0	----------DID NOT COMPLETE STUDY----------						

24* = Supervised removal of 1st Induction and Challenge Patch
DNC = Did not complete study
W = Inclement weather. Subject unable to report as scheduled. Observation recorded 96 hours post challenge application.

Table 2
Panel #20020513

Subject Data

Subject Number	Initials	Age	Sex
1		59	F
2		70	M
3		70	F
4		70	F
5		37	F
6		31	F
7		39	F
8		58	F
9		46	M
10		41	F
11		41	F
12		50	F
13		38	F
14		40	F
15		51	M
16		52	F
17		65	M
18		47	M
19		66	F
20		67	F
21		61	F
22		79	M
23		59	F
24		42	F
25		17	F
26		48	F
27		35	F
28		35	F
29		58	M

Table 2
(continued)
Panel #20020513

Subject Data

Subject Number	Initials	Age	Sex
30		41	F
31		32	F
32		47	F
33		67	F
34		43	F
35		57	F
36		42	F
37		55	F
38		47	F
39		55	M
40		18	F
41		41	F
42		75	M
43		34	M
44		72	M
45		66	F
46		65	F
47		65	M
48		54	F
49		41	F
50		43	F
51		54	F
52		52	F
53		39	F
54		35	F
55		63	F
56		46	M

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Carol Eisenmann, Ph.D.
Personal Care Products Council

DATE: May 20, 2022

SUBJECT: Diphenyl Dimethicone and Diphenylsiloxy Phenyl Trimethicone

ShinEtsu. 2022. Toxicity and hazardousness information of cosmetic silicone ingredients: Diphenyl Dimethicone 100%.

ShinEtsu. 2022. Toxicity and hazardousness information of cosmetic silicone ingredients: Diphenylsiloxy Phenyl Dimethicone 100%.

Toxicity and hazardousness information of cosmetic silicone ingredients

To: Personal Care Products Council
Test ingredient: Diphenyl Dimethicone 100%
Shin-Etsu Product Name: KF-54

(1) Guinea Pig Sensitization (Buehler)

Method: Twelve (6M:6F) Hartley albino, outbred, viral antibody free, guinea pigs (SPF Hartley guinea pig Aai: (HA) Outbred), 364-447 grams, each received three(3) topical, occluded applications of the test article during the induction period of three(3) weeks. An additional group of ten(5M: 5F) Hartley-strain guinea pigs, 378-446 grams, served as a control group. These animals did not receive induction applications. Two (2) weeks following the last induction application, the animals in the test group received a topical application of the test article to a dorsal, virgin site. At the same time, the control group animals received an identical dosage of the test article. Observations of irritation and other effects were recorded 7 and 24 hours after each induction application and 7, 24 and 48 hours following the challenge and rechallenge applications. The test article was used as received for the induction and the challenge dosages.

Conclusion: This test article is not a sensitizer in guinea pigs, under the conditions of this test.

(2) Primary Dermal Irritation in Rabbits

Method: Six (6) New Zealand white rabbits each received a single dermal application of one-half of one milliliter (0.5ml) of the test article on two (2) test sites, one (1) abraded and one (1) non-abraded. The test sites were occluded for 24 hours and were observed individually for erythema, edema, and other effects 24 and 72 hours after application. Mean scores from the 24 and 72 hour readings were averaged to determine the primary irritation index. The test article was used as received.

Results: Primary Irritation Index: 0.28

Conclusion: According to Federal Hazardous Substances Act Regulations, (16 CFR 1500.41), and under the conditions of this test,

this test article is not a primary dermal irritant.

Tested date;
1),2) Aug, 2003

May 20, 2022
M. Masuda
Silicone Division
Shin-Etsu Chemical Co., Ltd.

Toxicity and hazardousness information of cosmetic silicone ingredients

To: Personal Care Products Council
Test ingredient: Diphenylsiloxy Phenyl Trimethicone 100%
Shin-Etsu Product Name: KF-56A
(This ingredient is the solvent of KSG-18A.)

(1) Primary skin irritation study in rabbits

The primary skin irritation potential of the test item was investigated according to OECD test guideline no.404. The test item was applied by topical semi-occlusive application of 0.5mL to the intact left flank of each of three young adult New Zealand White rabbits. The duration of treatment was four hours. The scoring of skin reactions was performed 1,24,48 and 72 hours after removal of the dressing.

Based upon the referred classification criteria (commission Directive 2001/59/EC of August 2001), this test item is considered to be "not irritating" to rabbit skin.

(2) Local Lymph Node Assay in Mice

In order to study a possible contact allergenic potential of the test item, three groups each of four female mice were treated daily with the test item at concentrations of 25%, 50% in acetone: olive oil, 4:1(v/v) and 100% (undiluted) by topical application to the dorsum of each ear lobe (left and right) for three consecutive days. A control group of four mice was treated with the vehicle (acetone: olive oil, 4:1 (v/v) only.

Five days after the first topical application the mice were injected intravenously into a tail vein with radio-labelled thymidine (^{3}H-methyl thymidine). Approximately five hours after intravenous injection, the mice were sacrificed, the draining auricular lymph nodes excised and pooled per group. Single cell suspensions of lymph node cells were prepared from pooled lymph nodes which were subsequently washed and incubated with trichloroacetic acid overnight. The proliferative capacity of pooled lymph node cells was determined by the incorporation of ^{3}H-methyl thymidine measured in a β-scintillation counter.

All treated animals survived the scheduled study period.

No clinical signs were observed in any animals of the control group or Group 2 (25%). On the second application day, a slight ear swelling was observe at both dosing sites in all mice of Group 4 (100%, undiluted), persisting for a total of four days. In addition, on the third application day, a slight ear erythema was observed at both dosing sites in all mice of Group3 (50%) and Group 4 (100%, undiluted), persisting for a total of three days.

The results obtained (STIMULATION INDEX (S.I.));

Group2: S.I.=1.0 (test item concentration 25%)

Group3: S.I.=2.0 (test item concentration 50%)

Group4: S.I.=2.4 (test item concentration 100%)

Tested date;

1) Oct, 2004

2) Jun, 2004

May 17, 2022

M. Masuda
Silicone Division
Shin-Etsu Chemical Co., Ltd.

2022 FDA VCRP Data for Phenyl-Substituted Methicone Ingredients

INGREDIENT NAME	CATEGORY CODE AND DESCRIPTION		CPIS COUNT
Diphenyl Dimethicone			
Total Uses: 145			
Diphenyl Dimethicone	03C - Eye Shadow		32
Diphenyl Dimethicone	05A - Hair Conditioner		1
Diphenyl Dimethicone	05B - Hair Spray (aerosol fixatives)		1
Diphenyl Dimethicone	07A - Blushers (all types)		2
Diphenyl Dimethicone	07C - Foundations		9
Diphenyl Dimethicone	07E - Lipstick		64
Diphenyl Dimethicone	07F - Makeup Bases		5
Diphenyl Dimethicone	07G - Rouges		16
Diphenyl Dimethicone	07I - Other Makeup Preparations		1
Diphenyl Dimethicone	12A - Cleansing		1
Diphenyl Dimethicone	12C - Face and Neck (exc shave)		2
Diphenyl Dimethicone	12D – Body and Hand (exc shave)		1
Diphenyl Dimethicone	12F - Moisturizing		5
Diphenyl Dimethicone	12I – Skin Fresheners		1
Diphenyl Dimethicone	12J - Other Skin Care Preps		4
Diphenylsiloxy Phenyl Trimethicone			
Total Uses: 269			
Diphenylsiloxy Phenyl Trimethicone	03B	Eyeliner	5
Diphenylsiloxy Phenyl Trimethicone	03C	Eye Shadow	30
Diphenylsiloxy Phenyl Trimethicone	03D	Eye Lotion	5
Diphenylsiloxy Phenyl Trimethicone	03G	Other Eye Makeup Preparations	7
Diphenylsiloxy Phenyl Trimethicone	07A	Blushers (all types)	21
Diphenylsiloxy Phenyl Trimethicone	07B	Face Powders	12
Diphenylsiloxy Phenyl Trimethicone	07C	Foundations	27
Diphenylsiloxy Phenyl Trimethicone	07E	Lipstick	75
Diphenylsiloxy Phenyl Trimethicone	07F	Makeup Bases	1
Diphenylsiloxy Phenyl Trimethicone	07G	Rouges	1
Diphenylsiloxy Phenyl Trimethicone	07H	Makeup Fixatives	1
Diphenylsiloxy Phenyl Trimethicone	07I	Other Makeup Preparations	30
Diphenylsiloxy Phenyl Trimethicone	12A	Cleansing	5
Diphenylsiloxy Phenyl Trimethicone	12C	Face and Neck (exc shave)	10
Diphenylsiloxy Phenyl Trimethicone	12D	Body and Hand (exc shave)	4
Diphenylsiloxy Phenyl Trimethicone	12F	Moisturizing	28
Diphenylsiloxy Phenyl Trimethicone	12G	Night	5
Diphenylsiloxy Phenyl Trimethicone	12H	Paste Masks (mud packs)	2
Phenyl Dimethicone			
Total Uses: 8			
Phenyl Dimethicone	05B	Hair Spray (aerosol fixatives)	2

Phenyl Dimethicone	05G	Tonics, Dressings, and Other Hair Grooming Aids	2
Phenyl Dimethicone	07E	Lipstick	1
Phenyl Dimethicone	07F	Makeup Bases	1
Phenyl Dimethicone	12G	Night	1
Phenyl Dimethicone	12J	Other Skin Care Preps	1
Phenyl Methicone			
Total Uses: 10			
Phenyl Methicone	03D	Eye Lotion	1
Phenyl Methicone	07C	Foundations	2
Phenyl Methicone	08E	Nail Polish and Enamel	2
Phenyl Methicone	08G	Other Manicuring Preparations	1
Phenyl Methicone	12F	Moisturizing	2
Phenyl Methicone	12G	Night	2
Phenyl Trimethicone			
Total Uses: 781			
Phenyl Trimethicone	01B	Baby Lotions, Oils, Powders, and Creams	3
Phenyl Trimethicone	03A	Eyebrow Pencil	2
Phenyl Trimethicone	03B	Eyeliner	13
Phenyl Trimethicone	03C	Eye Shadow	98
Phenyl Trimethicone	03D	Eye Lotion	1
Phenyl Trimethicone	03G	Other Eye Makeup Preparations	23
Phenyl Trimethicone	04B	Perfumes	1
Phenyl Trimethicone	04E	Other Fragrance Preparation	2
Phenyl Trimethicone	05A	Hair Conditioner	42
Phenyl Trimethicone	05B	Hair Spray (aerosol fixatives)	51
Phenyl Trimethicone	05C	Hair Straighteners	6
Phenyl Trimethicone	05F	Shampoos (non-coloring)	4
Phenyl Trimethicone	05G	Tonics, Dressings, and Other Hair Grooming Aids	75
Phenyl Trimethicone	05I	Other Hair Preparations	38
Phenyl Trimethicone	06B	Hair Tints	4
Phenyl Trimethicone	06E	Hair Color Sprays (aerosol)	6
Phenyl Trimethicone	07A	Blushers (all types)	27
Phenyl Trimethicone	07B	Face Powders	32
Phenyl Trimethicone	07C	Foundations	66
Phenyl Trimethicone	07E	Lipstick	88
Phenyl Trimethicone	07F	Makeup Bases	19
Phenyl Trimethicone	07G	Rouges	4
Phenyl Trimethicone	07H	Makeup Fixatives	2
Phenyl Trimethicone	07I	Other Makeup Preparations	43
Phenyl Trimethicone	08B	Cuticle Softeners	1
Phenyl Trimethicone	10B	Deodorants (underarm)	1
Phenyl Trimethicone	11B	Beard Softeners	1

Phenyl Trimethicone	12A	Cleansing	2
Phenyl Trimethicone	12C	Face and Neck (exc shave)	31
Phenyl Trimethicone	12D	Body and Hand (exc shave)	16
Phenyl Trimethicone	12F	Moisturizing	58
Phenyl Trimethicone	12G	Night	2
Phenyl Trimethicone	12H	Paste Masks (mud packs)	1
Phenyl Trimethicone	12I	Skin Fresheners	4
Phenyl Trimethicone	12J	Other Skin Care Preps	9
Phenyl Trimethicone	13A	Suntan Gels, Creams, and Liquids	4
Phenyl Trimethicone	13B	Indoor Tanning Preparations	1
Trimethylsiloxyphenyl Dimethicone Total Uses: 47			
Trimethylsiloxyphenyl Dimethicone	03B	Eyeliner	1
Trimethylsiloxyphenyl Dimethicone	03G	Other Eye Makeup Preparations	1
Trimethylsiloxyphenyl Dimethicone	05A	Hair Conditioner	1
Trimethylsiloxyphenyl Dimethicone	07C	Foundations	3
Trimethylsiloxyphenyl Dimethicone	07E	Lipstick	29
Trimethylsiloxyphenyl Dimethicone	07I	Other Makeup Preparations	11
Trimethylsiloxyphenyl Dimethicone	12C	Face and Neck (exc shave)	1