Safety Assessment of Phenyl-Substituted Methicones as Used in Cosmetics

Status:	Draft Tentative Report for Panel Review
Release Date:	February 10, 2023
Panel Meeting Date:	March 6-7, 2023

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.; 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. Previous Panel member involved in this assessment: Daniel C. Liebler, 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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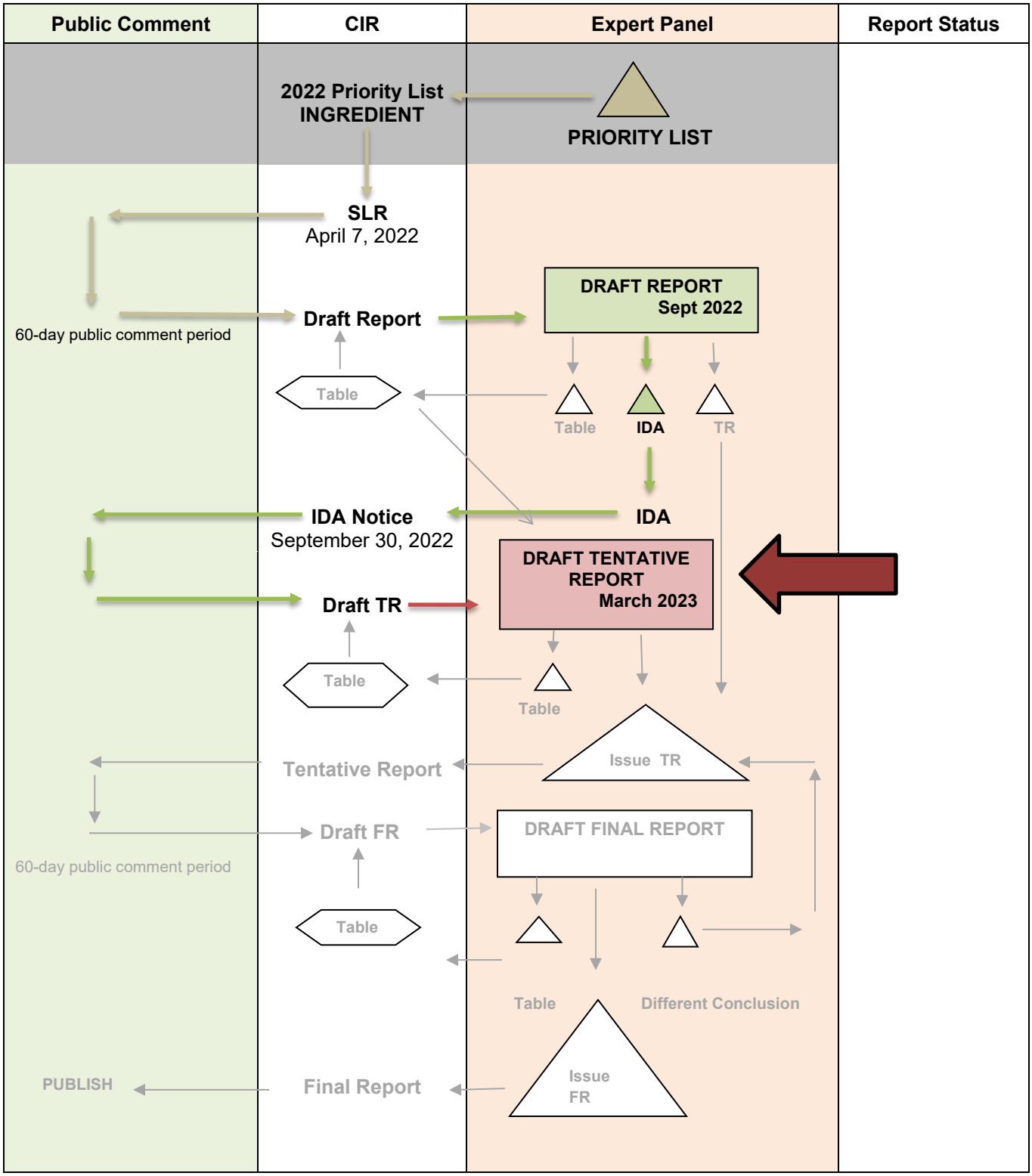
SAFETY ASSESSMENT FLOW CHART

INGREDIENT/FAMILY Phenyl-Substituted Methicones

MEETING March 2023



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: February 10, 2023
Subject: Safety Assessment of Phenyl-Substituted Methicones as Used in Cosmetics

Enclosed is a Draft Tentative Report of the Safety Assessment of Phenyl-Substituted Methicones as Used in Cosmetics (identified as *report_PhenylSubMethicones_032023* in the pdf). This is the second time the Panel is seeing a safety assessment of these 7 cosmetic ingredients. At the September 2022 meeting, a Draft Report was presented to the Panel. Upon review, the Panel issued an Insufficient Data Announcement (IDA) for the following data needs:

- Method of manufacture data and impurities (specific to cosmetic ingredients) for all ingredients
- Molecular weight ranges for all ingredients

Data which were received in response to the IDA have been incorporated and are highlighted in yellow in the report:

data1_PhenylSubMethicones_032023
- Anonymous. 2022. Method of manufacture and molecular weight – Diphenyl Dimethicone
- Anonymous. 2022. Method of manufacture and molecular weight – Phenyl Trimethicone

*data2_PhenylSubMethicones_032023_*
- Anonymous. 2022. Impurities and molecular weight – Diphenyl Dimethicone and Diphenylsiloxy Phenyl Trimethicone
- Anonymous. 2022. General manufacturing process of Diphenyl Dimethicone
- Anonymous. 2022. General manufacturing process of Diphenylsiloxy Phenyl Trimethicone

data3_PhenylSubMethicones_032023
- Anonymous. 2019. Clinical safety evaluation repeated insult patch test (lip balm containing 11% Diphenylsiloxy Phenyl Trimethicone).
- Anonymous. 2011. Clinical safety evaluation repeated insult patch test (product containing 20% Phenyl Trimethicone).

data4_PhenylSubMethicones_032023
- Anonymous. 2023. Phenyl Trimethicone (process flow diagram, impurities, molecular weight)

The Panel has previously published a safety assessment 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, as published in 2006. Since this ingredient is now included in this report, these previous reports are included in this package for your review (*originalreport_PhenylSubMethicones_032023; rereview2006_PhenylSubMethicones_032023*, respectively). The associated meeting minutes are also included for your review (*originalminutes_PhenylSubMethicones_032023*).

As per the Panel's request at the December 2022 meeting, an updated use table format has been implemented. The frequency and concentration of use is presented both cumulatively by likely duration and exposure and individually by product category.

Also included in this package, for your review, are a flow chart (*flow_PhenylSubMethicones_032023*), literature search strategy (*search_PhenylSubMethicones_032023*), ingredient data profile (*dataprofile_PhenylSubMethicones_032023*), ingredient history (*history_PhenylSubMethicones_032023*), and transcripts from the previous meeting (*transcripts_PhenylSubMethicones_032023*).

The Panel should carefully consider and discuss the data (or lack thereof), and the draft Abstract and draft Discussion presented in this report. A Tentative Report with a safe as used, safe with qualifications, insufficient, split, or unsafe conclusion should then be issued.

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 was presented to the Panel. The Panel issued an IDA with the following data needs:
- Method of manufacture and impurities (specific to cosmetic ingredients) for all ingredients
- Molecular weight ranges for all ingredients

Data received, by date:

November 14, 2022

- Anonymous. 2022. Method of manufacture and molecular weight – Diphenyl Dimethicone
- Anonymous. 2022. Method of manufacture and molecular weight – Phenyl Trimethicone

November 21, 2022

- Anonymous. 2022. Impurities and molecular weight – Diphenyl Dimethicone and Diphenylsiloxy Phenyl Trimethicone
- Anonymous. 2022. General manufacturing process of Diphenyl Dimethicone
- Anonymous. 2022. General manufacturing process of Diphenylsiloxy Phenyl Trimethicone

November 29, 2022

- Anonymous. 2019. Clinical safety evaluation repeated insult patch test (lip balm containing 11% Diphenylsiloxy Phenyl Trimethicone).
- Anonymous. 2011. Clinical safety evaluation repeated insult patch test (product containing 20% Phenyl Trimethicone).

January 13, 2023

- Anonymous. 2023. Phenyl Trimethicone (process flow diagram, impurities, molecular weight)

March 2023

A Draft Tentative Report is being presented to the Panel.

Phenyl-Substituted Methicones Data Profile* – March 6-7, 2023 – 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	X			X		
Diphenylsiloxy Phenyl Trimethicone	X	X	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	OX	X		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 (as of 01/17/2023)
((((((((((((((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) – 268/0

((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

SEPTEMBER 2022 PANEL MEETING – INITIAL REVIEW/DRAFT REPORT

Belsito Team – September 26, 2022

[Belsito team minutes have yet to be located]

Cohen Team – September 26, 2022

Dr. David Cohen - OK, let's move on to Phenyl-substituted methicones. This is the first time we're reviewing this draft report and we're looking at 7 derived ingredients. These are used as antifoaming agents and skin and or hair conditioning agents. We have highest concentration of use of 59.5% and non coloring shampoos and 28.5% in a leave on product. Several of these products are reported to be used near the eye, namely Diphenylsiloxy Phenyl Trimethicone at almost 20% in an eyeliner. And Diphenyl Dimethicone at 24.1% in lipsticks. We recently issued a recent amended report on 30 dimethicone, methicone and Methicone substituted polymers where we concluded that these were safe as used when formulated to be non irritating. Phenyl Trimethicone was adjudicated in 1986. And then reaffirmed in 2006. And are in this report now. There was a fair amount of material cause this came in three sections, right, we there was a lot of material on this. And we have sensitization data 28.67% on phenyl and trimethicone. And need on trimethyl, siloxane phenyl dimethicone. And some other and we have some irritation. And since it is the other data that looks good. I'll stop here and open it for comments. Susan, you want to kick off?

Dr. Susan Tilton - So well, I am in terms of including these together as a class, I don't have any concerns about that. In this case. I had noted the lack of chemistry, manufacturing and impurities data. For the ingredients that were part of this group. Outside of what was previously available just for phenyl trimethicone.

Dr. David Cohen – So we need method and manufacturing and impurities for the group. Largely right?

Dr. David Ross - You've got some manufacture info, right, but it's certainly had no impurity.

Dr. Susan Tilton - Yes, I.

Dr. David Ross - But you haven't got sufficient. You haven't got sufficient method of manufacture.

Dr. David Cohen - David, how would you word that?

Dr. David Ross - I think you're original fine. Just ask them that you know complete method of manufacture and impurities.

Dr. David Cohen - OK. Yeah, that's what I have here. You know, in some of those in some of the in the S1 supplement, one of the products that 2% trimethyl, siloxane phenyl dimethicone, they look like there may have been some sensitization signals, but the rest of the data and that may have been a product related thing because none of the other data seemed to support that so I just made note of it, but it really wasn't holding me up.

Dr. David Ross - So the sensitization data (*inaudible). I'm numbered these you know. Have to match max use I just don't know.

Dr. David Ross - Data on the developer you. Maximum use.

Dr. David Cohen - I'm getting like hammering feedback is. Is anyone hearing that?

Dr. David Ross - I'm.

Dr. Tom Slaga - Yeah, I am too.

Dr. David Ross - It's not my house.

Dr. Wilma Bergfeld - Nor mine.

Dr. Tom Slaga - Not fine.

Dr. Susan Tilton - Not here.

Dr. David Cohen - I've never ever said in my house, Eva, can you knock off the hammering? Umm, so I'm pretty sure it's not my house. OK so.

Dr. Tom Slaga - I heard it, but I don't. I don't know if it's here or not. I didn't see anything.

Dr. David Cohen - Uh, Tom, what was that time?

Dr. Tom Slaga - I'm.

Dr. David Cohen - I didn't. I didn't get what you said.

Dr. Tom Slaga - Yeah. Anyway, back to the ingredient. The irritation data I think it's relative pretty good. It looks and genotoxicity is OK. We have a similar compound the polymer that is safe.
But it is the first time that we've seen this. There was some concern about sensitization of 1 compound wasn't there?

Dr. David Cohen - There was a product that had two percent trimethyl siloxane phenyl dimethicone that. In the second week of testing, started to have a number signals. But we didn't see it anywhere else. We have trimethyl siloxane phenyl dimethicone tested neat in an HRIPT.

Dr. Tom Slaga - Yeah.

Dr. David Cohen - I don't know if we know the number of people. Ohh no 51 subjects and it looked like the overall, data on irritation and sensitization looked OK, the totality of it.

Dr. Tom Slaga - It's OK.

Dr. David Ross - Yeah.

Dr. Tom Slaga - It's OK. Yeah.

Preethi Raj (CIR) - Yeah. And Speaking of Tri--

Dr. Tom Slaga - Yeah, there's a weight of evidence I think is OK too.

Preethi Raj (CIR) - Sorry, Speaking of Trimethysiloxyphenyl Dimethicone, there is an HRIPT for 205 subjects where it was tested at 38.006%.

Dr. David Cohen - Yes, yeah. That's why I didn't put a lot of eggs in that one basket of that in the S1 supplement. It was a 2%, which and I don't know what the other 98% was in there, just didn't seem to resonate with the rest of the sensitization and irritation data we have. We'll see what the Belsito team comes out with. But we have an IDA for method of manufacturing and impurities. Anything else in our IDA?

Dr. Susan Tilton - I was just going to.

Dr. David Ross - I'm not sure whether you ask for any sensitization data. Did it or not. Seems like you're comfortable with that.

Dr. David Cohen - I'll, I'll take another look.

Dr. David Ross - And could I, uh, Table 3? I could maybe quick look at that Preethi had there was a that was my comment here. The dermal contact was listed at Max 1.3%. I thought it was 24%.

Preethi Raj (CIR) - I'm sorry. Where are you looking, Doctor Ross?

Dr. David Ross - Table 3.

Dr. David Cohen - Table 3. Yeah.

Preethi Raj (CIR) - Are you looking at dermal contact for the diphenyl dimethicone?

Dr. David Ross - You go down diphenyl dimethicone. Yeah, and go down to dermal contact. It's listed at, 1.3%.

Preethi Raj (CIR) - OK. Yep.

Dr. David Ross - I thought that would be changed to 24.1 but I don't know.

Preethi Raj (CIR) - Yeah, you might be right, actually, I'll fix it. Thank you.

Dr. Susan Tilton - And I guess that was.

Dr. David Cohen - That's a nice catch there, huh?

Preethi Raj (CIR) - Yeah.

Dr. Susan Tilton - That was one thing I was going to ask. There are and you know 4 Phenyl trimethicone compared to previous the studies that were published previously. I'm wondering if the test concentrations if the maximum use concentrations have now exceeded the maximum concentration tested. For some of the studies, the same 24% in lipstick, but I wasn't sure it was tested that high.

Dr. David Cohen - Define the diphenyl dimethicone is indeed 24%.

Dr. Susan Tilton - And it was tested at up to 15%?

Preethi Raj (CIR) - Yes.

Dr. David Cohen - A Diphenyl Dimethicone let me we have animal data on that but.

Preethi Raj (CIR) - You're looking at the subchronic oral. Looks like, right, Doctor Tilton? Yeah.

Dr. Susan Tilton - That's right.

Monice Fiume (CIR) - David, while you're looking, can I just interject, so, Doctor Ross, that 24.1 as represented in the table is actually correct. As the use tables are currently formulated, lipstick is represented under incidental ingestion and mucous membrane, but not as skin, not as dermal contact. It's mucous membrane and oral. Or incidental ingestion. So the table as presented right now is correct according to our current format.

Preethi Raj (CIR) - Thanks Monice.

Dr. David Ross - The maximum concentration for dermal is 1.3 by that read.

Monice Fiume (CIR) - That would be correct.

Dr. David Cohen - Can you just reiterate that it just explain that again? Ah, OK.

Monice Fiume (CIR) – So as the current format for our use table, if something is used in a lipstick, because it's applied to lips that's considered a mucus membrane exposure and not a dermal skin exposure.

Dr. David Cohen - OK, I got it. And Susan, your question was are Max use concentrations matching the sensitization or is this an or an oral study you're talking about?

Dr. Susan Tilton - This was the oral for Diphenyl Dimethicone, so related to the 24% that's in lipstick. It didn't seem like the maximum concentration tested was reflective of the maximum use. That it was.

Dr. David Cohen - For oral tox.

Dr. Susan Tilton - Lower for oral.

Dr. David Ross - Yeah, the.

Dr. David Cohen - I'm not sure. We've always looked at it like that.

Dr. David Ross - And NOAEL came in at what, 20 mg/kg/d--

Dr. Susan Tilton - Is that what it I'm trying to find it again?

Dr. David Ross - It's on page 20.

Preethi Raj (CIR) - It is, yeah, 20.

Dr. David Ross - The PDF.

Dr. Susan Tilton - OK.

Dr. David Ross - I thought, I mean, there's an awful lot of tox data with these and I, you know, with the acute oral and I thought that was OK and it's subchronic. Yeah, I mean, I you know, there was only two studies I would probably come from the. So that was a bit limited, but (*inaudible).

Dr. Susan Tilton C - Yeah.

Preethi Raj (CIR) - Yeah, (*inaudible) the NOAEL is in the DART section.

Dr. Susan Tilton C - I am OK.

Dr. David Ross - Yeah. Yeah, I didn't flag that (*inaudible). I have to say, but I had a question on the respiratory data, whether you thought that was OK.

Dr. Susan Tilton - With Phenyl Trimethicone.

Dr. David Ross - Umm.

Dr. Susan Tilton - Wasn't a lot of description there, but it was tested at an aerosol concentration. Again, that was lower than the Max use.

Dr. David Ross - 3%.

Dr. Susan Tilton - 3% compared to 15%. So if we are, I mean if there is data available at the Max, use concentration.

Dr. David Cohen - So I haven't I need a little help on this because I haven't heard that kind of Analogy before on the inhalational or the oral relating to Max use. It's something that I generally think of in terminal studies and contact irritation and sensitization. How do we how do we bridge that? Do we need, is inhalational tox going to have to match Max use I just don't know?

Dr. Susan Tilton - On this case, they don't report. They aren't. They didn't test high enough concentrations like they did with the oral to come out with a

Dr. David Cohen - OK.

Dr. Susan Tilton – NOAEL other than that the 3% would have no effect.

Dr. David Cohen - What? What PDF a number are you on again?

Dr. Susan Tilton - PDF number.

Dr. David Ross - That's on now.

Preethi Raj (CIR) - Is it 19?

Dr. David Ross - It's nine right at the bottom of 19. At least the inhalation data.

Preethi Raj (CIR) - Well, looking at the table again, I think the maximum reported concentration of use for Phenyl Trimethicone in sprays as 7.5 and the 15% you're seeing is for powders I think.

Dr. Susan Tilton - OK.

Dr. David Cohen - If that's the case, that's still a lot lower than what they reported here, right?

Dr. Tom Slaga - You know.

Dr. David Cohen - So could you articulate the data needs? Susan what's would I ask for?

Dr. Susan Tilton - So if there. So I would be interested to know if there are data available at concentrations for the inhalation. Short term toxicity studies that are closer to the Max, use concentrations. For

Dr. Tom Slaga - Or at Max.

Dr. Susan Tilton - Either the Hairspray or the face powders.

Dr. David Cohen - For Diphenylsiloxy Phenyl Trimethicone?

Dr. Susan Tilton - Uh for Phenyl Trimethicone?

Dr. David Cohen - Of the phenyl. We're Phenyl Trimethicone. OK. Alright, well, here, we'll hear what.
We have a few things. We have method of manufacturing and impurities and inhalation data closer to max use for trying to Phenyl Trimethicone. I'll review the sensitization data again. Was there anything else?

Preethi Raj (CIR) - I'm sorry, Doctor Cohen, could you reiterate what were you going to look at in that sensitization data?

Dr. David Cohen - I'm just going to look and make sure that the max use of the specific chemicals aligned, but I think we have I think it's OK because we have neat, we have very high concentration on this, but the team had asked me about it a little early. I think it's fine. I'm just going to, it's a note to myself.

Preethi Raj (CIR) - Thank you.

Dr. David Cohen - OK, so let's finish. Phenyl -substituted imethicone do what's the team like to do, we could break or we could make a run for glyceryl diesters. What's the overall feeling?

Full Panel – September 27, 2022

Dr. Wilma Bergfeld - Alright, well, let me call the question all those opposing? Abstaining? Approved. Safe. OK. We're moving on then to the Phenyl-substituted methicones, Dr. Belsito.

Dr. Don Belsito - Yes. So this is the first time that we're looking at this cosmetic ingredient group of seven ingredients in this. I won't read them all off. And it took three different PDF's to get us all the data. Reams and reams of data that were quite nice, except that we didn't have manufacturing impurities or molecular weight ranges for any of them. So we are going insufficient for those needs.

Dr. Wilma Bergfeld - David.

Dr. David Cohen - Yeah. I would second that. One thing that came up at our discussion for Phenyl Trimethicone. The inhalation tox was at 3% but the max use is much higher than that. And we wanted your thoughts on asking for additional respiratory tox that was more approximating the real life use.

Dr. Don Belsito - Well, that I guess is going to be an issue with airbrush where we know these are being used. So this will be a very clear statement in the airbrush in the discussion for airbrush, but I mean I think we have our standard boilerplate for respiratory toxicity in terms of inhalation, it didn't come up in my group, but I'll turn that over to Paul, Dan and Allan and Kurt?

Dr. Don Belsito - Don’t chime in all at once.

Dr. Paul Snyder - Like this was. This ingredient report actually had some of the best data we've ever had from the tox side. I mean it had dermal, oral, all the way from acute all the way up to developmental and repro. So there was no signal anywhere or no issue. Anything all the findings were at 20 milligrams or greater per kilogram and so we felt it was an extreme (*inaudible) to have a very safe tox profile and we didn't really talk about the inhalation and I didn't pick up on that on the on that inhalation. I know that there was acute and short term inhalation that I was comfortable with, so I would suspect those would be sufficient for any incidental exposure we can address that in discussion regarding the potential for incidental inhalation and address it to the levels that we have data on. So that's my two cents.

Dr. Curtis Klaassen - While the concentration of the compound in the inhalation study was low. It was for a long, much longer time than what humans would be exposed to, so that gives one some security.

Dr. Wilma Bergfeld - Allan.

Dr. David Cohen - Susan, Tom. Ohh sorry.

Dr. Allan Rettie - Yeah, I didn't have anything to add to that. I did have a comment, maybe we'll get to later about something's text, but I'm good with it.

Dr. Don Belsito - I mean. It's insufficient at this point. If you guys want to ask for that data, we can ask for it and come back to the whole respiratory issue later.

Dr. Wilma Bergfeld - OK. Well, we'll be in the minutes, so we know it's a discussion point that needs to be addressed.

Dr. Daniel Liebler - I agree with it.

Dr. David Cohen - Susan, any?

Dr. Wilma Bergfeld - Any other comments? Susan?

Dr. Susan Tilton - So I do agree with Kurt's comment that the cumulative exposure over time would exceed what you would expect from normal use so. And I also agree that as long as it's addressed in the discussion, the point with which I guess is a fairly boilerplate statement, then that would then that, you know is could be sufficient.

Dr. Wilma Bergfeld - OK. David, did you want to comment?

Dr. Tom Slaga - I agree. I agree with that.

Dr. Wilma Bergfeld - OK. Thanks, Tom. David. No.

Dr. David Cohen - You meant Dr. David Ross

Dr. Wilma Bergfeld - Ohh, I don't mean. Alright. That's two David's Sorry, I'm looking at Dr. David Ross. Thank you.

Dr. David Cohen – Yea.

Dr. Wilma Bergfeld - Any comment?

Dr. David Ross - No, I'm fine with it.

Dr. Wilma Bergfeld - How about you, David?

Dr. David Cohen - Yes. So we'll, we'll second uh, Don Belsito's motion.

Dr. Wilma Bergfeld - OK, so a second.

Dr. David Cohen - We came to the same conclusions.

Dr. Wilma Bergfeld - Yeah. And what you're asking for, the writer, I'm not sure I see who the writer is, but do you have the list that's needed?

Preethi Raj (CIR) - So, Doctor Belsito's team had said all are insufficient for method of manufacture and impurities and also molecular weight range is that it?

Dr. Don Belsito - Correct, yes.

Preethi Raj (CIR) - OK. Thank you.

Dr. Wilma Bergfeld - OK.

Dr. David Cohen - That's what we have.

Dr. Wilma Bergfeld - All right. Any other points of discussion? Hearing none, all those opposed? Abstaining? Approved as an IDA. All right, moving on to the last chemical and this particular advancing group, Doctor Cohen, that Trisodium Ethylenediamine Disuccinate.

JUNE 1985 PANEL MEETING

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.

Safety Assessment of Phenyl-Substituted Methicones as Used in Cosmetics

Status: Draft Tentative Report for Panel Review
Release Date: February 10, 2023
Panel Meeting Date: March 6-7, 2023

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.; 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. Previous Panel member involved in this assessment: Daniel C. Liebler, 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
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 (long-wavelength)/ ultraviolet radiation B (mid-wavelength)
VCRP	Voluntary Cosmetic Registration Program
wINCI; *Dictionary*	web-based *International Cosmetic Ingredient Dictionary and Handbook*

DRAFT ABSTRACT

The Expert Panel for Cosmetic Ingredient Safety (Panel) assessed the safety of 7 phenyl-substituted methicones as used in cosmetic formulations. These ingredients are reported to function in cosmetics mostly as anti-foaming agents and skin and/or hair conditioning agents. The Panel reviewed the available data to determine the safety of these ingredients, and concluded…[to be determined].

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, as published in 2006.[4] Excerpts of 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.

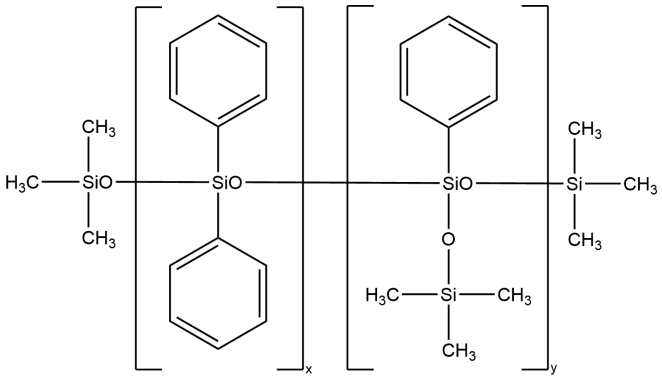


Figure 1. Diphenylsiloxy Phenyl Trimethicone (x and y are undefined)

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 and 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.

According to one supplier, a sample of Diphenyl Dimethicone had a number average molecular weight (MW) of 1711 g/mol, a weight average MW of 3105 g/mol, and a polydisperity index of 1.816.[8] Another supplier described the number average MW of Diphenyl Dimethicone to be > 1000 g/mol and the number average MW of Diphenylsiloxy Phenyl Trimethicone to be 500 - 1000 g/mol.[9] A sample of Phenyl Trimethicone was described by a supplier as having a number average MW of 725 g/mol, a weight average MW of 920 g/mol, and a polydisperity index of 1.27.[10] Another sample of Phenyl Trimethicone was deemed to contain greater than 70% material < 1000 g/mol when measured by conventional gel permeation chromatography against polystyrene standards.[11]

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.

Diphenyl Dimethicone

A supplier described the manufacture of Diphenyl Dimethicone as a five-step process, involving hydrolysis, polymerization, neutralization, distillation, and filtration.[8] The hydrolysis reaction produces diphenyl dimethyl silicone hydrolysate, which along with dimethylcyclosiloxane and methyl-ended siloxane, is added to the reactor and mixed with a base catalyst for synthesis. Upon neutralization, the reaction is terminated and the unreacted polymer is removed via distillation, prior to filtration and packaging. The general manufacturing process of Diphenyl Dimethicone is described by another supplier as the hydrolysis of a mixture of dichlorodiphenylsilane, dichlorodimethylsilane, and chlorotrimethylsilane, followed by catalyst polymerization.[12]

Diphenylsiloxy Phenyl Trimethicone

The general manufacturing process of Diphenylsiloxy Phenyl Trimethicone is described by a supplier as the hydrolysis of a mixture of trichlorophenylsilane, dichlorodiphenylsilane, and chloromethylsilane followed by catalyst polymerization.[13]

Phenyl Trimethicone

A supplier described the manufacture of Phenyl Trimethicone as a three-step process, involving hydrolysis, distillation, and filtration.[10] The hydrolysis reaction produces phenyl trimethicone hydrolysate, which is then distilled to remove low molecular weight impurities and filtered prior to packaging. In another method of manufacture provided by a supplier, silanes first undergo hydrolysis to produce Phenyl Trimethicone.[11] The resulting hydrolysis product is then stripped, filtered, and tested for quality prior to packaging.

Impurities

Diphenyl Dimethicone; Diphenylsiloxy Phenyl Trimethicone

According to a supplier, a sample of Diphenyl Dimethicone and a sample of Diphenylsiloxy Phenyl Trimethicone each contained < 0.1% of cyclotetrasiloxane, < 0.1% cyclopentasiloxane, and < 0.1% cyclohexasiloxane.[9]

Phenyl Trimethicone

A sample of Phenyl Trimethicone was described by a supplier as comprising ≤ 50 ppm methanol and ≤ 1 ppm benzene.[11]

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).[14] Diphenylsiloxy Phenyl Trimethicone is reported to be used in 269 formulations, and Diphenyl Dimethicone is reported to be used in 145 formulations (Table 3). All other ingredients are used in less than 50 formulations. The results from concentration of use surveys conducted by the Council in 2021 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).[15,16] Use concentration data were reported for Diphenylsiloxy Phenyl/Propyl Trimethicone in makeup bases at 5.3%, but no uses were received in the VCRP; however, 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%.[4,14,16] 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 aerosol 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.[17]

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.[18] 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.[19] 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.[20]

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.[19] 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.[21] 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.[22] 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 $\geq$ 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

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).[23] 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.[24] 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.[25] 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.[6,7,25] 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.[26]

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.[27,28] 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.[29,30] A lip balm containing 11% Diphenylsiloxy Phenyl Trimethicone was neither irritating or sensitizing in an occlusive HRIPT performed in 109 subjects.[31] A Marzulli-Maibach HRIPT of a formulation containing 0.2% Phenyl Methicone was performed in 107 subjects; the test article was neither irritating or sensitizing.[32] 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.[33,34] A product containing 20% Phenyl Trimethicone was neither irritating or sensitizing in an occlusive HRIPT performed in 53 subjects.[35] A concealer formulation containing 26.18% Phenyl Trimethicone was not sensitizing to 26 subjects in a maximization assay.[36] Similarly, a semi-occlusive HRIPT of a product containing 28.67% Phenyl Trimethicone was performed in 203 subjects; the test material was not sensitizing.[37] 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.[38,39] 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.[40-42]

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.[43] 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).[44] 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.[19] 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.[21] 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.[45]

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 Diphenylsiloxy 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 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 lip balm containing 11% Diphenylsiloxy Phenyl Trimethicone was neither irritating or sensitizing in an occlusive HRIPT performed in 109 subjects. A formulation containing 0.2% Phenyl Methicone was neither irritating or sensitizing in a Marzulli-Maibach HRIPT performed in 107 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. An occlusive HRIPT of a product containing 20% Phenyl Trimethicone (53 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% Trimethylsiloxyphenyl 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 rabbit 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).

DRAFT DISCUSSION

[Note: This Discussion is in the draft form, and changes will be made following the Panel meeting.]

This assessment reviews the safety of 7 phenyl-substituted methicones, as used in cosmetic formulations. The Panel concluded [TBD].

The Panel noted that the toxicological profile for these ingredients is comprehensive, with multiple routes and durations of exposure. Negative results for genotoxicity were considered to be robust along with data for dermal irritation or sensitization. Transient signs of irritation were observed in a 15-d cumulative irritation study, in which a serum containing 2% Trimethylsiloxyphenyl Dimethicone, was tested using 28 subjects. The Panel discussed that due to no further evidence of these ingredients causing irritation or sensitization, even when tested at higher concentrations, these results may be product-related.

The Panel also discussed the issue of incidental inhalation exposure resulting from these ingredients; 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 aerosol deodorants. In a short-term inhalation toxicity study, Phenyl Methicone, aspirated into a mist at a rate of 67.4 mg/min, administered whole body, at a concentration of 0.52 mg/l, was only circumstantially associated with moderate degenerative changes observed in the livers of cats and guinea pigs. However, the Panel noted that in aerosol products, the majority of droplets/particles would not be respirable to any appreciable amount. Furthermore, droplets/particles deposited in the nasopharyngeal or tracheobronchial regions of the respiratory tract present no toxicological concerns based on the chemical and biological properties of these ingredients. Coupled with the small actual exposure in the breathing zone and the low concentrations at which these ingredients are used (or expected to be used) in potentially inhaled products, the available information indicates that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic effects. A detailed discussion and summary of the Panel's approach to evaluating incidental inhalation exposures to ingredients in cosmetic products is available at https://www.cir-safety.org/cir-findings.

The Panel's respiratory exposure resource document (see link above] notes that airbrush technology presents a potential safety concern, and that no data are available for consumer habits and practices thereof. As a result of deficiencies in these critical data needs, the safety of cosmetic ingredients applied by airbrush delivery systems cannot be determined by the Panel. Therefore, the Panel has concluded the data are insufficient to support the safe use of cosmetic ingredients applied via an airbrush delivery system.

CONCLUSION

To be determined.

TABLES

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

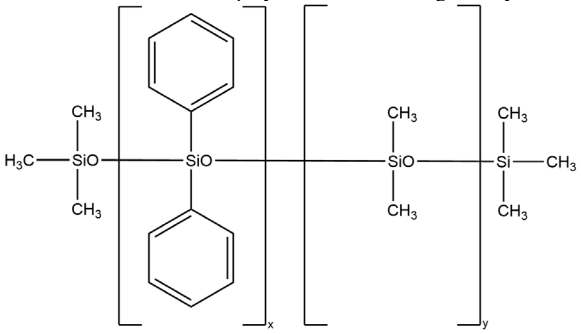
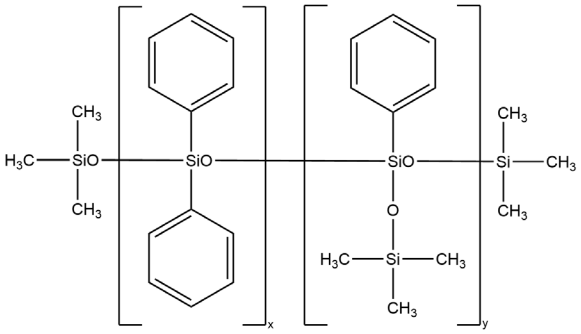
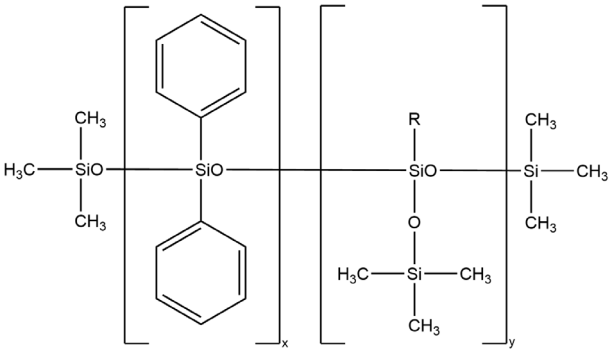
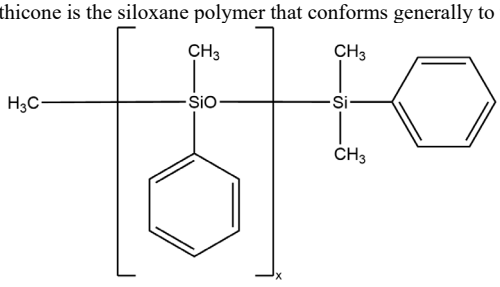
Ingredient/CAS No.	Definition	Function(s)
Diphenyl Dimethicone 68083-14-7	Diphenyl Dimethicone is a siloxane polymer that conforms generally to the structure: 	Antifoaming agents; Skin-conditioning agents - occlusive
Diphenylsiloxy Phenyl Trimethicone 352230-22-9	Diphenylsiloxy Phenyl Trimethicone is 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]

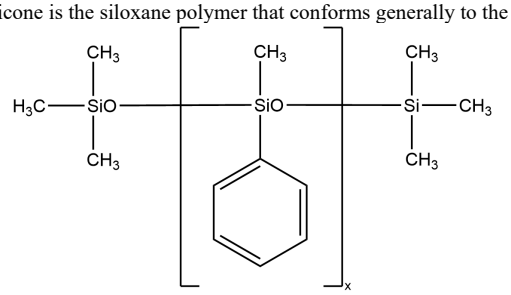
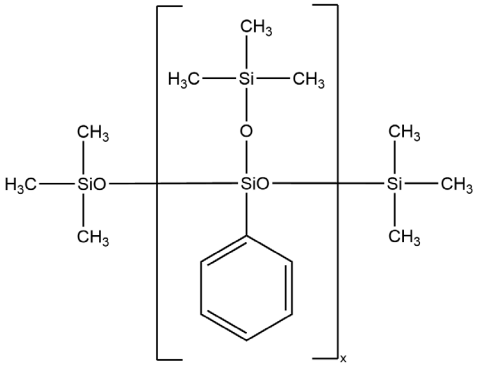
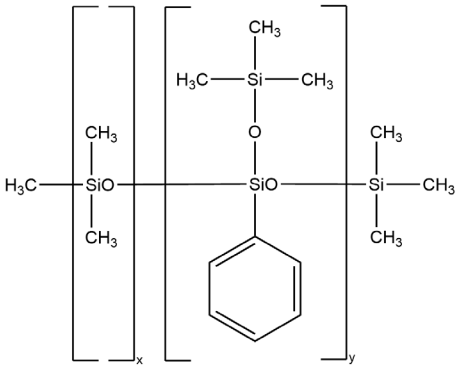
Ingredient/CAS No.	Definition	Function(s)
Phenyl Methicone 31230-04-3 63148-58-3	Phenyl Methicone is the siloxane polymer that conforms generally to the structure: 	Skin-conditioning agents - emollient
Phenyl Trimethicone 18758-91-3 18876-34-1 195868-36-1 2116-84-9 70131-69-0 73559-47-4	Phenyl Trimethicone 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. 2022 and historical frequency and concentration of use according to duration and exposure for Phenyl Trimethicone

	# of Uses		*Max Conc of Use (%)*	
	2022[14]	**2002[4]**	**2022[16]**	**2004[4]**
Totals	**781**	**279**	**0.1 – 59.5**	**0.0075-36**
summarized by likely duration and exposure*				
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
as reported by product category				
Baby Products				
Baby Lotions/Oils/Powders/Creams	3		NR	
Other Baby Products	NR		6.5	
Bath Preparations (diluted for use)				
Bath Oils, Tablets, and Salts		1		NR
Eye Makeup Preparations				
Eyebrow Pencil	2		8.8	
Eyeliner	13	1	3.4-16.5	2-6
Eye Shadow	98	77	2.4-17	4-13
Eye Lotion	1	NR	NR	0.008-1
Mascara		1		0.1-0.4
Other Eye Makeup Preparations	23	4	0.75	6-15
Fragrance Preparations				
Cologne and Toilet Water		NR		0.5
Perfumes	1	1	3	NR
Powders (dusting/talcum, excl aftershave talc)		1		NR
Other Fragrance Preparation	2	NR	0.5	0.5
Hair Preparations (non-coloring)				
Hair Conditioner	42	8	0.75-3	0.3-2
Hair Spray (aerosol fixatives)	51	23	0.5-7.5	0.1-18
Hair Straighteners	6			
Shampoos (non-coloring)	4	NR	59.5	1
Tonics, Dressings, and Other Hair Grooming Aids	75	31	0.51-9 (not spray); 2 (pump spray); 7 (aerosol)	5-11
Other Hair Preparations	38	7	3	0.5-2
Hair Coloring Preparations				
Hair Tints	4		NR	
Hair Rinses (coloring)				
Hair Color Sprays (aerosol)	6		NR	
Makeup Preparations				
Blushers (all types)	27	1	5.2	2-15
Face Powders	32	9	1.2-15.6	0.1-18
Foundations	66	17	7-12	2-22
Leg and Body Paints		NR		2
Lipstick	88	34	1-13.8	0.08-36
Makeup Bases	19	8	NR	NR
Rouges	4	2	2-4.8	NR
Makeup Fixatives	2		NR	
Other Makeup Preparations	43	13	12.1-24.8	0.0075-22
Manicuring Preparations (Nail)				
Cuticle Softeners	1		NR	
Nail Creams and Lotions		NR		0.5
Nail Polish and Enamel	NR		3	
Other Manicuring Preparations				
Personal Cleanliness Products				
Deodorants (underarm)	1	1	1.8-10.2 (not spray) 2.2 (aerosol)	NR

Table 2. 2022 and historical frequency and concentration of use according to duration and exposure for Phenyl Trimethicone

	# of Uses		*Max Conc of Use (%)*	
	2022[14]	**2002[4]**	**2022[16]**	**2004[4]**
Other Personal Cleanliness Products		1		NR
Shaving Preparations				
Aftershave Lotion		1		0.5-2
Beard Softeners	1		NR	
Preshave Lotions (all types)	NR	1	2.5	2
Other Shaving Preparations		NR		0.5
Skin Care Preparations				
Cleansing	2	4	NR	2-4
Face and Neck (exc shave)	31	3	3.4-13 (not spray)	4-6
Body and Hand (exc shave)	16	4	1.7 (not spray)	0.2-18
Moisturizing	58	15	0.8-22.7 (not spray)	0.8-3
Night	2	NR	NR	2
Paste Masks (mud packs)	1		NR	
Skin Fresheners	4		NR	
Other Skin Care Preparations	9	NR	0.5-4.9	2
Suntan Preparations				
Suntan Gels, Creams, and Liquids	4	2	0.1 (aerosol) 0.5 (pump spray)	0.5-9
Indoor Tanning Preparations	1	8		0.2-5
Other Suntan Preparations	NR	NR	6	2

NR – not reported

*likely duration and exposure is derived based on product category (see Use Categorization https://www.cir-safety.org/cir-findings)

**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.

Table 3. Frequency (2022)[14] and concentration (2021)[15] of use according to likely duration and exposure and by product category

	# 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**
summarized by likely duration and exposure*						
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
as reported by product category						
Baby Products						
Baby Lotions/Oils/Powders/Creams						
Other Baby Products						
Bath Preparations (diluted for use)						
Bath Oils, Tablets, and Salts						
Eye Makeup Preparations						
Eyebrow Pencil			NR	4.4		
Eyeliner			5	19.9		
Eye Shadow	32	NR	30	15		
Eye Lotion			5	NR		
Mascara						
Other Eye Makeup Preparations			7	NR		
Fragrance Preparations						
Cologne and Toilet Water						
Perfumes						

Table 3. Frequency (2022)[14] and concentration (2021)[15] of use according to likely duration and exposure and by product category

	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)
Powders (dusting/talcum, excl aftershave talc)						
Other Fragrance Preparation						
Hair Preparations (non-coloring)						
Hair Conditioner	1	NR	NR	1.2		
Hair Spray (aerosol fixatives)	1	0.9-1				
Hair Straighteners						
Shampoos (non-coloring)						
Tonics, Dressings, and Other Hair Grooming Aids			NR	3.5		
Other Hair Preparations						
Hair Coloring Preparations						
Hair Tints			NR	8.8		
Hair Rinses (coloring)			NR	1		
Hair Color Sprays (aerosol)	NR	0.1	NR	0.3		
Makeup Preparations						
Blushers (all types)	2	NR	21	4.7		
Face Powders			12	5.7		
Foundations	9	0.6-1.3	27	3.3-7.5		
Leg and Body Paints						
Lipstick	64	1.9-24.1	75	9.4-15.2		
Makeup Bases	5	NR	1	NR	NR	5.3
Rouges	16	NR	1	NR		
Makeup Fixatives			1	NR		
Other Makeup Preparations	1	NR	30	NR		
Manicuring Preparations (Nail)						
Cuticle Softeners						
Nail Creams and Lotions						
Nail Polish and Enamel						
Other Manicuring Preparations						
Personal Cleanliness Products						
Deodorants (underarm)			NR	0.5 (aerosol) 0.5 (not spray)		
Other Personal Cleanliness Products						
Shaving Preparations						
Aftershave Lotion						
Beard Softeners						
Preshave Lotions (all types)						
Other Shaving Preparations						
Skin Care Preparations						
Cleansing	1	NR	5			
Face and Neck (exc shave)	2	0.42 (not spray)	10	0.4-0.5 (not spray)		
Body and Hand (exc shave)	1	NR	4	5 (spray)		
Moisturizing	5	NR	28	1.7 (not spray)		
Night			5	NR		
Paste Masks (mud packs)			2	NR		
Skin Fresheners	1	NR				
Other Skin Care Preparations	4	NR	NR	2-9		
Suntan Preparations						
Suntan Gels, Creams, and Liquids						
Indoor Tanning Preparations						
Other Suntan Preparations						

Table 3. Frequency (2022)[14] and concentration (2021)[15] of use according to likely duration and exposure and by product category

	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)
	Phenyl Dimethicone		Phenyl Methicone		Trimethylsiloxyphenyl Dimethicone	
Totals	**8**	**0.0096 – 19.5**	**10**	**0.28**	**47**	**0.2 - 23**
summarized by likely duration and exposure*						
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
as reported by product category						
Baby Products						
Baby Lotions/Oils/Powders/Creams						
Other Baby Products						
Bath Preparations (diluted for use)						
Bath Oils, Tablets, and Salts						
Eye Makeup Preparations						
Eyebrow Pencil						
Eyeliner					1	NR
Eye Shadow	NR	2.1			NR	14
Eye Lotion			1	NR		
Mascara						
Other Eye Makeup Preparations					1	NR
Fragrance Preparations						
Cologne and Toilet Water						
Perfumes						
Powders (dusting/talcum, excl aftershave talc)						
Other Fragrance Preparation						
Hair Preparations (non-coloring)						
Hair Conditioner					1	0.5
Hair Spray (aerosol fixatives)	2	NR				
Hair Straighteners						
Shampoos (non-coloring)						
Tonics, Dressings, and Other Hair Grooming Aids	2	NR			NR	5
Other Hair Preparations					NR	5
Hair Coloring Preparations						
Hair Tints						
Hair Rinses (coloring)						
Hair Color Sprays (aerosol)						
Makeup Preparations						
Blushers (all types)						
Face Powders					NR	3.5
Foundations			2	NR	3	NR
Leg and Body Paints						
Lipstick	1	19.5			29	18-23
Makeup Bases	1	NR				
Rouges						
Makeup Fixatives						
Other Makeup Preparations					11	NR
Manicuring Preparations (Nail)						
Cuticle Softeners						
Nail Creams and Lotions						
Nail Polish and Enamel	NR	0.0096	2	NR	NR	0.2
Other Manicuring Preparations			1	NR		
Personal Cleanliness Products						
Deodorants (underarm)						
Other Personal Cleanliness Products						
Shaving Preparations						
Aftershave Lotion						

Table 3. Frequency (2022)[14] and concentration (2021)[15] of use according to likely duration and exposure and by product category

	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)
Beard Softeners						
Preshave Lotions (all types)						
Other Shaving Preparations						
Skin Care Preparations						
Cleansing						
Face and Neck (exc shave)			NR	0.28 (not spray)	1	NR
Body and Hand (exc shave)						
Moisturizing			2	NR	NR	20 (not spray)
Night	1	NR	2	NR		
Paste Masks (mud packs)						
Skin Fresheners						
Other Skin Care Preparations	1	NR				
Suntan Preparations						
Suntan Gels, Creams, and Liquids						
Indoor Tanning Preparations						
Other Suntan Preparations						

NR – not reported

*likely duration and exposure is derived based on product category (see Use Categorization https://www.cir-safety.org/cir-findings)

**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.

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.	[19]
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.	[20]
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.	[19]

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.	[23]
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	[24]
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	[24]
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	[25]
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.	[25]
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	[26]
			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	[27]
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	[28]
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	[29]

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.	30
Lip balm containing 11% Diphenylsiloxy Phenyl Trimethicone	N/A	~ 0.1 -0.15 g, applied neat	109 subjects	HRIPT. Similar procedure as described above. The 24-h challenge application was scored 24 and 72 h after application.	Not irritating or sensitizing	31
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	32
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.	33
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	34
Product containing 20% Phenyl Trimethicone	N/A	0.1-0.15 g, applied neat	53 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 and 72 h after application.	Not irritating or sensitizing	35
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.	36
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	37
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	38

Table 5. Dermal irritation and sensitization studies

Test Article	Vehicle	Concentration/Dose	Test Population	Procedure	Results	Reference
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.	[39]
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	[40]
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	[41]
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	[42]

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.	[19]
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.	[21]
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	[45]

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.

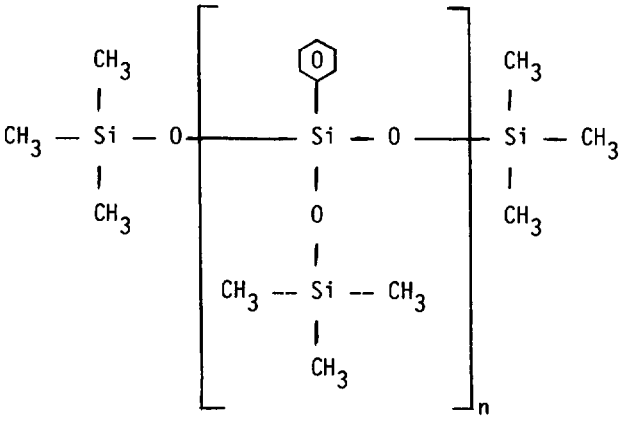
Phenyl Trimethicone is neither an irritant nor a sensitizer to humans. No photosensitization data are available on Phenyl Trimethicone; however, the UV absorption spectrum indicated only weak absorbance at 327 nm.

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.

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

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.

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: November 14, 2022

SUBJECT: Diphenyl Dimethicone and Phenyl Trimethicone

Anonymous. 2022. Method of Manufacture and Molecular Weight – Diphenyl Dimethicone.

Anonymous. 2022. Method of Manufacture and Molecular Weight – Phenyl Trimethicone.

Manufacturing Process

1. Hydrolysis : After water is first added to the reactor, Diphenyl silane and Dimethyl silane are dropped. This reaction produces Diphenyl Dimethyl Silicone Hydrolyzate.
2. Polymerization : Diphenyl Dimethyl Silicone Hydrolyzate, Dimethylcyclosiloxane and Methyl ended siloxane are added to the reactor and mixed. And Base catalyst is added to synthesize.
3. Neutralization : Proceed to neutralize to terminate the reaction.
4. Distillation : The unreacted polymer is distilled off.
5. Filter and Packing

Molecular weight ranges

	Mn	Mw	MP	PDI	%Poly <1000Da	%Poly <500Da	Retention Time(min)	Start Time (min)	End Timd (min)
Diphenyl Dimethicone	1711	3105	2663	1.816	14.542	3.335	19.221	16.333	22.317

Mn : Number average Molecular weight

Mw : Weight average Molecular weight

MP : Molecular weight of the highest peak

PDI : Polydispersity index

Manufacturing Process

1. Hydrolysis : After water is first added to the reactor, Phenyltrichlorosilane and Trimethylchlorosilane are dropped. This reaction produces Phenyl Trimethicone Hydrolyzate.
2. Distillation : Removal of low molecular weight substance by distillation
3. Filter and Packing

Molecular weight ranges

	Mn	Mw	MP	PDI	%Poly <1000Da	%Poly <500Da	Retention Time(min)	Start Time (min)	End Timd (min)
Phenyl Trimethicone	725	920	657	1.270	71.242	17.147	20.842	18.150	21.850

Mn : Number average Molecular weight

Mw : Weight average Molecular weight

MP : Molecular weight of the highest peak

PDI : Polydispersity index

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: November 21, 2022

SUBJECT: Diphenyl Dimethicone and Diphenylsiloxy Phenyl Trimethicone

Anonymous. 2022. Impurities and Molecular Weight – Diphenyl Dimethicone and Diphenylsiloxy Phenyl Trimethicone.

Anonymous. 2022. General Manufacturing Process of Diphenyl Dimethicone.

Anonymous. 2022. General Manufacturing Process of Diphenylsiloxy Phenyl Trimethicone.

November 2022

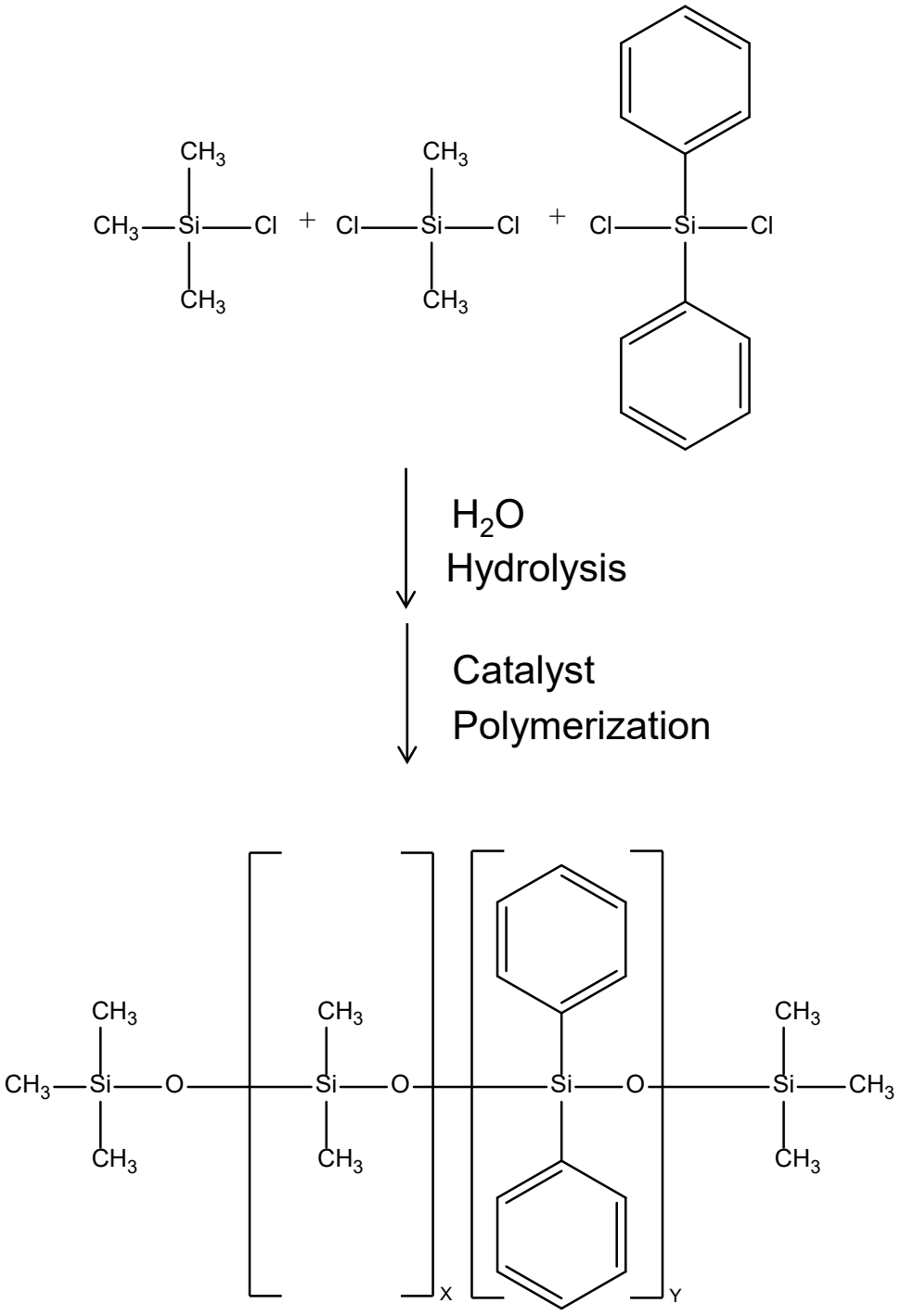
INCI Name: DiphenylDimethicone

Impurity			MW		
			Number average molecular weight(Mn)		
D4	D5	D6	**<500 Daltons**	**500-1000 Daltons**	**>1000 Daltons**
<0.1%	<0.1%	<0.1%			X

INCI Name: Diphenylsiloxy Phenyl Trimethicone

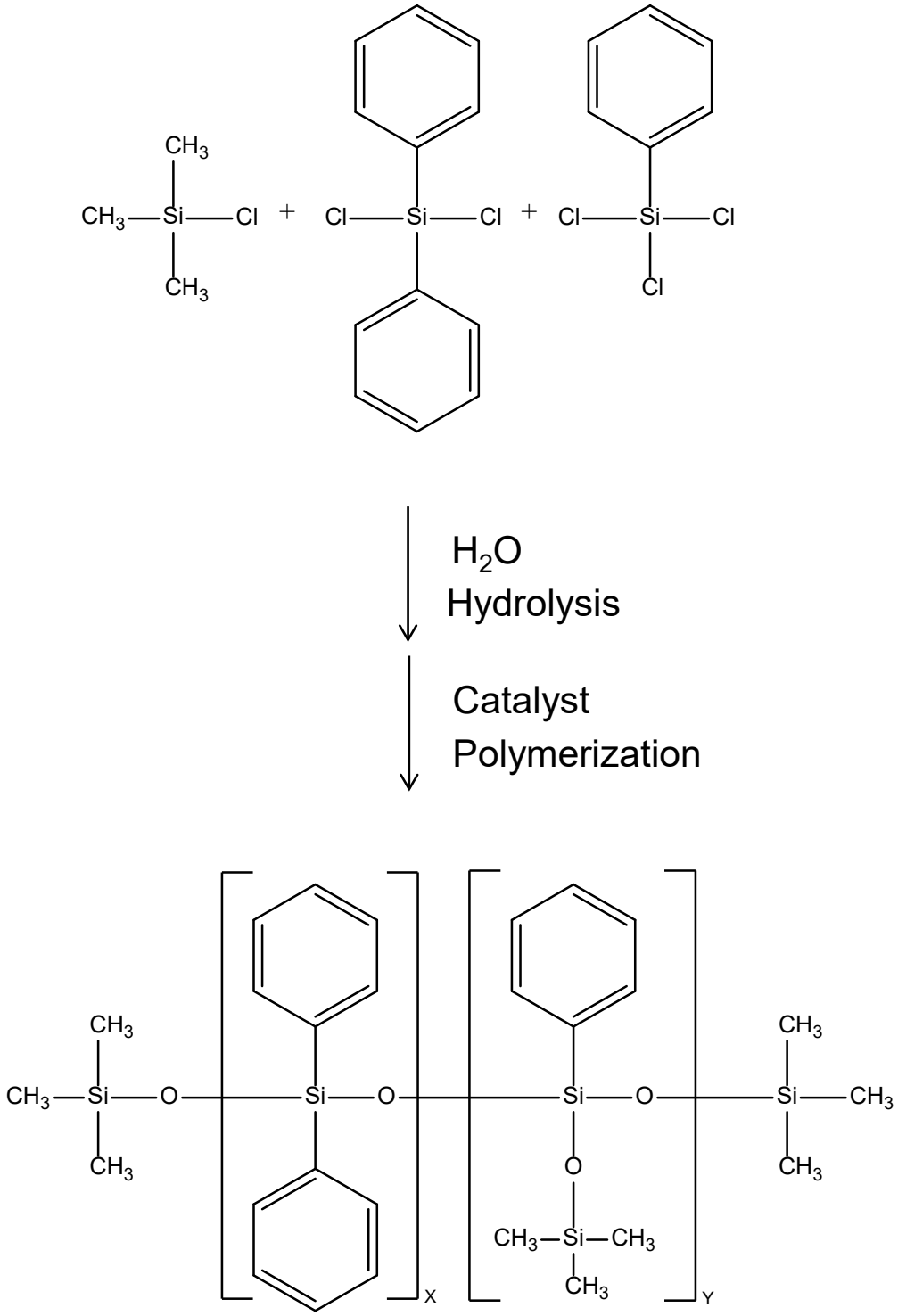
Impurity			MW		
			Number average molecular weight(Mn)		
D4	D5	D6	**<500 Daltons**	**500-1000 Daltons**	**>1000 Daltons**
<0.1%	<0.1%	<0.1%		X	

General Manufacturing Process of Diphenyl Dimethicone



November 2022

General Manufacturing Process of Diphenylsiloxy Phenyl Trimethicone



November 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: November 29, 2022

SUBJECT: Diphenylsiloxy Phenyl Trimethicone and Phenyl Trimethicone

Anonymous. 2019. Clinical safety evaluation repeated insult patch test (1ip balm containing 11% Diphenylsiloxy Phenyl Trimethicone).

Anonymous. 2011. Clinical safety evaluation repeated insult patch test (product containing 20% Phenyl Trimethicone).

.

[redacted]

FINAL REPORT

CLINICAL SAFETY EVALUATION

REPEATED INSULT PATCH TEST

lip balm containing 11% Diphenylsiloxy Phenyl Trimethicone

[redacted]

Sponsor

[redacted]

Sponsor Representative

[redacted]

Clinical Testing Facility

[redacted]

Date of Final Report

3-6-19

[redacted]

SIGNATURE PAGE

CLINICAL SAFETY EVALUATION

REPEATED INSULT PATCH TEST

[redacted]

[redacted] MD
Board-Certified Dermatologist
Medical Investigator

3/11/19
Date

[redacted]

QUALITY ASSURANCE STATEMENT

This study ([redacted] was conducted in accordance with the intent and purpose of Good Clinical Practice regulations described in 21 CFR Part 50 (Protection of Human Subjects – Informed Consent) and the Standard Operating Procedures of Essex Testing Clinic, Inc.

For purposes of this clinical study:

_X_	Informed Consent was obtained.
____	Informed Consent was not obtained.
_X_	An IRB review was not required.
____	An IRB review was conducted and approval to conduct the proposed clinical research was granted.

To assure compliance with the study protocol, the Quality Assurance Unit completed an audit of the applicable study records and report. This report is considered a true and accurate reflection of the testing methods and source data.

[redacted]
Manager, Quality Assurance

2 Mar 2019
Date

[redacted]

[redacted]

TABLE OF CONTENTS

[redacted]

[redacted]

CLINICAL SAFETY EVALUATION

REPEATED INSULT PATCH TEST

[redacted]

1.0 OBJECTIVE

The objective of this study was to determine the irritation and/or sensitization potential of the test article after repeated application under occlusive patch test conditions to the skin of human subjects (non-exclusive panel).

2.0 SPONSOR

[redacted]

2.1 Sponsor Representative

[redacted]

3.0 CLINICAL TESTING FACILITY

The study was conducted by:

[redacted]

4.0 CLINICAL INVESTIGATORS

Study Director:
Principal Investigator:
Medical Investigator:

[redacted]

5.0 STUDY DATES

Study initiation: January 9, 2019 (Panel No. 19017)
January 16, 2019 (Panel No. 19034)

Final evaluation: February 16, 2019 (Panel No. 19017)
February 22, 2019 (Panel No. 19034)

[redacted]

6.0 ETHICS

6.1 Ethical Conduct of the Study

This study was conducted in accordance with the intent and purpose of Good Clinical Practice regulations described in Title 21 of the U.S. Code of Federal Regulations (CFR), the Declaration of Helsinki and/or [redacted] Standard Operating Procedures.

6.2 Subject Information and Consent

This study was conducted in compliance with CFR Title 21, Part 50 (Informed Consent of Human Subjects). Informed Consent was obtained from each subject in the study and documented in writing before participation in the study. A copy of the Informed Consent was provided to each subject.

7.0 TEST MATERIAL

The test article used in this study was provided by:

[redacted]

It was received on December 17, 2018 and identified as follows:

	Test Article ID	Description
[redacted]	[redacted]	Light Pink Semi-Solid

8.0 TEST SUBJECTS

At least 100 male and female subjects ranging in age from 18 to 79 years were to be empanelled for this test.

The subjects chosen were to be dependable and able to read and understand instructions. The subjects were not to exhibit any physical or dermatologic condition that would have precluded application of the test article or determination of potential effects of the test article.

9.0 TEST PROCEDURE

The 9 Repeated Insult (occlusive) Patch Test (9-RIPT)[1] was conducted as follows:

9.1 Induction Phase

A sufficient amount of the test article (approximately 0.1 g – 0.15 g) was placed onto a Parke-Davis Readi-Bandage® occlusive patch (approximately 25 - 38 mg/cm^2 of test material) and applied to the back of each subject between the scapulae and waist, adjacent to the spinal mid-line. This procedure was performed by a trained technician/examiner and repeated every Monday, Wednesday and Friday until 9 applications of the test article had been made.

The subjects were instructed to remove the patch 24 hours after application. Twenty-four hour rest periods followed the Tuesday and Thursday removals and 48-hour rest periods followed each Saturday removal. Subjects returned to the Testing Facility and the site was scored by a trained examiner just prior to the next patch application.

If a subject developed a positive reaction of a level 2 erythema or greater during the Induction phase or if, at the discretion of the Study Director, the skin response warranted a change in site, the patch was applied to a previously unpatched, adjacent site for the next application. If a level 2 reaction or greater occurred at the new site, no further applications were made. However, any reactive subjects were subsequently Challenge patch tested.

9.2 Challenge Phase

After a rest period of approximately 2 weeks (no applications of the test article), the Challenge patch was applied to a previously unpatched (virgin) test site. The site was scored 24 and 72 hours after application. All subjects were instructed to report any delayed skin reactivity that occurred after the final Challenge patch reading. When warranted, selected test subjects were called back to the Clinic for additional examinations and scoring to determine possible increases or decreases in Challenge patch reactivity.

Dermal responses for both the Induction and Challenge phases of the study were scored according to the following 6-point scale:

0 = No evidence of any effect
+ = Barely perceptible (Minimal, faint, uniform or spotty erythema)
1 = Mild (Pink, uniform erythema covering most of the contact site)
2 = Moderate (Pink-red erythema uniform in the entire contact site)
3 = Marked (Bright red erythema with/without petechiae or papules)
4 = Severe (Deep red erythema with/without vesiculation or weeping)

All other observed dermal sequelae (eg, edema, dryness, hypo- or hyperpigmentation) were appropriately recorded on the data sheet and described as mild, moderate or severe.

[1] Marzulli FN, Maibach HI. (1976) Contact allergy: predictive testing in man. *Contact Dermatitis.* 2, 1-17.

[redacted]

9.0 TEST PROCEDURE (CONT'D)

9.3 Data Interpretation

Edema, vesicles, papules and/or erythema that persist or increase in intensity either during the Induction and/or Challenge phase may be indicative of allergic contact dermatitis. Allergic responses normally do not resolve or improve markedly at 72-96 hours.

Exceptions to typical skin reactions may occur. These may include, but not be limited to, symptoms of allergic contact sensitivity early in the Induction period to one or more test products. When this occurs in one subject, such a reaction usually suggests either an idiosyncratic response or that the subject had a pre-exposure/sensitization to the test material or component(s) of the test material or a cross-reactivity with a similar product/component. Data for such reactions will be included in the study report but will not be included in the final study analysis/conclusion of sensitization.

10.0 RESULTS AND DISCUSSION

(See Table 1 for Individual Scores)

A total of 114 subjects (26 males and 88 females ranging in age from 19 to 78 years) were empanelled for the test procedure. One hundred nine (109/114) subjects satisfactorily completed the test procedure on Test Article: [redacted] Five (5/114) subjects discontinued for personal reasons unrelated to the conduct of the study. Discontinued subject data are shown up to the point of discontinuation, but are not used in the Conclusions section of this final report.

Induction Phase Summary

Test Article	Induction Scores (Number of Responses)						Evidence of Irritation
	0.5	1	2	3	4	Other	
[redacted]	0	0	0	0	0	0	No

Challenge Phase Summary

Test Article	Challenge Scores (Number of Responses)						Evidence of Sensitization
	0.5	1	2	3	4	Other	
[redacted]	0	0	0	0	0	0	No

There was no skin reactivity observed at any time during the course of the study.

11.0 CONCLUSIONS

Under the conditions of a repeated insult (occlusive) patch test procedure conducted in 109 subjects, Test Article: [redacted] was "Dermatologist-Tested" and was not associated with skin irritation or allergic contact dermatitis in human subjects.

TABLE 1

INDIVIDUAL SCORES

REPEATED INSULT PATCH TEST - OCCLUSIVE

Test Article: [redacted]

Subj.	Induction Evaluation Number									Challenge Virgin Site	
No.	1	2	3	4	5	6	7	8	9	24hr	72hr
1	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0
4	Discontinued										
5	0	0	0	0	0	0	0	0	0	0	0
6	0	0	Discontinued								
7	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0	0	0	0
21	0	0	0	0	0	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0	0	0	0
25	Discontinued										
26	0	0	0	0	0	0	0	0	0	0	0
27	0	0	0	0	0	0	0	0	0	0	0
28	0	0	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0	0	0	0
30	0	0	0	0	0	0	0	0	0	0	0

Scale:0 = No evidence of any effect
+ = Barely perceptible (Minimal, faint, uniform or spotty erythema)
1 = Mild (Pink, uniform erythema covering most of the contact site)
2 = Moderate (Pink-red erythema uniform in the entire contact site)
3 = Marked (Bright red erythema with/without petechiae or papules)
4 = Severe (Deep red erythema with/without vesiculation or weeping)

TABLE 1 (CONT'D)

INDIVIDUAL SCORES

REPEATED INSULT PATCH TEST - OCCLUSIVE

Test Article: [redacted]

Subj.	Induction Evaluation Number									Challenge Virgin Site	
No.	1	2	3	4	5	6	7	8	9	24hr	72hr
31	0	0	0	0	0	0	0	0	0	0	0
32	0	0	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0	0
34	0	0	0	0	0	0	0	0	0	0	0
35	0	0	0	0	0	0	0	0	0	0	0
36	0	0	0	0	0	0	0	0	Discontinued		
37	0	0	0	0	0	0	0	0	0	0	0
38	0	0	0	0	0	0	0	0	0	0	0
39	0	0	0	0	0	0	0	0	0	0	0
40	0	0	0	0	0	0	0	0	0	0	0
41	0	0	0	0	0	0	0	0	0	0	0
42	0	0	0	0	0	0	0	0	0	0	0
43	0	0	0	0	0	0	0	0	0	0	0
44	0	0	0	0	0	0	0	0	0	0	0
45	0	0	0	0	0	0	0	0	0	0	0
46	0	0	0	0	0	0	0	0	0	0	0
47	0	0	0	0	0	0	0	0	0	0	0
48	0	0	0	0	0	0	0	0	0	0	0
49	0	0	0	0	0	0	0	0	0	0	0
50	0	0	0	0	0	0	0	0	0	0	0
51	0	0	0	0	0	0	0	0	0	0	0
52	0	0	0	0	0	0	0	0	0	0	0
53	0	0	0	0	0	0	0	0	0	0	0
54	0	0	0	0	0	0	0	0	0	0	0
55	0	0	0	0	0	0	0	0	0	0	0
56	0	0	0	0	0	0	0	0	0	0	0
57	0	0	0	0	0	0	0	0	0	0	0
58	0	0	0	0	0	0	0	0	0	0	0
59	0	0	0	0	0	0	0	0	0	0	0

Scale:0 = No evidence of any effect
+ = Barely perceptible (Minimal, faint, uniform or spotty erythema)
1 = Mild (Pink, uniform erythema covering most of the contact site)
2 = Moderate (Pink-red erythema uniform in the entire contact site)
3 = Marked (Bright red erythema with/without petechiae or papules)
4 = Severe (Deep red erythema with/without vesiculation or weeping)

[redacted]

TABLE 1 (CONT'D)

INDIVIDUAL SCORES

REPEATED INSULT PATCH TEST - OCCLUSIVE

Test Article: [redacted]

Subj.	Induction Evaluation Number									Challenge Virgin Site	
No.	1	2	3	4	5	6	7	8	9	24hr	72hr
1	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	Discontinued	
16	0	0	0	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0	0	0	0
21	0	0	0	0	0	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0	0	0	0
25	0	0	0	0	0	0	0	0	0	0	0
26	0	0	0	0	0	0	0	0	0	0	0
27	0	0	0	0	0	0	0	0	0	0	0
28	0	0	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0	0	0	0
30	0	0	0	0	0	0	0	0	0	0	0

Scale:0 = No evidence of any effect
+ = Barely perceptible (Minimal, faint, uniform or spotty erythema)
1 = Mild (Pink, uniform erythema covering most of the contact site)
2 = Moderate (Pink-red erythema uniform in the entire contact site)
3 = Marked (Bright red erythema with/without petechiae or papules)
4 = Severe (Deep red erythema with/without vesiculation or weeping)

[redacted]

TABLE 1 (CONT'D)

INDIVIDUAL SCORES

REPEATED INSULT PATCH TEST - OCCLUSIVE

Test Article: [redacted]

Subj. No.	Induction Evaluation Number									Challenge Virgin Site	
	1	2	3	4	5	6	7	8	9	24hr	72hr
31	0	0	0	0	0	0	0	0	0	0	0
32	0	0	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0	0
34	0	0	0	0	0	0	0	0	0	0	0
35	0	0	0	0	0	0	0	0	0	0	0
36	0	0	0	0	0	0	0	0	0	0	0
37	0	0	0	0	0	0	0	0	0	0	0
38	0	0	0	0	0	0	0	0	0	0	0
39	0	0	0	0	0	0	0	0	0	0	0
40	0	0	0	0	0	0	0	0	0	0	0
41	0	0	0	0	0	0	0	0	0	0	0
42	0	0	0	0	0	0	0	0	0	0	0
43	0	0	0	0	0	0	0	0	0	0	0
44	0	0	0	0	0	0	0	0	0	0	0
45	0	0	0	0	0	0	0	0	0	0	0
46	0	0	0	0	0	0	0	0	0	0	0
47	0	0	0	0	0	0	0	0	0	0	0
48	0	0	0	0	0	0	0	0	0	0	0
49	0	0	0	0	0	0	0	0	0	0	0
50	0	0	0	0	0	0	0	0	0	0	0
51	0	0	0	0	0	0	0	0	0	0	0
52	0	0	0	0	0	0	0	0	0	0	0
53	0	0	0	0	0	0	0	0	0	0	0
54	0	0	0	0	0	0	0	0	0	0	0
55	0	0	0	0	0	0	0	0	0	0	0

Scale:0 = No evidence of any effect
+ = Barely perceptible (Minimal, faint, uniform or spotty erythema)
1 = Mild (Pink, uniform erythema covering most of the contact site)
2 = Moderate (Pink-red erythema uniform in the entire contact site)
3 = Marked (Bright red erythema with/without petechiae or papules)
4 = Severe (Deep red erythema with/without vesiculation or weeping)

[redacted]

FINAL REPORT

CLINICAL SAFETY EVALUATION

REPEATED INSULT PATCH TEST

product contains 20% Phenyl Trimethicone

[redacted]

Sponsor

[redacted]

Sponsor Representative

[redacted]

Clinical Testing Facility

[redacted]

[redacted]

Date of Final Report

3-2-11

[redacted]

[redacted]

SIGNATURE PAGE

CLINICAL SAFETY EVALUATION

REPEATED INSULT PATCH TEST

[redacted]

[redacted]

Laboratory Manager
Study Director

2/24/11
Date

[redacted] PhD, DABT, BCFE
Scientific Director
Principal Investigator

2-28-11
Date

[redacted] MD
Board-Certified Dermatologist
Medical Investigator

2/18/11
Date

[redacted]

QUALITY ASSURANCE STATEMENT

This study ([redacted]) was conducted in accordance with the intent and purpose of Good Clinical Practice regulations described in 21 CFR Part 50 (Protection of Human Subjects – Informed Consent) and the Standard Operating Procedures of Essex Testing Clinic, Inc.

For purposes of this clinical study:

X	Informed Consent was obtained.
____	Informed Consent was not obtained.
X	An IRB review was not required.
____	An IRB review was conducted and approval to conduct the proposed clinical research was granted.

To assure compliance with the study protocol, the Quality Assurance Unit completed an audit of the applicable study records and report. This report is considered a true and accurate reflection of the testing methods and source data.

[redacted] 25 Feb 2011

Manager, Quality Assurance — Date

[redacted]

[redacted]

TABLE OF CONTENTS

[redacted]

[redacted]

CLINICAL SAFETY EVALUATION

REPEATED INSULT PATCH TEST

[redacted]

1.0 OBJECTIVE

The objective of this study was to determine the irritation and/or sensitization potential of the test article after repeated application under occlusive patch test conditions to the skin of human subjects (non-exclusive panel).

2.0 SPONSOR

[redacted]

2.1 Sponsor Representative

[redacted]

3.0 CLINICAL TESTING FACILITY

The study was conducted by:

[redacted]

4.0 CLINICAL INVESTIGATORS

Study Director:
Principal Investigator:
Medical Investigator:

[redacted]

5.0 STUDY DATES

Study initiation: December 29, 2010

Final evaluation: February 11, 2011

[redacted]

[redacted]

6.0 ETHICS

6.1 Ethical Conduct of the Study

This study was conducted in accordance with the intent and purpose of Good Clinical Practice regulations described in Title 21 of the U.S. Code of Federal Regulations (CFR), the Declaration of Helsinki and/or [redacted] Standard Operating Procedures.

6.2 Subject Information and Consent

This study was conducted in compliance with CFR Title 21, Part 50 (Informed Consent of Human Subjects). Informed Consent was obtained from each subject in the study and documented in writing before participation in the study. A copy of the Informed Consent was provided to each subject.

7.0 TEST MATERIAL

The test article used in this study was provided by:

[redacted]

It was received on December 16, 2010 and identified as follows:

	Test Article I.D.	Description
[redacted]	[redacted]	Brown Semi-Solid

*The test article was supplied as a composite by the Sponsor.

8.0 TEST SUBJECTS

At least 50 male and female subjects ranging in age from 18 to 79 years were to be empanelled for this test.

The subjects chosen were to be dependable and able to read and understand instructions. The subjects were not to exhibit any physical or dermatologic condition that would have precluded application of the test article or determination of potential effects of the test article.

[redacted]

[redacted]

9.0 TEST PROCEDURE

The 9 Repeated Insult (occlusive) Patch Test (9-RIPT) was conducted as follows:

9.1 Induction Phase

A sufficient amount of the test article (approximately 0.1 g – 0.15 g) was placed onto a Parke-Davis Readi-Bandage® occlusive patch (approximately 25 - 38 mg/cm^2 of test material) and applied to the back of each subject between the scapulae and waist, adjacent to the spinal mid-line. This procedure was performed by a trained technician/examiner and repeated every Monday, Wednesday and Friday until 9 applications of the test article had been made.

The subjects were instructed to remove the patch 24 hours after application. Twenty-four hour rest periods followed the Tuesday and Thursday removals and 48-hour rest periods followed each Saturday removal. Subjects returned to the Testing Facility and the site was scored by a trained examiner just prior to the next patch application.

If a subject developed a positive reaction of a level 2 erythema or greater during the Induction phase or if, at the discretion of the Study Director, the skin response warranted a change in site, the patch was applied to a previously unpatched, adjacent site for the next application. If a level 2 reaction or greater occurred at the new site, no further applications were made. However, any reactive subjects were subsequently Challenge patch tested.

9.2 Challenge Phase

After a rest period of approximately 2 weeks (no applications of the test article), the Challenge patch was applied to a previously unpatched (virgin) test site. The site was scored 24 and 72 hours after application. Due to inclement weather during the test procedure, 1 of the 55 subjects was challenged one week later than originally scheduled to allow sufficient time between the Induction and Challenge phases of the study. Also during the Challenge phase, 54 of the 55 subjects missed the 24-hour reading when the Testing Facility was closed due to the inclement weather. All subjects were evaluated at 72 hours and were instructed to report any delayed skin reactivity that occurred after the final Challenge patch reading. When warranted, selected test subjects were called back to the Clinic for additional examinations and scoring to determine possible increases or decreases in Challenge patch reactivity.

Dermal responses for both the Induction and Challenge phases of the study were scored according to the following 6-point scale:

0 = No evidence of any effect
+ = Barely perceptible (Minimal, faint, uniform or spotty erythema)
1 = Mild (Pink, uniform erythema covering most of the contact site)
2 = Moderate (Pink-red erythema uniform in the entire contact site)
3 = Marked (Bright red erythema with/without petechiae or papules)
4 = Severe (Deep red erythema with/without vesiculation or weeping)

All other observed dermal sequelae (eg, edema, dryness, hypo- or hyperpigmentation) were appropriately recorded on the data sheet and described as mild, moderate or severe.

[redacted]

[redacted]

9.0 TEST PROCEDURE (CONT'D)

9.3 Data Interpretation

Edema, vesicles, papules and/or erythema that persist or increase in intensity either during the Induction and/or Challenge phase may be indicative of allergic contact dermatitis. Allergic responses normally do not resolve or improve markedly at 72-96 hours.

Exceptions to typical skin reactions may occur. These may include, but not be limited to, symptoms of allergic contact sensitivity early in the Induction period to one or more test products. When this occurs in one subject, such a reaction usually suggests either an idiosyncratic response or that the subject had a pre-exposure/sensitization to the test material or component(s) of the test material or a cross-reactivity with a similar product/component. Data for such reactions will be included in the study report but will not be included in the final study analysis/conclusion of sensitization.

10.0 RESULTS AND DISCUSSION

(See Table 2 for Individual Scores)

A total of 55 subjects (10 males and 45 females ranging in age from 23 to 75 years and 16 of whom had sensitive skin) were empanelled for the test procedure. Fifty-three (53/55) subjects satisfactorily completed the test procedure on Test Article: [redacted] Two (2/55) subjects discontinued for personal reasons unrelated to the conduct of the study. Discontinued panelist data are shown up to the point of discontinuation, but are not used in the Conclusions section of this final report.

Induction Phase Summary675

Test Article	Induction Scores (Number of Responses)						Evidence of Irritation
	0.5	1	2	3	4	Other	
[redacted]	0	0	0	0	0	0	No

Challenge Phase Summary

Test Article	Challenge Scores (Number of Responses)						Evidence of Sensitization
	0.5	1	2	3	4	Other	
[redacted]	0	0	0	0	0	0	No

There was no skin reactivity observed at any time during the course of the study.

11.0 CONCLUSIONS

Under the conditions of a repeated insult (occlusive) patch test procedure conducted in 53 subjects (30% with sensitive skin), Test Article: [redacted] was "Dermatologist-Tested" and was not associated with skin irritation or allergic contact dermatitis in human subjects.

[redacted]

TABLE 1

SUBJECT DEMOGRAPHICS

Test Article: [redacted]

Subject No.	Initials	Age	Sex	Race	Sensitive Skin	Subject No.	Initials	Age	Sex	Race	Sensitive Skin
1	[redacted]	71	M	CA	Yes	29	[redacted]	67	F	CA	No
2	[redacted]	41	F	BA	Yes	30	[redacted]	43	M	BA	No
3	[redacted]	49	F	CA	Yes	31	[redacted]	44	F	CA	Yes
4	[redacted]	50	F	CA	No	32	[redacted]	44	F	HS	No
5	[redacted]	36	F	CA	No	33	[redacted]	49	F	CA	Yes
6	[redacted]	42	F	BA	No	34	[redacted]	46	F	CA	Yes
7	[redacted]	38	F	BA	Yes	35	[redacted]	30	F	CA	No
8	[redacted]	56	F	BA	No	36	[redacted]	26	M	BA	No
9	[redacted]	37	F	HS	No	37	[redacted]	38	F	HS	No
10	[redacted]	75	F	CA	No	38	[redacted]	36	F	BA	No
11	[redacted]	71	F	CA	Yes	39	[redacted]	45	F	CA	No
12	[redacted]	56	F	BA	Yes	40	[redacted]	68	M	CA	No
13	[redacted]	47	F	CA	No	41	[redacted]	44	F	CA	No
14	[redacted]	23	F	CA	No	42	[redacted]	39	F	CA	No
15	[redacted]	41	M	CA	No	43	[redacted]	47	F	BA	Yes
16	[redacted]	51	F	CA	No	44	[redacted]	56	M	BA	Yes
17	[redacted]	49	F	BA	No	45	[redacted]	73	F	CA	No
18	[redacted]	50	F	CA	No	46	[redacted]	71	F	CA	No
19	[redacted]	53	F	CA	Yes	47	[redacted]	39	M	CA	No
20	[redacted]	29	F	CA	Yes	48	[redacted]	68	F	CA	Yes
21	[redacted]	49	F	BA	No	49	[redacted]	63	M	CA	No
22	[redacted]	75	M	CA	No	50	[redacted]	50	F	CA	No
23	[redacted]	49	F	CA	No	51	[redacted]	45	F	CA	Yes
24	[redacted]	49	F	BA	No	52	[redacted]	40	F	CA	Yes
25	[redacted]	42	F	CA	No	53	[redacted]	61	F	OT	No
26	[redacted]	42	F	CA	No	54	[redacted]	45	M	CA	No
27	[redacted]	51	F	CA	No	55	[redacted]	54	F	CA	No
28	[redacted]	55	F	CA	No						

BA = Black/African American
CA = Caucasian
HS = Hispanic
OT = Other

Shaded area = Discontinued subject

[redacted]

TABLE 2

INDIVIDUAL SCORES

REPEATED INSULT PATCH TEST - OCCLUSIVE

Test Article: [redacted]

Subj. No.	Induction Evaluation Number 1	2	3	4	5	6	7	8	9	Challenge Virgin Site 24hr	72hr
1	0	0	0	0	0	0	0	0	0	-	0
2	0	0	0	0	0	0	0	0	0	-	0
3	0	0	0	0	0	0	0	0	0	-	0
4	0	0	0	0	0	0	0	0	0	-	0
5	0	0	0	0	0	0	0	0	0	-	0
6	0	0	0	0	0	0	0	0	0	-	0
7	0	0	0	0	0	0	0	0	0	-	0
8	0	0	0	0	0	0	0	0	0	-	0
9	0	Discontinued									
10	0	0	0	0	0	0	0	0	0	-	0
11	0	0	0	0	0	0	0	0	0	-	0
12	0	0	0	0	0	0	0	0	0	-	0
13	0	0	0	0	0	0	0	0	0	-	0
14	0	0	0	0	0	0	0	0	0	-	0
15	0	0	0	0	0	0	0	0	0	-	0
16	0	0	0	0	0	0	0	0	0	-	0
17	0	0	0	0	0	0	0	0	0	-	0
18	0	0	0	0	0	0	0	0	0	-	0
19	0	0	0	0	0	0	0	0	0	-	0
20	0	0	0	0	0	0	0	0	0	-	0
21	0	0	0	0	0	0	0	0	0	-	0
22	0	0	0	0	0	0	0	0	0	-	0
23	0	0	0	0	0	0	0	0	0	-	0
24	0	0	0	0	0	0	0	0	0	-	0
25	0	0	0	0	0	0	0	0	0	-	0
26	0	0	0	0	0	0	0	0	0	-	0
27	0	0	0	0	0	0	0	0	0	-	0
28	0	0	0	0	Discontinued						
29	0	0	0	0	0	0	0	0	0	-	0
30	0	0	0	0	0	0	0	0	0	-	0

Scale:0 = No evidence of any effect
+ = Barely perceptible (Minimal, faint, uniform or spotty erythema)
1 = Mild (Pink, uniform erythema covering most of the contact site)
2 = Moderate (Pink-red erythema uniform in the entire contact site)
3 = Marked (Bright red erythema with/without petechiae or papules)
4 = Severe (Deep red erythema with/without vesiculation or weeping)

- = no reading

[redacted]

TABLE 2 (CONT'D)

INDIVIDUAL SCORES

REPEATED INSULT PATCH TEST - OCCLUSIVE

Test Article: [redacted]

Subj. No.	Induction Evaluation Number 1	2	3	4	5	6	7	8	9	Challenge Virgin Site 24hr	72hr
31	0	0	0	0	0	0	0	0	0	-	0
32	0	0	0	0	0	0	0	0	0	-	0
33	0	0	0	0	0	0	0	0	0	-	0
34	0	0	0	0	0	0	0	0	0	-	0
35	0	0	0	0	0	0	0	0	0	-	0
36	0	0	0	0	0	0	0	0	0	-	0
37	0	0	0	0	0	0	0	0	0	-	0
38	0	0	0	0	0	0	0	0	0	-	0
39	0	0	0	0	0	0	0	0	0	-	0
40	0	0	0	0	0	0	0	0	0	-	0
41	0	0	0	0	0	0	0	0	0	-	0
42	0	0	0	0	0	0	0	0	0	-	0
43	0	0	0	0	0	0	0	0	0	-	0
44	0	0	0	0	0	0	0	0	0	-	0
45	0	0	0	0	0	0	0	0	0	-	0
46	0	0	0	0	0	0	0	0	0	-	0
47	0	0	0	0	0	0	0	0	0	-	0
48	0	0	0	0	0	0	0	0	0	-	0
49	0	0	0	0	0	0	0	0	0	-	0
50	0	0	0	0	0	0	0	0	0	0	0
51	0	0	0	0	0	0	0	0	0	-	0
52	0	0	0	0	0	0	0	0	0	-	0
53	0	0	0	0	0	0	0	0	0	-	0
54	0	0	0	0	0	0	0	0	0	-	0
55	0	0	0	0	0	0	0	0	0	-	0

Scale:0 = No evidence of any effect
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- = no reading

[redacted]

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

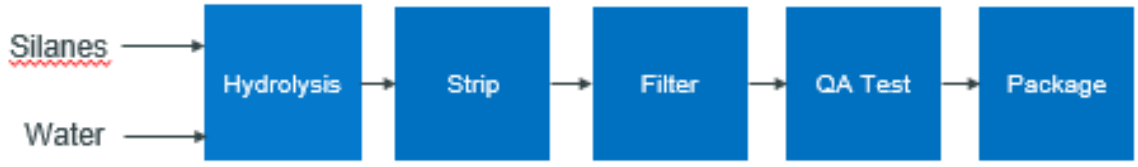
DATE: January 13, 2023

SUBJECT: Phenyl Trimethicone

Anonymous. 2023. Phenyl Trimethicone (process flow diagram, impurities, molecular weight).

Phenyl Trimethicone

Process Flow Diagram



Impurities

Methanol at a level ≤ 50 ppm

Benzene at a level ≤ 1 ppm

Molecular Weight

Greater than 70% of this material is less than 1000 Daltons, measured by conventional GPC against polystyrene standards.