Amended Safety Assessment of Dimethicone, Methicone, and Substituted-Methicone Polymers as Used in Cosmetics

Status:	Draft Final Amended Report for Panel Review
Release Date:	November 13, 2020
Panel Meeting Date:	December 7-8, 2020

The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; David E. Cohen, M.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; Lisa A. Peterson, Ph.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. Previous Panel member involved in this assessment: James G. Marks, Jr., M.D. The Cosmetic Ingredient Review (CIR) Executive Director is Bart Heldreth, Ph.D. This safety assessment was prepared by Preethi S. Raj, Senior Scientific Analyst/Writer, CIR.

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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 Writer/Analyst, CIR
Date: November 13, 2020
Subject: Amended Safety Assessment of Dimethicone, Methicone, and Substituted-Methicone Polymers

A Draft Final Amended Report of the Amended Safety Assessment of Dimethicone, Methicone, and Substituted-Methicone Polymers is enclosed for your review (*methic122020rep*). The Expert Panel for Cosmetic Ingredient Safety (Panel) first published a safety assessment of dimethicone, methicone, and substituted-methicone polymer ingredients in 2003, with the conclusion that the 20 ingredients named in that report are safe as used in cosmetic products. The original report is included for your use (identified as *methic122020orig* in the pdf).

At the June 2020 Panel meeting, a Draft Amended Report was presented to the Panel, along with 11 additional ingredient suggestions from the CIR Science and Support Committee. The Panel approved the addition of 10 ingredients, excluding, Simethicone. Due to an observed potential for irritation at the present concentrations of use, the Panel issued a Tentative Amended Report for these 30 ingredients, with a conclusion of safe as used when formulated to be non-irritating to the skin and the eye.

This is the first time that the Panel has issued a conclusion with the caveat, "when formulated to be non-irritating to the skin and the eye." Three issues make formulating to be "non-irritating to the eye" a departure from prior Panel conclusions. The first is that eye exposure is incidental; thus, formulating for accidental exposures of unknown doses, creates a unique challenge. The second issue is that most of the reported uses for these ingredients are not categorized for use in the "eye area." The third issue is that the Panel has historically utilized conclusion caveats based on concentration or use/product types, instead of organ exposures. For instance, with regard to formaldehyde, the Panel concluded (**emphasis** added):

> …that formaldehyde and methylene glycol are safe for use in cosmetics when formulated to ensure use at the minimal effective concentration, but in no case should the formalin concentration exceed **0.2%** (w/w), which would be 0.074% (w/w) calculated as formaldehyde or 0.118% (w/w) calculated as methylene glycol. Additionally, formaldehyde and methylene glycol are safe in the present practices of use and concentration in **nail hardening products**. However, formaldehyde and methylene glycol are unsafe in the present practices of use and concentration in **hair smoothing products** (a.k.a. **hair straightening products**).

It is, of course, the prerogative of the Panel to continue with a new conclusion type if they deem such is warranted. However, the Panel should consider if a historically common approach may equally/better serve the Panel's intentions.

Since the last review, concentration and frequency of use data for the added ingredients (*methic122020data; methic122020FDA*, respectively), as well as newly identified published data, have been incorporated into the report (highlighted in yellow). Additionally, comments on the Tentative Amended Report (*methic122020pcpc*) were received from the Council and have been considered.

Minutes from recent and previous meetings (*methic122020min),* a flow chart (*methic122020flow*), the history of these ingredients (*methic122020hist*), and a search strategy document (*methic122020strat*) are also included, as is a data profile identifying the presence of information in the original and current report (*methic122020prof*).

The Panel should consider the newly added data, and review the Abstract, Discussion, and Conclusion. The Panel should be prepared to issue a Final Amended Report.

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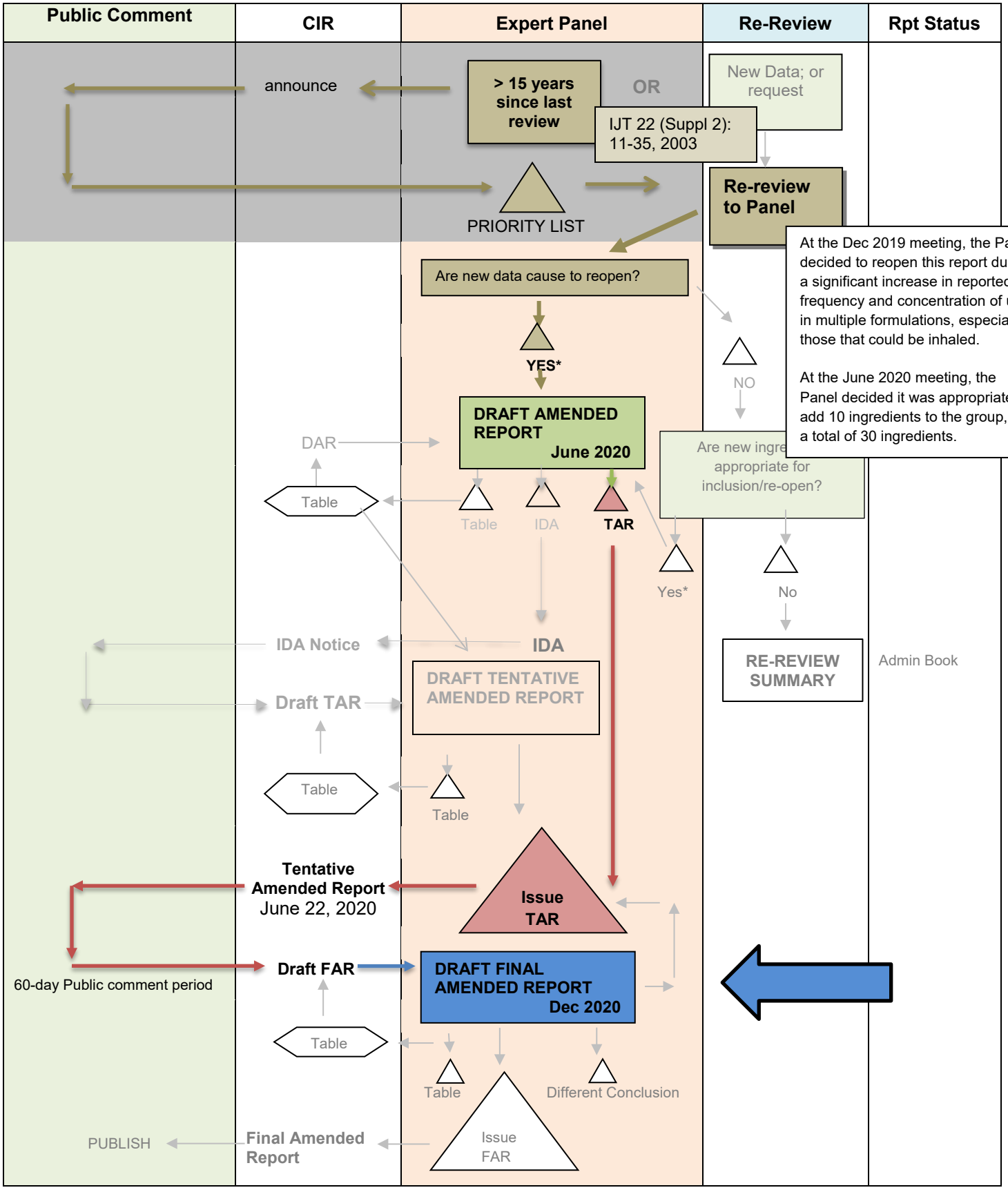
RE-REVIEW FLOW CHART

INGREDIENT/FAMILY Dimethicone, Methicone, and Substituted-Methicone Polymers

MEETING December 2020



*If Draft Amended Report (DAR) is available, the Panel may choose to review; if not, CIR staff prepares DAR for Panel Review.

CIR History of

Dimethicone, Methicone, and Substituted-Methicone Polymers (formerly 20, now, 30 ingredients)

August 1998: Scientific Literature Review published

June 1999 Panel Meeting: The first draft report was assessed, and the Panel issued an IDA for methods of manufacture, UV absorption data, and dermal reproductive and developmental toxicity data.

September 1999 Panel Meeting: The Panel unanimously concluded that the ingredients in the Methicone ingredient family are safe for use in cosmetics, with the understanding that forthcoming reports would include discussion on cautionary elements (such as the potential for inhalation exposure), and information on chemistry, delivery systems, and Dimethicone use levels. The issuance of a Tentative Report was approved.

September 1999: Tentative Report published

February 2000 Panel Meeting: The Panel requested for clarification of minor differences between the reported use of Dimethicone polymers by the cosmetics industry and the FDA. A skin irritation study describing necrosis was attributed to mineral spirits, and not Dimethicone, and was hence removed. The Panel voted unanimously in favor of issuing a Final Report with a safe as used conclusion.

February 2000: Final Report published

December 2019: A Re-Review was presented to the Panel. Due to substantial increases in frequency of use and concentrations of use for these ingredients, the Panel unanimously agreed to reopen this report.

June 2020: A Draft Amended Report was presented to the Panel, along with 11 additional ingredient suggestions (including Simethicone), from the CIR Scientific Support Committee. The Panel approved the addition of 10 ingredients, excluding Simethicone, and issued a Tentative Amended Report.

July 2020: Council comments on the Tentative report were received.

October 2020: Concentration of use data for 10 Methicones add-on ingredients were received.

December 2020: A Draft Final Amended Report is being presented to the Panel.

Methicones Data Profile* – December 7-8, 2020 – Preethi S. Raj

	Use				Toxico-kinetics			Acute Tox			Repeated Dose Tox			DART		Genotox		Carci		Dermal Irritation			Dermal Sensitization				Ocular Irritation		Clinical Studies	
	New Rpt	Old Rpt	Method of Mfg	Impurities	log P/log K_{ow}	Dermal Penetration	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
Amino Bispropyl Dimethicone	X																												
Aminopropyl Dimethicone	X																												
Amodimethicone	X	O																											
Amodimethicone Hydroxystearate																													
Behenoxy Dimethicone	X	O																											
C20-24 Alkyl Dimethicone	X																												
C20-24 Alkyl Methicone																													
C24-28 Alkyl Dimethicone																													
C24-28 Alkyl Methicone		O																											
C26-28 Alkyl Dimethicone	X																												
C26-28 Alkyl Methicone																													
C30-45 Alkyl Dimethicone	X	O						X																					
C30-45 Alkyl Methicone	X																												
C30-60 Alkyl Dimethicone	X																												
C32 Alkyl Dimethicone																													
Capryl Dimethicone	X																												
Caprylyl Methicone	X				X	X	X	X	X			X			X	X	X				X			X			X		
Cetearyl Methicone	X	O																											
Cetyl Dimethicone	X	O	O	O																									
Dimethicone	X	O	O	O	O	OX	OX	OX	OX	O	OX	OX	O	OX	O	OX	O	O	OX		OX	O	O	X	OX			OX		O X
Dimethoxysilyl Ethylenediaminopropyl Dimethicone	X																												
Hexyl Dimethicone	X																												
Hexyl Methicone										O																			
Hydroxypropyldimethicone																													
Methicone	X	O						O	O	O																		O	
Stearamidopropyl Dimethicone																													
Stearoxy Dimethicone	X	O	O	O																									
Stearyl Dimethicone	X	O	O	O																									
Stearyl Methicone	X																												
Vinyldimethicone	X							O	O	O															O			O		

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

[Methicones (years 1998 forward)- 10/10/2020]

Ingredient	CAS #	Info Base	PubMed	TOXNET	FDA	EU	ECHA	IUCLID	SIDS	ECETOC	HPVIS	NICNAS	NTIS	NTP	WHO	FAO	NIOSH	FEMA	Web
Amino Bispropyl Dimethicone	**189959-16-8** 999002112 243842-22-0	✓	1/0	NR	NR	✓*	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	
Aminopropyl Dimethicone	977185264 **99363-37-8**	✓	1/0	NR	NR	✓*	✓*	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	
Amodimethicone	977091647 106842-44-8 **68554-54-1** 71750-79-3	✓	2/0	1?	NR	✓*	✓*	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	
Amodimethicone Hydroxystearate	NR	✓	1/0	NR	NR	✓*	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	
Behenoxy Dimethicone	**977136745 193892-43-2**	✓	1/0	NR	NR	✓*	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	
C20-24 Alkyl Dimethicone	**200074-76-6**	✓	0/0	NR	NR	✓*	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	
C24-28 Alkyl Dimethicone	**192230-29-8**	✓	4/0	NR	NR	✓*	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	
C26-28 Alkyl Dimethicone	NR	✓	0/0	NR	NR	NR	NR	NR	NR	NR	NR	✓*	NR	NR	NR	NR	NR	NR	
C30-60 Alkyl Dimethicone	NR	✓	0/0	NR	NR	✓*	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	
C32 Alkyl Dimethicone	NR	✓	0/0	NR	NR	✓*	NR	NR	NR	NR	NR	NR	✓*	NR	NR	NR	NR	NR	
C20-24 Alkyl Methicone	**200074-77-7**	✓	0/0	NR	NR	✓*	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	
C24-28 Alkyl Methicone	**189378-12-9** 158061-44-0	✓	1/0	NR	NR	NR	✓*	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	
C26-28 Alkyl Methicone	**189378-12-9**	✓	0/0	NR	NR	✓*	✓*	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	
C30-45 Alkyl Methicone	977144016 **189378-12-9** 246864-88-0	✓	1/0	NR	NR	NR	✓*	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	
C30-45 Alkyl Dimethicone	**170831386**	✓	1/0	NR	NR	NR	NR	NR	NR	NR	NR	✓	NR	NR	NR	NR	NR	NR	
Capryl Dimethicone	NR	✓	0/0	1/0	NR	✓*	NR	NR	NR	NR	NR	NR	✓*	NR	NR	NR	NR	NR	
Caprylyl Methicone	**17955-88-3**	✓	0/0	0/0	NR	✓*	✓	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	
Cetearyl Methicone	**977183359**	✓	1/0	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	
Cetyl Dimethicone (Cetyl dimethicone 25)	977114263 **191044-49-2**	✓	11/1	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	
Dimethicone (Dimethylpolysiloxane, Dimethylsilicone fluid/oil, Polydimethylsiloxane)	9016-00-6 **9006-65-9**	✓	23/5	✓	NR	NR	NR	NR	NR	✓	NR	✓*	NR	✓*	NR	✓	NR	NR	
Dimethoxysilyl Ethylenediaminopropyl Dimethicone	**71750-80-6**	NR	1/0	NR	NR	NR	✓*	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	
Hexyl Dimethicone	NR	✓	9/0	1/0	NR	✓*	NR	NR	NR	NR	NR	NR	✓*	NR	NR	NR	NR	NR	

Ingredient	CAS #	Info Base	PubMed	TOXNET	FDA	EU	ECHA	IUCLID	SIDS	ECETOC	HPVIS	NICNAS	NTIS	NTP	WHO	FAO	NIOSH	FEMA	Web
Hexyl Methicone	**1873-90-1**	✓	1/0	NR	NR	NR	✓*	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	
Hydroxypropyldimethicone	**102782-61-6**	✓	2/0	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	
Methicone	63148-57-2 **9004-73-3**	✓	2/1	NR	NR	NR	NR	NR	NR	NR	NR	✓*	NR	NR	NR	NR	NR	NR	
Stearamidopropyl Dimethicone	110475-03-1	✓	1/0	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	
Stearoxy Dimethicone	**68554-53-0**	✓	1/0	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	
Stearyl Dimethicone	977094464 **67762-83-8**	✓	2/0	✓*	NR	NR	NR	NR	NR	NR	NR	✓*	NR	NR	NR	NR	NR	NR	
Stearyl Methicone	**977130247** 67762-83-8	✓	2/0	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	
Vinyldimethicone	**53529-60-5**	NR	1/0	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	

Bolded CAS number -number most recognized by
NR – not reported or available
✓ - data is available
✓*- in database, but data is not available or relevant
total # of hits/total # useful

Search Strategy

[*total # of hits / # hits that were useful*]
[*In PubMed*- 622/4]
Group search; note: also searched for ingredients individually
((((((((((((((((((stearoxy dimethicone) OR dimethicone) OR dimeticone) OR methicone) OR amino bispropyl dimethicone) OR aminopropyl dimethicone) OR amodimethicone) OR amodimethicone hydroxystearate) OR behenoxy dimethicone) OR c24-28 alkyl methicone) OR c30-45 alkyl methicone) OR c30-45 alkyl dimethicone) OR cetearyl methicone) OR cetyl dimethicone) OR dimethoxysilyl ethylenediaminopropyl dimethicone) OR hexyl methicone) OR hydroxypropyldimethicone) OR stearamidopropyl dimethicone) OR stearyl dimethicone) OR stearyl methicone) OR vinyl dimethicone) AND [search terms listed below]

Search for add-on ingredients in Pubmed and TOXNet (10/10/2020):
((((((((((((((c20-24 alkyl dimethicone) OR (200074-76-6)) OR (c24-28 alkyl dimethicone)) OR (192230-29-8)) OR (c26-28 alkyl dimethicone)) OR (c30-60 alkyl dimethicone)) OR (c32 alkyl dimethicone)) OR (200074-77-7)) OR (c20-24 alkyl methicone)) OR (189378-12-9)) OR (c26-28 alkyl methicone)) OR (capryl dimethicone)) OR (17955-88-3)) OR (caprylyl methicone)) OR (hexyl dimethicone)) AND (toxicity) – 1/0

tox [subset] AND c20-24 alkyl dimethicone -0/0;
OR c24-28 alkyl dimethicone – 1/0;
OR c26-c28 alkyl dimethicone -0/0;
OR c30-60 alkyl dimethicone – 0/0;
OR c32 alkyl dimethicone - 0/0;
OR c20-24 alkyl methicone – 0/0;
OR c26-28 alkyl methicone – 0/0;
OR capryl dimethicone – 1/0;
OR caprylyl methicone – 0/0;
OR hexyl dimethicone – 9/0

[*In PubChem,TOXNet, ECETOC, NICNAS, ECHA, Google, Google Scholar, Research Gate*-12/7]
Linear silicones; Linear polysiloxanes; Method of manufacturing; Impurities, Dermal toxicity; Dermal sensitization; Dermal irritation; In vivo toxicity; In vitro toxicity; Toxicity; Eye irritation; Ocular irritation; Vaginal irritation; Cytotoxicity; Genotoxicity; Carcinogenicity; Mutagenicity; Developmental toxicity; Reproductive toxicity; Safety; Epidemiology; Silicone animal studies

LINKS

Search Engines

- Pubmed (- http://www.ncbi.nlm.nih.gov/pubmed)
- Toxnet (https://toxnet.nlm.nih.gov/); (includes Toxline; HSDB; ChemIDPlus; DART; IRIS; CCRIS; CPDB; GENE-TOX)

appropriate qualifiers are used as necessary
search results are reviewed to identify relevant documents

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;,
- EAFUS: http://www.accessdata.fda.gov/scripts/fcn/fcnnavigation.cfm?rpt=eafuslisting&displayall=true
- 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/InformatioNRnDrugs/default.htm
- http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/UCM135688.pdf
- FDA Orange Book: https://www.fda.gov/Drugs/InformatioNRnDrugs/ucm129662.htm
- OTC ingredient list: https://www.fda.gov/downloads/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cder/ucm135688.pdf
- (inactive ingredients approved for drugs: http://www.accessdata.fda.gov/scripts/cder/iig/
- HPVIS (EPA High-Production Volume Info Systems) - https://ofmext.epa.gov/hpvis/HPVISlogon
- NIOSH (National Institute for Occupational Safety and Health) - http://www.cdc.gov/niosh/
- NTIS (National Technical Information Service) - http://www.ntis.gov/
- NTP (National Toxicology Program) - http://ntp.niehs.nih.gov/
- Office of Dietary Supplements https://ods.od.nih.gov/
- FEMA (Flavor & Extract Manufacturers Association) - http://www.femaflavor.org/search/apachesolr_search/
- 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/
- IUCLID (International Uniform Chemical Information Database) - https://iuclid6.echa.europa.eu/search
- OECD SIDS (Organisation for EcoNRmic 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
- NICNAS (Australian National Industrial Chemical NRtification and Assessment Scheme)- https://www.nicnas.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

JUNE 1999 PANEL MEETING – ORIGINAL ASSESSMENT/DRAFT REPORT

Full Panel – June 14-15, 1999

Dr. Schroeter indicated that his Team determined that an informal data request consisting of the following items should be issued:

(1) Methods of manufacture
(2) UV absorption data
(3) Dermal reproductive and developmental toxicity data

Dr. Belsito noted that after reviewing numerous reproductive toxicity studies, his Team identified minimal effects on the seminal vesicles that were considered insignificant by Dr. Carlton, and, overall, determined that the available data in the report are sufficient for evaluating the safety of this group of ingredients. However, Dr. Belsito said that his Team recommended that the report be tabled due to concern that a body of data from Industrial Bio-Test Laboratories (which, in the past, has come under question) should be removed from the document.

Dr. Bergfeld noted that, on the preceding day, Dr. Schroeter's Team had a lengthy discussion on testicular effects (decreased spermatogenesis and testicular size) that were reported.

Dr. Shank indicated that his Team has not seen these data, from Industrial Bio-Test. He agreed that all of the Industrial Bio-Test data should be removed from the present report, but also indicated that the findings have generated concern over the effects of these chemicals on the testis.

Dr. Bergfeld noted that another question that was raised in Teams relates to the inhalation toxicity of these chemicals. She recalled that the particle size was considered small, giving rise to little or no concern about potential pulmonary effects. She recommended that this concern be included in the report discussion at a future date.

The Panel voted unanimously in favor of tabling the Stearoxy Dimethicone report.

Dr. Bergfeld said that the report is being tabled with the understanding that the data from Industrial Bio-Test Laboratories will be removed, and that there will be a special look at testicular size and spermatogenesis in reproductive toxicity studies and a special note on inhalation toxicity and particle size in various products.

Dr. Andersen said that in the announcement of the results for this meeting, he will indicate that if any interested party has data relative to decreased spermatogenesis or particle size issues, the Panel would appreciate the submission of these data.

SEPTEMBER 1999 PANEL MEETING - ORIGINAL ASSESSMENT/DRAFT TENTATIVE REPORT

Full Panel – September 9-10, 1999

Dr. Belsito recalled that the Draft Report on these ingredients was reviewed at the June 14-15, 1999 Panel meeting, and, at that time, the data needs were related primarily to inhalation exposure. He noted that because information on the particle size of Dimethicones used in the inhalation study was not received, his Team was unable to evaluate the safety of the Dimethicone group in aerosolized products. However, these ingredients were considered safe as used in other cosmetics products. Dr. Belsito also noted that the Panel made the decision to delete all reproductive toxicity studies that were performed at a testing facility whose test results are regarded as suspect.

Dr. Schroeter noted that the ingredients being reviewed are high molecular weight compounds that are not absorbed, and, therefore, are safe. He also said that the issue of inhalation exposure will have to be addressed in the report discussion.

Dr. Bergfeld asked if the Panel is accepting the proposed safe as used conclusion, with a restriction on the use of these ingredients in aerosolized products.

Concerning the aerosol restriction, Dr. McEwen recalled that the Panel recently addressed the question of inhalation toxicity in another safety assessment by considering the particle size and by developing (using the published literature) a kind of algorithm as to what would or would not be considered a safe particle size. Thus, Dr. McEwen recommended that the Panel conclude that these ingredients are unsafe at certain particle sizes, rather than conclude that these ingredients are unsafe for use in aerosolized products.

Dr. Shank recalled that information on the particle size of Hexyl Methicone (mass median aerodynamic diameter [MMAD] = 0.27 μm), not a cosmetic ingredient, is included in the inhalation toxicity study in the report text. He noted that this study indicates that methicone derivatives have the potential for inhalation toxicity.

Dr. Bergfeld confirmed that this is the only inhalation toxicity study in which information on particle size was given.

Dr. Shank commented that if large particles were used in the other inhalation toxicity studies, then there would be no respiration and the results would be negative.

Dr. McEwen said that, usually, the particle size in an aerosol (10, 15, or 20 μm) is much greater than 0.27 μm. He noted that particles 10-20 μm in diameter are not respirable.

Dr. Bailey said that in the absence of data to demonstrate Dr. McEwen's point, the question of inhalation toxicity remains open.

Dr. Shank asked if the Panel could conclude that the ingredients are safe as used as long as there are no respirable particles.

Dr. Belsito said that the Panel could indicate that the ingredients are safe when formulated so as to avoid particle sizes that are less than a certain diameter.

Dr. Andersen noted that, in this case, the particle size that is respirable is known, but the ingredient particle sizes in cosmetic products are not known.

Ms. Fise said that the Panel has the option of saying that the available data are insufficient until sufficient data for evaluating the safety of these ingredients have been received.

Dr. Bergfeld recalled that the Panel has addressed the issue of pesticide contamination in a way that is similar to what was proposed today for the Stearoxy Dimethicone ingredient family. She said that the Panel has indicated in the report discussion for botanical ingredients certain limitations on pesticide impurities, because data on the pesticide content of these ingredients were not provided.

Ms. Fise proposed that the Panel request information on particle size, such that the Panel can determine exactly what the particle size in cosmetics should be.

Dr. McEwen noted that this information has been provided on other ingredients that have been reviewed by the Panel.

Dr. Andersen said that CIR has information on what is respirable, but does not have data on particle size for products containing the Dimethicones.

Dr. David Bower (with RT Vanderbilt now, formerly with ISP) noted that a similar discussion on particle size took place during the Panel's review of PVP (polyvinylpyrollidone), which is no longer used in cosmetics. He recalled that he was the toxicologist at ISP who provided CIR with data on this ingredient, and said that the following information/comments may be helpful in the present review: Anhydrous hair sprays typically have a particle size (MMAD) of 60 to 80 μm. Typically, less than 1% is under 10 μm. Pump hair sprays and aqueous aerosols typically have a particle size of 80 μm or higher (as much as 120 μm), with much less than 1% under 10 μm. So, if the Panel is concerned about the inhalation dynamics of plasticizers used in hair sprays at a level of approximately 1%, or even less, the following calculations can be done: In the hair spray, 8% resin contains 1% Dimethicone. So, the concentration of Dimethicone in the hair spray is 0.08%, of which less than one-half of 1% is respirable. Calculations such as this can be used to get around the problem of what is respirable and how much is actually exposed.

Dr. Belsito noted that the Panel's concern about inhalation exposure should be included in the report summary and discussion. He said that the exposure assessment described by Dr. Bower (including information on the average particle size in a spray versus a pump) will be incorporated. He added that it is the Panel's expectation that this will be the particle size of any Dimethicone-containing spray, and that it is not respirable.

Dr. Schroeter said that the Panel's conclusion will be safe for use, with the understanding that a report discussion containing cautionary elements and information on chemistry, the delivery systems, and use levels of the Dimethicones will be developed.

The Expert Panel unanimously concluded that the ingredients in the Stearoxy Dimethicone ingredient family are safe for use in cosmetics, with the understanding that a report discussion containing cautionary elements and information on chemistry, the delivery systems, and use levels of the Dimethicones will be developed. The issuance of a Tentative Report on this group of ingredients was approved.

FEBRUARY 2000 PANEL MEETING – ORIGINAL ASSESSMENT/DRAFT FINAL REPORT

Full Panel – February 14-15, 2000

Dr. Schroeter recalled that a Tentative Report with a safe as used conclusion on these ingredients was issued at the September 9-10, 1999 Panel meeting, and that the additional data available since then do not warrant any change in this conclusion. Dr. Schroeter also noted a discrepancy between the uses of Dimethicone polymers in cosmetics reported by FDA (7 uses) versus those that were received from the cosmetics industry (10 uses).

Drs. Bergfeld and Belsito agreed that the basis for the difference in reported uses should be clarified.

Dr. Belsito requested deletion of the skin irritation study (rabbits) on a mixture of Dimethicone and mineral spirits from the CIR report. He noted that the necrosis observed was due to the mineral spirits, and not Dimethicone. The Panel voted unanimously in favor of issuing a Final Report with a safe as used conclusion on the Stearoxy Dimethicone ingredient family.

DECEMBER 2019 PANEL MEETING – PRESENT ASSESSMENT/ INITIAL REVIEW: REREVIEW

Belsito Team – December 9, 2019

DR. BELSITO: Methicones. Okay. We first published the safety assessment in 2003, considered unlikely for any of the polymers to be absorbed into the skin because of large molecular weight. We concluded that they were safe as used in cosmetic products. We had limited inhalation exposure. There were a few ingredients that were used in aerosols.

It's been 15 years, and so it's time to look to see if we need to re-review. The frequency and concentration of use have generally increased in the ingredients quite significantly. The reported frequency of dimethicone has increased to 12-, almost 13,000 from 1,600.

A report of maximum concentration of dimethicone has also increased from 80 to 85. The rest of the others, really not significant. So, it's really dimethicone we're looking at.

So, I thought that the new and existing data covered dermal, eye, and lip. The major question was inhalation. And the only other thing would be the low molecular weight polymers, and I was wondering if we could use language like as used in foods, in our discussion about low molecular weight polymers of good manufacturing process. But inhalation would be the issue.

Are we happy with that? Particularly, if we have some statement about low molecular weight polymers? So, in 2019 the concentration in powders has gone up from 30 percent, in '98, to 53 percent in powders.

DR. SNYDER: In sprays it's gone from 16 to 85. And there was inhalation data on PDF Page 35 and 36 of the old report. And in the discussion of the old report, on page 44, PDF 44, they discussed the particle size distribution being one percent, less than ten microns.

So, if we just had that and didn't have these significant increased uses, and significant increased percentages, I'd probably say okay. But there's a little bit -- in a little bit of a gray zone there with now going from 16 percent to 85 percent concentration use in a spray.

Are we assured or are we reassured that in a 15-year period, that the particle size distribution is consistent with what it was previously. We have no new data on particle size distribution.

DR. BERGFELD: I put reopen.

DR. LIEBLER: Yeah, I said the same thing. I was originally a little uncertain about whether we should reopen this, but the dramatic increase in concentration of use and the numbers of uses.

I said reopen because of those things. We also have significant new data; some of which should be addressed even though it would appear likely that the conclusion may not change. But I think we can't do the level of diligence we're responsible for by just affirming the original conclusion and not reopening it.

DR. BERGFELD: Plus, we have new --

DR. LIEBLER: Microphone.

DR. BERGFELD: In addition, we have new ways of attacking or approaching inhalation. So, we have to update that.

DR. BELSITO: Okay. I mean, that's what I thought was going to be the issue was inhalation. Okay.

MS. FIUME: So, can I ask -- so this will eventually come back as a draft report; so we can't do any type of data requests right now, but we can give a heads up to industry in our post-meeting announcement.

So besides particle size distribution, is there any other piece of information that you think -- I know this isn't a full review, but just based on the preliminary look, that you might need, that we could just give a heads up, saying this type of information could help the panel come to a decision.

DR. SNYDER: Certainly, any additional inhalation data.

MS. RAJ: Did you have concerns about not having DART data and there's been, I think, a slight increase in -- or some documentation of baby product use?

DR. SNYDER: I would defer to Dan, but I think this is still too large to be absorbed, correct?

DR. LIEBLER: Yeah, I basically would agree.

DR. BELSITO: Yeah, we're going to put language about GMP and low molecular weight polymer, so I think that will --

MR. GREMILLION: Is that essentially saying formulated to be non-respirable, putting language in there? When you say the language about the molecular weight?

DR. LIEBLER: That's -- we've never been able to get away with formulate to be non-respirable.

MR. GREMILLION: Well, yeah. See, I'm trying to get an idea --

DR. BELSITO: No, eliminating the molecular weight polymers is to eliminate the issue of dermal absorption.

DR. LIEBLER: And systemic toxicity. Two different things.

DR. BELSITO: Yeah.

DR. LIEBLER: Yeah, two different issues. Yeah.

MR. GREMILLION: The other question I wanted to ask is a reference to, like, a case study with a premature baby. Does that, you know, point to any particular inhalation data that you might want to see? I mean, it seems like they concluded that it wasn't the dimethicone, but it struck me as interesting.

DR. BELSITO: These were for asthmatic, no?

MR. GREMILLION: This was on page 19.

MS. RAJ: Well, I think the other ingredient in that product, I think, are known to be irritants from what I heard -- especially, the Peruvian balsam oil, I was told.

DR. BELSITO: Yeah.

MR. GREMILLION: Yeah.

DR. BELSITO: I think Tom is talking about the case report for the premature infant --

MR. SNYDER: Yeah.

DR. BELSITO: -- who developed pneumonitis.

MR. SNYDER: Mineral oil, yeah, yeah.

DR. BELSITO: Mineral oil, yeah. And the Peruvian balsam for the eosinophilia, yeah.

DR. BERGFELD: Tt has vitamin E in it, very similar to those inhaled products.

MS. RAJ: And the authors did refer to the panel, if you noticed, to, I guess, be assured that it wasn't caused by the dimethicone.

DR. BELSITO: That's circular argument for us.

Okay. So, we're going to reopen, primarily concentrating on particle size, distribution and any additional inhalation toxicity.

Oh my, read-across. This is our last one?

DR. KLAASSEN: Yes.

Marks Team – December 9, 2019

DR. MARKS: And next is methicones. And I'm going to probably delay this a minute until Tom gets here. Oh, yeah.

So this is a re-review document. There are 20 ingredients, and a safety assessment was first published in 2003. The Panel came to a conclusion based on its large -- these are polymers -- concluded they were safe.

So every 15 years or so, Lisa, we take a look back at the ingredient's conclusion and then see if there's new data, whether the conclusion should be changed or modified. And our decision is whether we should reopen or not now.

So there's been a marked increase in -- we moved on to methicones, Tom.

DR. SLAGA: Okay.

DR. MARKS: And this is a rereview assessment of dimethicone, methicone, and a substantive methicone polymers. 2003, it was safe. Marked number of increased uses, concentration of dermal uses has also increased. In the original report, there was no sensitization at 100 percent dimethicone. I felt we didn't need to reopen, but Ron, Tom?

DR. SHANK: Oh, the other team's going to love this. We may want to reopen --

DR. MARKS: Oh, you may? Okay.

DR. SHANK: -- for extensive impurity data on the ingredients other than dimethicone. Because it was -- new data suggested that the polymers may contain significant levels of low molecular weight impurities. That's on page 14.

We have plenty of toxicity data on dimethicone itself, but not the others. So, the impurity issue may make read across difficult.

MS. RAJ: I think that language that I've taken from the review was more in the context of, during the process of making these polymers, it may not be 100 percent, that specific polymer. Like there may be, I guess, these other -- I don't know what you'd call them -- intermediates. In other words, it may not be 100 percent of what you're trying to create.

That's, I think, more what that's saying.

DR. SHANK: Okay.

DR. MARKS: So, let me make sure. So you're suggesting maybe we should open this for clarification of the impurities of these polymers?

DR. SHANK: Other than dimethicone, yes. But the number of uses of the other ingredients, other than dimethicone, was pretty small.

DR. ANSELL: So, where was this statement?

DR. MARKS: Page 14.

DR. SHANK: Page 14.

MS. RAJ: In impurities.

DR. SHANK: Let me find it. I'm not too fast.

MS. RAJ: It's the second paragraph.

DR. MARKS: "Therefore, it may be worth considering at high molecular weight linear methicones may contain impurities that are not just shorter counterparts with low molecular weights." Is that what you were focusing on, Ron?

DR. SHANK: Yes.

DR. MARKS: "But possibly other siloxane polymers with physicochemical properties, which could affect dermal penetration and/or cellular toxicity." Ohhh. I highlighted that, but I didn't focus on it.

DR. SHANK: I figured that would be a red flag for the B team.

DR. SLAGA: And it would give the opportunity to add this additional data we had to the report, if we reopen. Because we got a lot more, and there was very little before.

DR. ANSELL: Is this new data, that polymerization results in a spectrum of materials including --

MS. RAJ: It was a pretty recent review, yes, that I took that from. At the time -- I'm not sure if I've received it since -- but I think there was a conference paper, or something, talking about dermal penetration of low molecular weight silicone polymers.

DR. ANSELL: Because typically, we would not recommend reopening, unless there were new applications or new information which justified the amount of work that would go into not only the industry side, but the Panel side.

So, I don't know where that would fit in terms of we didn't consider polymerization results in a spectrum -- a distribution of molecular weights. So, if this is suggesting something new, then you guys can decide if it's just -- that's how --

DR. SLAGA: If we have the same conclusion, we don't reopen it. Yeah. I mean, that's what I originally put down.

DR. MARKS: Don't reopen?

DR. SLAGA: Yeah, don't reopen. And then I just put a note that there's a good bit of data in here, though. And sometimes you like to put it in the report.

DR. MARKS: Yeah. I had that at the bottom. A synopsis of new data.

DR. SLAGA: Yeah, but it doesn't change the conclusion, this data.

DR. SHANK: But that can go in the summary.

DR. MARKS: Yes.

DR. SLAGA: Yeah.

DR. SHANK: We don't have to reopen it to add the new data.

MS. RAJ: And I guess you weren't concerned with the increase in mucus membrane exposure for lipstick concentration?

DR. SHANK: I wasn't. That was for dimethicone, wasn't it?

MS. RAJ: Yeah.

DR. SHANK: Yeah.

DR. MARKS: I hear now, Ron -- because we're going to be -- our team is going to be moving. Do we not reopen, and then handle this in the re-review summary?

DR. SLAGA: That's what I would say. Yeah.

DR. MARKS: And then if we say that, what are we going to say? Because you raised the issue of what are these impurities. Do we need clarification?

DR. SLAGA: No.

DR. MARKS: Because in the re-review summary, if we need clarification, then we need to reopen it. I guess the other is --

DR. SHANK: I was anticipating tomorrow's discussion. And if there's consistency, I'm sure the impurity issue will come up. It doesn't bother me that much, and I wouldn't reopen it just for that.

DR. HELDRETH: I'm looking back at the original reference that Preethi used. The impression I'm getting isn't so much that they're talking about impurities, per se; it's just the natural distribution of chain links when you do polymerization.

For instance, for most polymerization reactions, you're not going to get all of the -- exactly what molecular weight. You're going to get a median value where most of the chain links are, and then it's going to be this bell-shaped curve of longer or shorter chain links in that situation.

I think that's what the author was getting at there.

DR. SHANK: Okay. Then what I would recommend is, not to put it under impurities. It's a distribution of molecular weight of the polymers. And I understand that. That's fine. I was thinking of some kind of monomer or other chemical that might be there.

MS. RAJ: Would you put it under method of manufacture then, or where would you put it?

DR. PETERSON: Chemical characteristics.

DR. SHANK: Chemical composition.

DR. PETERSON: Composition.

DR. SHANK: Chemical properties.

MS. RAJ: Okay.

DR. SHANK: And not call it impurities.

DR. HELDRETH: You could have it as a its own statement right before. Under chemical and physical properties right before hexyl methicone. You could have it as a general statement about --

DR. MARKS: Chemical properties.

DR. SHANK: The main chemists may see it differently than I do.

DR. MARKS: What do you think?

DR. PETERSON: I agree. If the issue is really that the polymer lengths are different, and that's the issue and not impurities, then it belongs up in chemical/physical properties.

DR. SHANK: Thank you.

MS. RAJ: Okay. Thank you.

DR. MARKS: Okay. So, with that in mind, it seems like it would be pretty straight forward. We're going to move not reopen. And then we put clarification maybe -- I'm not sure that's the best way, now, to put it. But in the re-review summary, we clarify -- we move the distribution of polymers to the chemical property section, something like that.

DR. HELDRETH: Yeah. If the full panel agrees tomorrow not to reopen this, most of this text just completely disappears. Because we're just going to condense down to a re-review summary, and that paragraph wouldn't really exist in the end product.

DR. SHANK: Okay. Because the way it's worded here, it sounds like they're worried about things other than just smaller polymers.

DR. ANSELL: Right. That we've discovered a new monomer, which -- not potentially affect, but was unknown.

DR. HELDRETH: Yeah. The exact language in the source document says, "Due to the specifics of the polymerization reaction, it results in a product that must be treated as a mixture of polymers, including oligomers with variable chain links and consequently variable molecular weights."

DR. SHANK: Okay. That's different.

DR. ANSELL: Which is true of many of the compounds we've spoke about, including the ethoxylation.

MS. RAJ: So, in the re-review summary, I guess, do you have anything specifically that you would want to mention?

DR. MARKS: I mean, it's interesting because the way it's worded now it caused concern, and in the impurities section.

If we note it in the chemical properties section, that there's a distribution of polymers, it can be as simple as that and don't say anything more. Although, I think most of us would know that any polymer there's going to be a distribution of length. But we could put it in there to be explicit. Does that sound good, Ron?

DR. SHANK: Yes.

MS. RAJ: I guess, would you have any language that, in spite of significant increase of use and in these certain categories, like why the panel feel safe about these ingredients?

DR. MARKS: Oh, because the data supports its safety. So, increased use doesn't create any concerns, unless it was a new use in which we had not considered the safety prior, such as perhaps on babies or on inhalation or something like that.

MS. RAJ: There is currently no DART data, which I'm sure you guys noticed.

DR. MARKS: Yeah. What I interpreted -- there were increased numbers of uses, but the products being used were virtually the same. The concentration on a leave-on was increased. But again, it wasn't like there was a whole new category. Is that how you interpret that?

DR. SHANK: Yes.

DR. MARKS: So, tomorrow I'm going to move not reopen. And then, do we want to bring -- I guess even though it's editorial, should we bring up the issue of the clarification of impurities on page 14, and moving that? Or just put that as a discussion here today, which is public knowledge, and not even bring it up tomorrow, unless the Belsito team has concerns about it?

DR. HELDRETH: That's right. Unless it's really the basis for your decision.

DR. MARKS: And you've heard everything, so I won't mention it tomorrow. Okay?

MS. RAJ: Thank you.

Full Panel – December 10, 2019

DR. MARKS: So, this is a re-review of the safety assessment of dimethicone, methicone, and substituted methicone polymers. There are 20 ingredients which were evaluated in 2003, and the panel concluded these were ingredients that were safe as used in cosmetics. Our team felt that that conclusion could remain the same and we move not to reopen.

DR. BERGFELD: Is there a second?

DR. BELSITO: No.

DR. BERGFELD: Okay.

DR. BELSITO: We felt that the increases in number of uses was so extremely high, including increase concentrations in products that could be aerosolized, that to do due diligence we needed to reopen this report.

DR. MARKS: I guess, if we don't have any tox alerts; just because the uses go up -- and noted, yeah, marked increase in the number of uses and the concentration of dermal uses including.

DR. BELSITO: Yeah, the dermal didn't bother us; it was the marked increases in the potential inhalation.

DR. MARKS: And we had quite a discussion about "impurities." And we felt that actually what was meant in this tentative memo -- or report -- was that it was really a distribution of polymers. And so we would move to the chemical properties section. But, inhalation didn't come up in our discussion so, I guess, clarify, was there an inhalation tox alert?

DR. BELSITO: Paul, you want to comment?

DR. SNYDER: No, there wasn't any specific alert; it was just that the uses went from 1600 to 13,000. And the greatest increase in concentration was the spray use; it went from 16 percent to 85 percent for sprays, 30 percent to 53 percent for powders.

So we thought just we could proceed to relook at it. We could reaffirm the conclusion, but we thought we'd like to see, you know, some additional information -- if there was any additional information regarding particle distribution or anything like that we could gleam from these increased uses and things.

Because obviously there's got to be new data in regard to the monomer content, I think would be an issue also as impurities. And, there was limited acute inhalation data in the old report.

DR. BERGFELD: Ron?

DR. SHANK: Using our usual wordage about particle size and distribution in the respiratory tract is not sufficient? Rather than opening it in a re-review summary, couldn't you just repeat what we say about the respiration of particles?

DR. SNYDER: That's an option. I think that's still on the table. I think just because we reopen doesn't mean that we're going to change anything; it's just that we want to look at the data a little bit more carefully and see where we're at. Because this is a significant change in uses and concentration used, compared to the old report.

DR. LIEBLER: If it had been a modest change in usage, but an increase in concentration, I would be certainly open to reaffirming the original conclusion and not reopening the report. It's just that on top of the concentration increase, the dramatic increase in number of uses, I felt it was due diligence for us -- I think I used that term in our discussion -- for us to open the report, even if we may end up in the same place.

DR. BERGFELD: Marks team?

DR. SHANK: Okay.

DR. MARKS: Sure, because we're deciding on the side of being safe. So, of course we endorse that. So we'll second. I'll withdraw my motion, and I'll second the motion to reopen this safety assessment.

DR. BERGFELD: So, all those in favor of reopening Methicone? Thank you, unanimous.

Okay, moving ahead, and I think the discussion well outlines what is needed. Moving on to Dr. Belsito's ingredient.

JUNE 2020 PANEL MEETING – PRESENT ASSESSMENT: SECOND REVIEW: DRAFT AMENDED REPORT

Belsito Team – June 8, 2020

DR. BELSITO: At the December meeting we had a re-review of 20 ingredients to determine if safety assessment should be reopened. And we decided because of a significant increase in reported frequency in concentration of use, the multiple formulations, especially ones that could be inhaled -- we decided to reopen the report and look for more data on particle size, distribution and inhalation toxicity. Additional data has not been received. And then it wasn't clear to me. Are we adding simethicone into this report?

MS. RAJ: Yes. Sorry, go ahead.

DR. HELDRETH: We've been asked to.

DR. LIEBLER: Preethi, go ahead, and then I'll follow.

MS. RAJ: Yes, simethicone along with ten other ingredients, I believe, have been proposed by the SSC.

DR. LIEBLER: So this was one of the things I referred to in my initial presentation that was brought to Lisa and I to discuss. If you go to PDF page 71, down near the end of the report, it's the CIR SSC memo where they propose adding several other ingredients, which begin at the bottom of the page and go on to the next page -- so capryl dimethicone, hexyl dimethicone, and several others, including -- and then in the third paragraph from the bottom on that page, "We think simethicone defined as a mixture of dimethicone with an average chain length of 200 to 350 dimethylsiloxane units and Silica to be added to this report."

So Lisa and I agreed that the ingredients at the bottom of this page and the top of the next page -- so let's see. That's five plus five -- so ten additional ingredients are fine to add. They certainly are chemically similar enough. They would belong with the ingredients in the remaining part of the report.

The only hang up is simethicone. And it may not be a problem, but it's a mixture of basically a dimethicone polymer in silica. And so as we are all well aware of the issues surrounding silica, it all depends on what kind of silica is in this. If it's synthetically produced amorphous silica, it's probably no problem. And it also depends on how much is routinely in this. If it's possibly crystalline silica or contaminated with crystalline silica, it would be an issue.

And having said all that, of course, this is a widely used over-the-counter medicinal ingredient, so it's probably okay. But based on the information that we currently have before us, we don't know.

DR. BELSITO: So what would we need, Dan? We would need the cosmetic definition of what simethicone is? Or would we assume that it's the same as the OTC drug?

DR. LIEBLER: So that would be one thing we would need to know. And then the method of manufacture, composition, and impurities should take care of it. As long as it's satisfactorily addressed in our description of that ingredient. I think it would be okay. And I think the ten ingredients other than simethicone are no-brainer additions. They make perfect sense.

Simethicone also may be a nearly no-brainer addition. We just need a little bit better documentation on what this is. Because it's the only ingredient that's a mix of a dimethicone polymer and something else, in this case silica.

DR. BELSITO: Okay. So we're going to go with adding in all and questionably silica -- simethicone, rather.

DR. LIEBLER: Right.

DR. BELSITO: And the information that we need on simethicone is what kind of silica is in it?

DR. LIEBLER: Right. So we'll need physical properties, chemical-physical properties, method of manufacture, and impurities. That should cover us there.

MS. RAJ: Thank you.

DR. BELSITO: So we hand it back in and we sort of give a hint this is what we need. Is that what you're suggesting?

DR. LIEBLER: Correct.

DR. KLAASEN: (Inaudible) being used to (Inaudible).

DR. BELSITO: I'm sorry, Curt. You broke up.

DR. KLAASEN: (Inaudible) if we're adding this chemical with the potential of silica in it, (Inaudible) how it's being used. If it's being used in any inhalation -- if it's likely to be inhaled or not.

DR. BELSITO: Well, we would get that in terms of when we see where it's used, right?

DR. KLAASEN: Oh, for sure. (Inaudible).

DR. LIEBLER: The simethicone says there's 519 uses, two of which are face powders. We have that data already.

MS. RAJ: Yeah. It's in the March to June supplement, I believe.

DR. LIEBLER: I doubt we're going to have a problem here, but Curt put his finger on the right point. This is mainly an inhalation issue, and it's going to depend on what silica is in this.

DR. KLAASEN: Correct.

DR. BELSITO: Well, I mean, we'll find out when we see the data, right?

DR. LIEBLER: Yeah.

MS. RAJ: So just to clarify, is this going to be a parallel IDA, and then would I, as the writer, be trying to pull in new data for these ingredients that we're going to add?

DR. LIEBLER: What do we do when we're sort of adding new ingredients to a report that's just starting? I mean, it's not really an IDA. We haven't presented the available data. We haven't even been able to pull in the available data yet.

DR. HELDRETH: So the stage of the report, last time you saw it, we were bringing it to you to see if you wanted to reopen this as a re-review. And you said thumbs up. In the interim, afterwards we and the Scientific Support Committee suggested some additions. So those are available for you to look at now. And currently this is a draft amended report before you. So two options now are to either go forward with a conclusion and issue a draft report with a conclusion or to put out an insufficient data announcement for whatever data needs you feel there are.

DR. SNYDER: Well, we received the inhalation data that we need to clarify the inhalation issue. But the request to add these additional ingredients has raised a concern for some missing data related to the silica involved. So, I think, Don, we need to -- we got data to clear the inhalation issue. We got data also that these are very large (Inaudible) new ones. But I think Dan is right with the point about the silica. That needs to (Inaudible).

DR. BELSITO: Then that would go with the no-brainer idea. Adding simethicone is not a no-brainer.

DR. LIEBLER: Yeah. One thing we can do, if you want to accelerate this report, is we don't include simethicone. We do that in some other way at some other time. And then I think our data needs are largely met. But if we add simethicone to this, we're literally at square one for a key ingredient.

DR. ANSELL: Yeah. We can't reopen and then conclude insufficient. I mean, if the materials can't be supported by the existing data, then they don't belong in the family. To the extent that the simethicone has a question mark on it, I'd be interested in how to resolve that -- that question mark. But insufficient isn't one of the choices.

DR. BELSITO: All right. Even the OTC use of simethicone is oral. It's not for -- there's no inhalation exposure, right?

DR. LIEBLER: Yeah.

DR. ANSELL: It's not recommended for aerosols.

DR. BELSITO: Okay. I mean, I think that what I'm hearing is we add an "all, except simethicone" and go with a "safe-as-used" conclusion.

DR. LIEBLER: Yeah. That's fine.

MS. RAJ: And I'm guessing in the discussion we wouldn't need to make mention of simethicone then, right?

DR. LIEBLER: Right. Right. Like it never happened.

DR. HELDRETH: It will get reviewed again. Just not here.

DR. LIEBLER: Yeah. That's right.

MS. RAJ: Any particular language you would like to see in the discussion?

DR. BELSITO: "Formulated to be nonirritant." Is that going to be part of our conclusion? Let me see. We just changed to Microsoft 365, so I apologize. But this is not the way I'm used to seeing the document discussion. Obviously, "particle size for potential inhalation." And then I had a question about the ocular issues. It's used up to 37.8 percent in an eye area. Is that problematic?

DR. SNYDER: I didn't ping that, so.

DR. LIEBLER: Let's see. Which table is that? Oh, I'm sorry. I'm thinking of the ocular tox data. I guess it's not summarized in the table.

MS. RAJ: No, it's not in the table. This was in the cosmetic use section you'll see that. It's page 20, I believe.

DR. BELSITO: Page 25 on dimethicone.

MS. RAJ: Under the cosmetic use section for the report, it's page 19 where I see that at the last paragraph.

DR. SNYDER: Yeah. I mean, I think, Don, that would be covered. If there's any issue it would be right in that irritation. So I guess the -- I mean, that was the whole reason we opened this because increase frequency of use and increase concentration of use, along with the inhalation. So I thought we were okay clearing it.

DR. BELSITO: But if you look at page -- under the ocular data --

DR. LIEBLER: Page 25 of the PDF.

DR. BELSITO: Yeah. 25. Ocular irritants -- actually on 26. It says, "Although there appear to be better ocular tolerance for medical-grade dimethicone, it also caused some corneal changes." I mean, I think it at least deserves some discussion. I mean, I'm presuming -- I'm not used to these doses and viscosities that they're giving and how that impacts upon the cosmetic viscosities in a finished formulation.

DR. LIEBLER: Yeah. Preethi, on the beginning of the ocular irritation section, which is PDF 25 at the bottom, in the italics it says, "Most ocular irritation studies using rabbits classified dimethicone as a mild to minimal irritant." Then it says, "The most common finding was a conjunctival reaction. However, a few studies reported severe reactions." And then, "Similar to dimethicone, methicone and vinyldimethicone also produced conjunctival reactions."

That's why I was asking is there a table with data on studies. Because in the rest of the paragraphs, except for that short line on C30-45 alkyl dimethicone, they all report some degree of reaction involving ocular irritation to these compounds. So it seems like fairly commonly observed. But a lot would depend on dose.

And in the case of this one thing Don mentioned, medical grade dimethicone producing somewhat better ocular tolerance. So that's kind of vague. I think we need to better document the data. And then this does need to be addressed in the discussion.

DR. SNYDER: But you have to remember this is part of a re-review. So that italicized is from an old report we think was -- we already said safe as used. And we are aware of this ocular irritation previously.

DR. BELSITO: Yeah. But the eye -- concentration in the eye and eye products has gone up significantly from when we last looked at it. It's now 37.8.

MS. RAJ: Yeah. I'm not seeing a table for ocular data in the original report. But I think there were like a few studies mentioned, which, as Dr. Snyder said, was summarized in italics here.

DR. LIEBLER: I think if the rationale driving this concern in reopening the report is increased frequency of use and increased concentration of use, we need to try and square that with the concentrations that produce the effects in these studies.

MS. RAJ: And I guess you mentioned something about viscosities. So are the viscosities, I guess, presented in this report not something you normally see in clinical use or --

DR. BELSITO: I've just never seen data where they're talking about different viscosities of, you know, the same material. I mean, it's just foreign to me.

DR. HELDRETH: For this particular report, the viscosity is a direct result of the degree of polymerization. So the higher the viscosity that you see, the longer the polymer chains are. So it's an indirect way of telling you how big these molecules are.

MS. RAJ: Yeah. That makes sense.

DR. BELSITO: So it says medical-grade dimethicone, which has a viscosity of 1000 centimeters squared per second, was safer. Do we have information on what cosmetic grade dimethicone is? We don't.

DR. LIEBLER: No.

DR. HELDRETH: The thing is it can vary from manufacturer to manufacturer, from formulation to formulation. I mean, you can attenuate the degree of polymerization for all of these very easily with heat and time, and there's even some additives that can further the propagation or slow it down or completely terminate it when it's smaller.

DR. BELSITO: Now, since we're adding in a whole bunch of other ingredients other than simethicone, there still may be data that we didn't look at and that's not in this report, correct?

DR. HELDRETH: Yes. We will do an extensive double check to make sure that there's no other data on these additions.

DR. BELSITO: Okay. I mean, so then how do we proceed if there could be other data that might change our conclusions?

DR. HELDRETH: As Jay alluded to, you know, these should all be no-brainer additions. The data that's already in the report should support the additions that the panel is making today.

DR. BELSITO: Okay.

DR. HELDRETH: If it doesn't, you know, you can decide not to add those in. But we will make sure that there's no other data on these additions. It may be somewhat unlikely that we'll find additional data on these add-ons since they are very specific to the cosmetic industry.

DR. LIEBLER: Yeah. I want to just clarify that our recommendation -- the recommendation I made and Lisa made to include these ingredients that the SSC recommended was based on chemical similarity and similarity for use. We didn't see any data on these. And Bart's probably right, we may not get much specific data on these -- much additional data. But it wasn't an assessment of the data or the safety. It was simply an assessment of the chemical similarity that these belong together in the same report.

DR. BELSITO: Okay. I mean, I'm fine with that. I'm just trying to clarify where we're going here. So I guess in the discussion we would not need, I think, to talk about certainly the significant increase in use concentration. And I think where we really need to probably stress -- and I'll ask Curt, Dan and Paul -- exactly wording is the inhalation issues.

I think that, basically, in our conclusion I think we would have to say "formulated to be nonirritating both to skin and eye," which is sort of different, because usually we talk just about skin. But here we're getting data that the dimethicone, which is 37.8 in an eye preparation, could potentially have significant irritation potential.

DR. SNYDER: And, Don, I reviewed the old report here quickly, and there was one study with dimethicone that there was no ocular irritation at 10 and 29 percent. But there was at 35 percent. And then in the summary in the old document -- the original report -- they talked about the conjunctival reaction of being mild to minimal but no severe reactions. And then we must have been comfortable that we weren't anywhere near that 35 percent positive reaction. I think we do need to address that in the re-review.

DR. ANSELL: I'd just add that while the data is relevant in assessing its ocular irritation, the intentional addition to an ocular product would not be a cosmetic. So at these high concentrations, the potential for irritation is relevant but not necessarily at the concentrations from a cosmetic application.

DR. SNYDER: Yeah. But I think this is akin to the incidental ingestion -- incidental inhalation because there is -- the one that has the 39 percent is (Inaudible). So there could be an incidental exposure of the eye, even though it's not intended to be used on the eye.

DR. LIEBLER: Yeah. That's it.

MS. RAJ: So would it be sufficient to say that at that concentration that we mentioned, the 39.5 percent, there may be an incidental exposure to the eye? But that, I guess, at that level of concentration is not very, I guess, prevalent for eye use or -- I'm not really sure how to say that.

DR. LIEBLER: No, you can't really put it that way. We know that there is ocular irritation voided from the old report. Paul, you said it was about 35 percent?

DR. SNYDER: Yeah. They tested it at 10 and 29 and 35. 10 and 29 did not cause any irritation, but 35 did.

DR. LIEBLER: Yeah. So if we have an ingredient used at 37 percent in a product that's going to be applied around the eye, there's a potential for ocular exposure and ocular irritation. So we have insufficient data to support the safety -- at this point, we have insufficient data to support ocular safety at that concentration of use.

DR. BELSITO: Well, in the study on PDF page 26, where they are looking at the ocular irritancy of dimethicone, it looks like, from what I can read -- this is the first paragraph at the top -- this was pure dimethicone.

MS. RAJ: Wait. Which page are you on again, Dr. Belsito?

DR. BELSITO: PDF page 26. It says "Ocular irritancy of dimethicone was evaluated in a study group: three mice, three guinea pigs, three rabbits -- five separately-manufactured samples of dimethicone. For the test, a drop of dimethicone was instilled once daily." So it sounds like it's pure dimethicone. And it says, "The authors opined that ocular irritancy and inflammatory effects of silicone fluids may be pH-dependent." So it sounds like it could be formulated to be nonirritant depending upon the pH.

MS. RAJ: Yeah. I remember this particular study. I think their emphasis was more on the pH of these samples than necessarily viscosity or other things.

DR. BELSITO: Yeah. But again, it was 100 centimeters squared per second was the -- and the medical grade. So that means, Bart, this was an even longer chain. Is that right? Or shorter?

DR. HELDRETH: The high viscosity --

DR. BELSITO: Medical grade is supposed to be 1,000 viscosity.

DR. HELDRETH: -- readings are going to be longer chain. Whereas lower viscosity we're talking smaller molecules.

DR. BELSITO: Okay. So this is a smaller molecule of (Inaudible) centimeters squared. Again, we don't know what cosmetic grade methicone is. I'm not an ocular toxicologist. Would one predict that a shorter chain would be more irritant than a longer chain?

DR. SNYDER: According to these authors, it wouldn't matter. It would matter about the pH of the fluid, the (Inaudible). So I think we could go with the caveat that you said -- when formulated not induce ocular irritation -- concentration of use. Yeah.

DR. BELSITO: Right. That's the way I interpreted it, for skin a well.

DR. SNYDER: Yeah.

DR. LIEBLER: Yeah. And I think we still need to note it in the discussion to come back to the original question Preethi posed to us.

DR. SNYDER: I think the discussion -- we'll have to bring in that old data that there was ocular irritation at 35 percent, and the current concentration of use exceed that. We do need to discuss that.

DR. BELSITO: Right. And then bring in the fact that, in this study, it appeared that there was a pH effect on that irritation so that it could be formulated presumably at 37.8 percent to be not irritating to the eye.

MS. RAJ: Okay. Thank you.

DR. KLAASEN: (Inaudible) popular irritancy test before which all guinea pigs on the eight to ten. (Inaudible). What's going on there?

DR. BELSITO: You keep breaking up on me, Curt. I didn't really fully understand your question.

DR. KLAASEN: I guess, in this study, by eight to ten on the screen there, all of the guinea pigs had died. It's more than just a little irritation.

DR. BELSITO: Which study are you on?

DR. KLAASEN: It's on the screen here.

MS. RAJ: It's the same one.

DR. KLAASEN: The one you have been talking about.

DR. BELSITO: Oh yeah, okay.

DR. SNYDER: Yeah. That was 100 percent applied every day for ten days.

DR. KLAASEN: Yeah.

DR. LIEBLER: That's still surprising.

DR. KLAASEN: That's what I was saying. I mean --

DR. BELSITO: That is weird. I've never heard of animals dying from an ocular study.

DR. KLAASEN: Correct. Usually the worst I've ever seen is blindness.

DR. BELSITO: Yeah.

DR. KLAASEN: Not death. But okay.

DR. SNYDER: Well, if you look at the old report, there is an awful, awful lot of ocular irritation data in that old report. Again, I think that this is (Inaudible) we have one that says only three guinea pigs -- three guinea pigs and three rabbits. It appears to be that there is an irritation issue. (Inaudible) it looks like somewhere around the mid -- 30 percent or more. So I think we can alleviate that with the "when formulated to be nonirritating to the eye."

DR. BELSITO: Yeah. And it may be nice to actually create a table on this and to bring in an italicized version as we do when we're quoting data from the old report -- all of the ocular studies were published or that we referenced in the old report and then these new ones.

DR. SNYDER: We're starting to trickle down a little bit into that -- this not being a no-brainer. I guess this is an add-on. This is the main -- never mind.

DR. BELSITO: Yeah. This is not an add-on. This is something we've already ruled on. So I mean --

DR. SNYDER: Which is pretty intuitive that we reopened because of that increased concentration of use.

DR. BELSITO: Right. That's exactly the reason we reopened.

DR. SNYDER: We need to address it.

DR. ANSELL: So I think it's appropriate to talk about the formulated to be nonirritating based on the data. But in the discussion, we shouldn't conclude or imply that 37 percent directly injected to the eye is equivalent to a cosmetic ingredient which contains 37 percent.

DR. BELSITO: No, I think we can put that in the discussion and say that, obviously, the cosmetic is not intended to be applied to the eye. But given our concerns that there could be, you know, incidental exposure -- accidental exposure to the eye, that we would hope that a cosmetic that was meant to be applied to the eye area would be one where they've looked at ocular irritancy and adjusted pH, or whatever, to avoid that.

DR. ANSELL: Right. Right.

DR. LIEBLER: Yeah. I just think that this is an important enough issue, since it is the reason we reopened the report, that we need lay out the data in a table, including the data that was referred in the previous report, just to indicate -- just to allow us to take one more look, when we look at this, I guess, in September again, to make sure that we can calibrate our assessment and our discussion appropriately. Because I think just saying "formulated not to be irritating," I mean, it basically may be okay. But given the high concentration of use, it pushes us into the toxic range in at least one study. This study with the rats and rabbits dying is very unusual and not toxicologically plausible for this kind of a chemical. So there must have been something else going on. I think it's incumbent on us to look at the full body of available data on tox on these for ocular.

MS. RAJ: Yeah. And I will say that this study is a bit unique with providing the pH values of the samples. I don't think other studies would necessarily provide that. But I'll try to make it as comprehensive as possible -- the table.

DR. LIEBLER: If it's 100 percent dimethicone, it doesn't even have a pH.

DR. BELSITO: Yeah.

DR. LIEBLER: It's nonaqueous.

DR. BELSITO: Okay. A few other points in the document. On PDF page 21 for dimethicone, the new data, "dimethicone when used as a condom lubricant was detectible." I presume it was in blood, but that's not mentioned. Do you see what I'm talking about, Preethi?

MS. RAJ: Yes, I don't think it was in blood, Dr. Belsito. I think they had externally swabbed areas that were in contact with the condom that had the dimethicone on it.

DR. BELSITO: Okay. Well, we just need to clarify where that was detectible.

MS. RAJ: Okay.

DR. BELSITO: And I had a question. Okay. I guess that's answered now -- that I understand that centimeters squared per second is viscosity. It was under the product toxicity oral studies.

DR. HELDRETH: Yeah.

MS. RAJ: And I guess the panel was okay with this notation for viscosities because I think we got a comment from council about that.

DR. LIEBLER: Well, the standard units are pascal-seconds, which is a kilogram per meter per second. So you have a mass -- I mean, you get this. It should be in it. It's not represented here. That may be what they're referring to.

MS. RAJ: Okay.

DR. HELDRETH: You know, we just -- Preethi reported them as we found them, but if you would prefer, we could convert them all to the pascal-seconds if that'd be helpful.

DR. LIEBLER: I think that would be standard usage for viscosity.

MS. RAJ: Thank you. Did you have more comments, Dr. Belsito?

DR. BELSITO: I did, but my screen just went blank. Does anyone else have any other comments while I'm trying to get this all back up here?

DR. SNYDER: I did not.

DR. BELSITO: Okay.

DR. KLAASEN: Fine.

DR. BELSITO: Okay. Here we go. On PDF page 23, it says -- just a clarification, this is on the chronic tox study for dimethicone. It says test article increases in ocular opacities in 300 milligrams of the females and 1000 milligrams, you said, of males and females. I presume that's just of males, correct? Because the females it was three. Or, I guess, was it both sexes at 1000? Okay.

MS. RAJ: Yeah.

DR. BELSITO: Yeah. Fine. My misreading. It must have been late. Okay. So --

DR. SNYDER: Yeah. The better wording for that would be at 300 and greater for females and at a 1000 for males. That would make that more clear.

DR. BELSITO: Okay.

MS. RAJ: Okay. Thank you.

DR. BELSITO: So we're going to add in everything except simethicone. We're going to see if there's any additional data out there for the add-ins. In the discussion, we're going to point out that, while we don't expect the eye makeup to be applied to the eye, we are concerned given the concentration that there could be incidental exposure. So it should be formulated to be nonirritating. We're going to talk about particle size and respiration. And our conclusion will be "safe when formulated to be nonirritating to the eye and the skin." Is that correct?

DR. LIEBLER: Yes.

DR. BELSITO: Does anybody have any wording, particularly for inhalation? Paul, Dan, Curt?

DR. KLAASEN: No.

DR. SNYDER: I mean, if the inhalation toxicity profile was minimal, and we received adequate data to suggest that there's no issue.

MS. RAJ: Was the data from -- I think it was the SCHSC citing the micron sizes and, you know, where it would sit in the respiratory system if inhaled? Would that be language that's useful to bring in?

DR. SNYDER: Yes, because that goes with our boilerplate where the particle size percentages (inaudible) and micron.

DR. BELSITO: Okay. Anything else? Okey-doke.

MS. RAJ: Thank you.

DR. BELSITO: Curt, Paul, Dan, we're all happy?

DR. KLAASEN: Yeah. We're happy.

DR. BELSITO: Okay. Okay. So then we're moving on to pomegranate. Oh, the --

MS. RAJ: There's Tris --

DR. BELSITO: Oh, Tris. Yeah, I keep skipping over that one, Bart, for some reason. And I was fine with all the comments that council made on the methicones. You guys as well?

DR. KLAASEN: Yes.

DR. LIEBLER: Yes.

DR. SNYDER: Yup.

Marks Team – June 8, 2020

DR. MARKS: And Lisa, you're going to be really on the hot spot with this one. Let me bring that up here. Look at Preethi's memo from February 21st.

The Panel first published the safety assessment of dimethicone, methicone, and substituted-methicone polymers in 2003 with a conclusion that these ingredients were safe. At the December 2019 Panel meeting, we were presented with a re-review of these 20 ingredients. There was a significant increase of reported uses -- frequency of use and concentration. And we wanted -- the Panel consensus was to get more data on particle size and distribution, inhalation toxicity. To date, additional data have not been received. What else?

And then, we actually in December felt that we didn't want -- our team felt that we didn't need to reopen, but now we have the issue of adding ingredients as well as dealing with the inhalation toxicity. That was the biggest concern in December. The CIR Science Committee, SSC, and the new Grouping/Clustering Working Group -- that's you, Lisa -- I assume you proposed adding 11 ingredients, including simethicone which is a mixture of silica and dimethicone.

DR. PETERSON: Yeah.

DR. MARKS: My feeling is -- even though that said the silica in simethicone is amorphous silica, is this a no-brainer?

DR. PETERSON: Um, so, yeah.

DR. MARKS: Let's see. So I think the key is the goal posts have changed a little since December because we aren't dealing with the issue of reopening for adding ingredients. And there -- besides the simethicone, there are 11 other ingredients. And then Alex's comments -- here there were comments that I thought our team should address -- is she mentions, should there be limits on other substitutes like carbon chain lengths, saturation, other molecules other than carbon. So actually, things have changed a bit since December.

Does the team want to reopen? Or I shouldn't say reopen; we've already reopened it. Do we want to proceed with adding 10 or 11 ingredients? Are these no-brainers, or do we want to go back to not reopen and deal as, I think, Ron Shank suggested the inhalation toxicity in the re-review discussion? So a lot -- sort of a couple different issues. So Lisa, Ron, and Tom, your comments?

DR. PETERSON: So, if I may add first, both Dan and I didn't feel that the simethicone should be added because of the silica, and there would be questions around that. And in terms of a group, it adds some different concerns than the other ones would have. So my recommendation, which would be probably also Dan's recommendation, is that this simethicone doesn't really belong as part of this group, but the other ones do.

DR. SHANK: I agree. The silicon dioxide has not been reviewed by the Panel, and so I don't think it's a no-brainer to add the simethicone silicon dioxide. The others I guess are okay, but not the -- I would not add the simethicone.

DR. MARKS: I'm trying to get my notes as to what the (inaudible), so there'd be ten that would be added, Lisa, to the draft.

DR. PETERSON: Yeah. I believe so.

DR. MARKS: Where do I have that? I know I put that list in here.

DR. EISENMANN: You have reviewed the -- the silica is the synthetic amorphous silica that you just completed review of.

DR. MARKS: I realize that, Carol. I guess, even though it says that it's amorphous silica and we concluded that amorphous silica would stay safe, to me, it reopened the silica issue all over again. As you can tell, I was a little bit -- I was definitely hesitant about it and, Lisa, you and Dan sounds like reinforce that concern. It's not a no-brainer. Where are the --

MS. RAJ: So it's on page 71 of the PDF. You'll see the PCPC memo with the add-on suggestions.

DR. MARKS: Yeah. Okay. Yeah. Capryl Dimethicone, Hexyl Dimethicone, then the C20-24 goes up the different carbon lengths here. So Lisa, you think these -- in the past when we've added ingredients in a rereview, we used the term "no-brainer" -- that you could take all the data you already have in the report and just add these on and either read across or they would tag along and not require a large discussion as we might have to do as you mentioned with the simethicones. So Lisa, you and Dan were fine that these shouldn't be an issue, and I'll ask that same question to Ron Shank and Tom Slaga. From your viewpoint, these add ons are not an issue?

DR. SHANK: Correct, except for the simethicone.

DR. MARKS: Okay.

DR. SHANK: The others are okay.

DR. MARKS: So there's no question in my mind that it's reopening because we're adding ingredients.

DR. PETERSON: And then, if there's data associated with them, that probably should be added too, right?

DR. SHANK: Pardon me?

DR. PETERSON: If there's data associated with these compounds, that should be added to the report as well.

DR. SHANK: Oh, yes. So we need to handle the inhalation toxicology issue -- aerosols containing 85 percent dimethicone.

DR. PETERSON: And we didn't really get any information about particle size.

DR. SHANK: Right.

MS. RAJ: Well, there was the resource document, I think, from SEHSC. I'm trying to remember. That should be, I think, in the data supplement file.

DR. SHANK: Yes?

DR. PETERSON: The March to June supplement?

MS. RAJ: No, data supplement, June 2020. It's on page 6.

DR. SHANK: I don't remember.

DR. MARKS: Are you talking about within the last week?

MS. RAJ: No, not the last week. This was sent --

DR. MARKS: If it's June 2020, we're talking about in the last couple of days. I don't remember seeing that supplement, but maybe I missed it.

MS. RAJ: No, this was sent in March.

MS. FIUME: That supplement came in the original mailing with the other reports, but the name of it was "data supplement" rather than a report name. It would have been on your original flash drive.

DR. MARKS: Okay. And do you know which page that is for Ron?

MS. RAJ: Page 6. Page 6 of 17. Would it help for me to share the screen?

DR. PETERSON: Yeah. That would be awesome.

DR. MARKS: Yeah. That'd be great because I have 72 pages in the document I'm looking at. So 6 of 17 --

MS. RAJ: Okay. Okay. Can everybody see?

MS. FIUME: No.

DR. SHANK: No. Oh.

MS. FIUME: Yeah. Now we can, Preethi. Now it's there.

MS. RAJ: Okay.

DR. SHANK: Yeah. I have it.

MS. RAJ: Yeah. I was thinking you all could possibly use language from here because -- tell me if there's an area where you'd like me stop but -- it has this diagram here I think towards the end and all this language about like how, if particles are between 10 and 100 micrometers, it shouldn't be deposited.

DR. PETERSON: Yeah. But it doesn't say what size the particles are if they are sprayed out.

MS. RAJ: Hmm.

DR. PETERSON: That was my concern. I've seen -- I understand all this but --

MS. RAJ: Okay.

DR. PETERSON: -- there's no information about with the particular chemicals what size are those particles.

MS. RAJ: Okay. As in for the data we have you mean?

DR. PETERSON: Yeah.

MS. RAJ: Okay.

DR. PETERSON: Because you can't assume -- I am uncomfortable with assuming that it's going to be a certain size. But, you know, there are scientists that measure these things.

MS. RAJ: Yeah. I was thinking you might use some language from here.

DR. PETERSON: But we don't know what size they are. So if we knew what size they were, then we could use the language there. That makes sense to me. But we don't know what the size of the particles are.

MS. RAJ: Okay.

DR. MARKS: So would that be an insufficient data announcement?

DR. BERGFELD: Yeah. I think it would be.

DR. EISENMANN: But the difficulty is you're never going to get particle size for every single product because they're highly variable. I mean, this is the issue we go round and round. You need this information, but it's all dependent on the -- it's not just dependent on this ingredient. It's dependent on the formulation. It's dependent on the product, the spray nozzle. There's a whole lot of variables, and it changes from one -- I mean it's very difficult for me to describe, but it changes with each product.

DR. PETERSON: Yeah. I mean I understand that, but for us to say a blanket statement that it's safe because we think this is what's going to happen because we expect the particle size to be X, Y, and Z, we don't really --

DR. EISENMANN: Maybe we need to say the particle size needs to be X, Y, and Z.

MS. KOWCZ: This is Alex, Lisa. Is it possible to -- to maybe have a range, Dr. Marks, where it would be acceptable to the Expert Panel instead of having a specific micron size, have a range of it?

DR. MARKS: Ron and --

DR. BERGFELD: Dr. Marks, if we're confident less than --

DR. MARKS: Ron, I'm going to rely on you in terms of this is -- obviously, if we're really -- that's an important issue. It probably needs to be in the conclusion. And somehow, you know, just as we say, it does not cause -- formulated not to cause sensitivity. Do we put on something to the effect this does not -- formulated with particle size not to cause inhalation toxicity? Other ways we've handled it is have a robust discussion about the inhalation toxicity.

And I think we're ready to go to a tentative report. It doesn't sound like we're going to get any more data, even though, Lisa, you bring up the issue of the particle size. Carol brings up some in terms of that's probably not going to be the whole story. Do we handle it in a conclusion to alert the formulators or the manufactures, or do we handle it all in the discussion?

DR. PETERSON: Well, there is an inhalation study that basically says there wasn't a problem. I mean, so I only raise the particle size because I think that was something that was requested and as a -- you know, I don't want to go down a rabbit hole, but I have trouble with that statement about, if it's this size, then this. But if we don't know what size it is, I'm not sure that we can argue it's safe in the discussion. But if there's been inhalation testing that shows that it's safe -- and there was one study on page -- it's an inhalation study. It's on the bottom of -- I'll have to get to the page.

DR. MARKS: Actually, Ron suggested in December we just use the inhalation resource document and not reopen it. That was, of course, not taking in consideration the suggestion adding ten more ingredients. But Ron, do you still like that?

DR. SHANK: Yes.

DR. MARKS: You said, if there's an inhalation study to support its safety, and then just deal with the inhalation as we've done in the past with the resource document and don't even mention inhalation in the conclusion?

DR. SHANK: Correct.

DR. MARKS: So Ron Shank, you would be in --

DR. SHANK: Rely on the resource document. It explains very well the role of particle size and solubility and chemical reactivity. So if the methicones are formulated such that they are not respired into the deep lung, it should be a no problem from inhalation.

MR. GREMILLION: Can I -- this is Thomas from CFA. This sounds like just to confirm -- we're saying formulated to be non-respirable is --

DR. MARKS: No, that would be a conclusion. That's what I was talking about, Thomas. We would say it's safe, and then in the discussion before that, we would use the resource document to tell the formulators our position as far as inhalation toxicity. That's how I interpret it. Is that correct, Ron?

DR. SHANK: Yes. Yes.

MR. GREMILLION: I mean, I guess it seems like having it in the conclusion would have the advantage of being a clearer flag on potential respiratory risk.

DR. PETERSON: On the bottom of page 22 is the inhalation study. The mice died, but everybody else is fine.

DR. MARKS: Tom, I haven't heard from you. What's your feelings? Just keep it simple with a safe conclusion, add the ten ingredients, and rely on the inhalation toxicity resource document which would appear in the discussion to further elucidate this? And, of course, Preethi, you would include that -- emphasize out that study of safety that Lisa mentioned.

MS. RAJ: Dr. Peterson, where were you looking again?

DR. PETERSON: It's on the bottom of --

DR. SHANK: It's on page 22.

DR. PETERSON: Yeah, 22.

MS. RAJ: Okay.

DR. PETERSON: It's from the previous report.

MS. RAJ: Okay. Is this the, I guess, short-term tox or --

DR. PETERSON: Well, it was a 28-day study. Yeah, short term.

MS. RAJ: Okay. Thank you.

DR. MARKS: Tom, I don't know whether your speaker works or not -- your mic. Are you okay with proceeding in that manner?

DR. SLAGA: (no audible response)

DR. BERGFELD: I couldn't hear you.

DR. SLAGA: (no audible response)

DR. BERGFELD: (Inaudible)

DR. MARKS: I have a feeling, Tom, you don't have your mic on. Monice, does Tom have his mic muted?

DR. BERGFELD: I can't hear her either.

DR. MARKS: It says muted. Well, Tom, raise your hand if you don't like the conclusion. So I'm going to move tomorrow that a tentative report be issued with safe for all the ingredients including adding the ten new ones. And the exception of that, of course, is we aren't going to include simethicone because of the silica issue. And in the discussion, we'll include the inhalation resource document to emphasize the issues with the inhalation toxicity with these -- the lack thereof. Does that sound good, Ron and Lisa?

DR. SHANK: Yes.

DR. PETERSON: Yep.

DR. SHANK: Yes.

DR. MARKS: And then, Tom --

DR. SLAGA: Yeah.

DR. MARKS: I assume you say yes too?

DR. SLAGA: Yes.

DR. MARKS: Okay. Yeah. I can hear you just briefly. Okay. Any other comments before we finish with these? Okay. If not, okay. We'll move onto the next ingredient or ingredients. Let's see. Tris Citrate.

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DR. MARKS: Okay. Again, I'm working off of two computers and three screens, so I can't exactly -- yeah, I have a lot of comments about this. So, let me see, this is a draft amended report on the safety assessment of Dimethicone, Methicone, and Substituted-Methicone Polymers, from Preethi's February 21st memo. And, in 2003 these ingredients were declared safe by the Panel. And in December 2019, we decided to reopen to review the inhalation toxicity more closely. There was a marked increase in use and concentration since the original report in 2003. And, Paul, if I remember correctly you was particularly concerned about the spray and what the inhalation toxicity might be.

Since that memo, the CIR SCC Committee -- and Lisa and Dan, I don't know if you participate in this new group and clustering working group at that point -- but, it was proposed that 11 ingredients be added including Simethicone. And if you want, I'll read off the other 10 ingredients. Any rate, Simethicone, we had difficulty including as a no-brainer since it's a mix of silica and Dimethicone. And, even though the silica is supposedly amorphous silica, we felt there would be some issues about inhalation toxicity. Even though on Wave 2 there was some clarification about amorphous silica, aerosol formation, particle size, etcetera.

The other ingredients, which were proposed to be added was Capyrl Dimethicone; Hexyl Dimethicone C20-40, 24-28, 26-28, 30-60, and then 32, 20-20 Alkyl Dimethicone, and then Capyrl Methicone, and C20-24 Alkyl Methicone, 26-28 Alkyl Methicone.

Our team felt that we could move forward with an amended tentative report, safe with the added 10 ingredients. And we would rely on the inhalation resource document in the discussion to confirm the safety of these ingredients. So, that's a motion.

DR. BERGFELD: Dr. Belsito, you want to respond?

DR. BELSITO: Yeah, so, we had issues particularly with the ocular toxicity because this is used in products, up to 37.8 percent, around the eye area. And while, of course, they are not meant to be applied to the eye they could accidentally get into the eyes since there are being used around the area. So, we went safe when formulated to be non-irritating -- and this is a new conclusion -- to the skin and the eye.

DR. MARKS: No problem. Do you include the other 10 ingredients?

DR. BELSITO: Yes. And we did not include Trimethicone for the same reason that you brought up.

DR. BERGFELD: So, a friendly amendment to Dr. Marks for (audio skips). Dr. Marks?

DR. MARKS: Yeah, that's fine.

DR. BERGFELD: A friendly amendment then.

DR. MARKS: I'll retract my motion, and I will second Don's motion.

DR. BERGFELD: Okay.

DR. MARKS: Concerning formulated to be non-irritating. And you said that --

DR. BELSITO: To skin and eye.

DR. MARKS: Yes.

DR. BERGFELD: That's new.

DR. MARKS: Yes. Well, the new would also be the 10 ingredients too, adding that. So, again, it would be an amended tentative report for both, for those changes in conclusion.

DR. BERGFELD: Amended tentative. Okay? So, we have a motion that's been seconded, amended tentative conclusion. Any other discussion regarding this motion, or this ingredient?

DR. MARKS: I'll let Lisa, Ron and Tom speak if you have any problems with including the irritation.

DR. SHANK: No problems.

DR. PETERSON: No problems.

DR. SLAGA: No problem.

DR. LIEBLER: I'd like to just point out that this is a good example of what our sort of chemist clustering group, with basically Lisa and I, were able to do here. Council has suggested adding ingredients to the report. They came to us first, via Bart. We both discussed them. We came to a pretty quick consensus, and then we were ready to report back to our teams.

I suggest that if we have any future additional ingredients in a certain situation, that this is a good way to handle it. That way the teams can kind of start off on the same footing with respect to our assessment of the chemistry and the suitability including ingredients. Lisa and I can advise our teams. Teams can come to an appropriate conclusion, in this case we were in sync and that's good.

DR. BERGFELD: (Audio skip) favor of this conclusion of an amended tentative report, raise your hand.

DR. MARKS: You were kind of breaking up, Wilma.

DR. BERGFELD: I am breaking up? All right -- now I'm okay?

DR. MARKS: Yeah, now you're better, but I think we all got the message to vote on Don's motion.

DR. BERGFELD: I didn't see Paul vote.

DR. SNYDER: I'm sorry.

DR. BERGFELD: Okay. Any opposed? None? This is then a final report, unanimous.

MS. RAJ: Excuse me?

DR. BERGFELD: Yes.

MS. RAJ: Sorry, Dr. Bergfeld, may I ask a few questions to the Panel?

DR. BERGFELD: Yes, absolutely.

MS. RAJ: So, I know in the Belsito team you had mentioned creating an ocular irritation table, bringing in data from the old report. I just wanted to clarify is that absolutely necessary?

Because I was told, you know, besides making all the data, I guess, available to the Panel in these reports, when it finally goes to the final stage we'll have to remove the old data anyways. So, I just wanted some clarity on that.

DR. SNYDER: I think what we wanted was in the discussion to talk about the new study where there were rabbits, guinea pig and mice, I think, they were treated and there were some pretty profound ocular results. And, in the old report there was also some positive irritation to the eye at 30 percent, and we have a highest concentration of use at 38 percent. That's why we -- but I think we can capture that in the discussion. I don't think we need to (audio skip).

MS. RAJ: Thank you, Dr. Snyder. And, also, specific language that can be added from the inhalation resource document in the discussion?

DR. SNYDER: Yes, around particle size.

MS. RAJ: Particle size? So, is this referring to particle size distribution in different types of products?

DR. BERGFELD: Paul, did you hear that question?

DR. SNYDER: Yeah, I mean, I guess we normally discuss that in the discussion (audio skip) the particle size, minimize the less than 10 microns, you know, according to the boilerplate.

MS. RAJ: Okay. I just wanted to see if there was anything in particular that is, I guess, different from standard boilerplate that should be added.

DR. SNYDER: I didn't have any thoughts.

DR. BERGFELD: Any other questions or comments then? Have we satisfied you, then, with what you need to do for us?

MS. RAJ: I think so.

DR. BERGFELD: Okay. Thank you.

MS. RAJ: Thank you.

DR. BERGFELD: Thank you for your question. All right, Dr. Belsito, the Sulfites.

Amended Safety Assessment of Dimethicone, Methicone, and Substituted-Methicone Polymers as Used in Cosmetics

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The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; David E. Cohen, M.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; Lisa A. Peterson, Ph.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. Previous Panel member involved in this assessment: James G. Marks, Jr., M.D. The Cosmetic Ingredient Review (CIR) Executive Director is Bart Heldreth, Ph.D. This safety assessment was prepared by Preethi S. Raj, Senior Scientific Analyst/Writer, CIR.

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ABSTRACT

The Expert Panel for Cosmetic Ingredient Safety (Panel) assessed the safety of 30 dimethicone, methicone, and substituted-methicone polymers; 20 of these ingredients were previously reviewed by the Panel, and 10 are reviewed herein for the first time. Most of these ingredients are reported to function as skin and hair conditioning agents. The Panel reviewed relevant new data, including frequency and concentration of use, as well as exposure type, and considered data from the previous report. The Panel concluded that these ingredients are safe in cosmetics in the present practices of use and concentration as described in this safety assessment when formulated to be non-irritating to the skin and eye.

INTRODUCTION

In 2003, the Expert Panel for Cosmetic Ingredient Safety (Panel) published a final report on the safety assessment of 20 dimethicone, methicone, and substituted-methicone polymers.[1] Based on the available data, the Panel concluded that the ingredients named in that report are safe as used in cosmetic products. According to the Cosmetic Ingredient Review (CIR) Procedures, the Panel evaluates the conclusions of previously-issued reports approximately every 15 years. In December 2019, the Panel determined that this safety assessment should be re-opened due to an increase in the overall frequency of use for ingredients in this group. The Panel also determined that it is appropriate to include an additional 10 alkyl dimethicone and methicone ingredients (denoted in red below); the complete family of 30 ingredients comprises:

Amino Bispropyl Dimethicone
Aminopropyl Dimethicone
Amodimethicone
Amodimethicone Hydroxystearate
Behenoxy Dimethicone
C20-24 Alkyl Dimethicone
C20-24 Alkyl Methicone
C24-28 Alkyl Dimethicone
C24-28 Alkyl Methicone
C26-28 Alkyl Dimethicone
C26-28 Alkyl Methicone
C30-45 Alkyl Dimethicone
C30-45 Alkyl Methicone
C30-60 Alkyl Dimethicone
C32 Alkyl Dimethicone
Capryl Dimethicone
Caprylyl Methicone
Cetearyl Methicone
Cetyl Dimethicone
Dimethicone
Dimethoxysilyl Ethylenediaminopropyl Dimethicone
Hexyl Dimethicone
Hexyl Methicone
Hydroxypropyldimethicone
Methicone
Stearamidopropyl Dimethicone
Stearoxy Dimethicone
Stearyl Dimethicone
Stearyl Methicone
Vinyl 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 as skin conditioning agents, hair conditioning agents, and/or viscosity increasing agents.[2] Additional functions are also reported for some ingredients (Table 1).

Excerpts from the summary of the 2003 report are included throughout the text of this re-review document, as appropriate, and are *identified by italicized text.* (This information is not included in the Summary section.) For complete and detailed information, please refer to the original report on the methicone polymer ingredients, which can be accessed on the CIR website (https://www.cir-safety.org/ingredients).

This safety assessments 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 in an European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC) report, on the European Chemicals Agency (ECHA) website, and in Australian Industrial Chemicals Introduction Scheme (AICIS) assessments.[3-7] Please note that most of the toxicology studies described in these documents were summaries, and it is these summary data that are reported when cited in this safety assessment.

CHEMISTRY

Definition and Structure

The ingredients in this report are all siloxane polymers. Each silicone atom is further substituted with hydrogen, methyl, or other substituents (Figure 1). "Methicone" (CAS No. 9004-73-3) means that most of the silicone atoms in the polymer backbone each have 1 methyl group and 1 hydrogen atom, while "Dimethicone" (CAS No. 9006-65-9) means that

most silicone atoms in the polymer back bone have 2 methyl substituents. The remaining ingredients in this report have 1 or 2 of the substituents on the silicone atoms replaced with an alternative functional group (e.g., Hexyl Methicone (CAS No. 1873-90-1) is substituted with hexyl-chains (C6)). The definitions and idealized structures of all the ingredients included in this report are provided in Table 1.

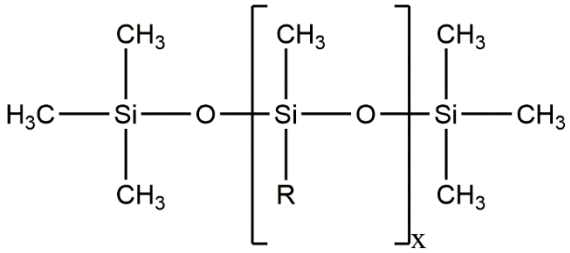


Figure 1. Methicones, wherein R is hydrogen, methyl, or other substituents

The polymerization of linear methicones, however, often results in a mixture of polymers (chains of variable lengths and molecular weights, including oligomers) and cyclic compounds.[8] Dimethicone is a mixture of fully methylated linear siloxane polymers end-blocked with trimethylsiloxy units.[2] Methicone is a linear monomethyl polysiloxane. The other ingredients included in this review are siloxane polymers of Dimethicone and Methicone.

Viscosity is expressed in both dynamic and kinematic measurements, and is directly correlated with molecular weight and the degree of polymerization of a molecule, i.e., the longer the polymer chains, the more viscous the liquid polymer.[3] Most of the viscosities reported in previous and current data have been described in kinematic centistokes (cSt; cm^2/s), and are converted to the standard, dynamic, Pascal*second (Pa·s; kg/m·s), where specific gravity, or relative density, values were available. To do this, the product of centistoke and specific gravity, or relative density, values, was divided by 1000, to attain Pa·s values. Specifically, a median reported relative density value of 950 has been used for the conversion of Dimethicone samples described in the ECETOC report.[3]

Chemical Properties

Dimethicone is a white, almost odorless fluid polymer.[1] Specifications for Dimethicone stated that the color and odor are specified by the buyer. Also specified by the buyer are the refractive index at 25℃ (within the range of 1.4000 to 1.4035), and the kinematic viscosity (provided that the specified mean viscosity at 25℃ is not less than 20 centistokes [cs] and not greater than ± 5% of the specified mean). It contains 98.5% to 101.1% Dimethicone and the total acid number is 0.01 maximum. One supplier of Dimethicone noted that 100 and 350 cs fluids are generally used for cosmetics.

C30-45 Alkyl Dimethicone

C30-45 Alkyl Dimethicone is a an off-white solid, which occurs in small pellets, at standard temperature and pressure.[4] This ingredient has a melting point of 63 - 74 °C and is considered insoluble in water.

Caprylyl Methicone

At atmospheric pressure, Caprylyl Methicone is a liquid at 20 °C, has a melting/freezing point at -20 °C, a boiling point at 263 °C, and a calculated partition coefficient (log P_{ow}) of 9 at 20 °C.[6] This ingredient also has a molecular weight of 335 g/mol, a relative density of 0.84 at 20 °C, a viscosity of 0.0027 kg/m·s at 20 °C, a vapor pressure of 0.64 Pa at 25 °C, and a water solubility of 2.8 x 10^{-5} mg/l.

Hexyl Methicone

At atmospheric pressure, Hexyl Methicone is a liquid at 20 °C, has a melting/freezing point at < -20 °C, a boiling point at 232 °C, and a log P_{ow} > 6.2 at 40 °C.[7] Additionally, Hexyl Methicone has a relative density of 0.83 at 20 °C and a water solubility of 0.011 mg/l at 20 °C.

Method of Manufacture

Stearoxy Dimethicone is produced by the reaction of dichloropolydimethylsiloxane with stearyl alcohol.[1] Dimethicone is produced by polymerization/equilibration. Cetyl Dimethicone is produced by hydrosilylation of C_{16} alpha-olefins. Stearyl Dimethicone is produced by hydrosilylation of C_{18} alpha-olefins.

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

Impurities

One supplier of these ingredients noted that Stearoxy Dimethicone, Dimethicone, Cetyl Dimethicone, and Stearyl Dimethicone contain no antioxidants or preservatives.[1] *Heavy metals are at 5 ppm maximum, and D4/D5 cyclomethicone is at less than 1%.*

C30-45 Alkyl Dimethicone

The Australian National Industrial Chemicals Notification and Assessment Scheme (NICNAS) noted that C30-45 Alkyl Dimethicone can potentially contain residual monomers which are classified as hazardous according to the *Globally Harmonised System of Classification and Labelling of Chemicals (GHS)*.[4] As per Australian chemical manufacturing guidelines, however, these are not present above the cut off concentrations for classification.

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

USE

Cosmetic

The safety of the cosmetic ingredients addressed in this assessment is evaluated based on data received from the US Food and Drug Administration (FDA) and the cosmetics industry on the expected use of these ingredients in cosmetics. Use frequencies of individual ingredients in cosmetics is collected from manufacturers and reported by cosmetic product category in the FDA Voluntary Cosmetic Registration Program (VCRP) database. Use concentration data are submitted by the cosmetic industry in response to a survey, conducted by the Personal Care Products Council (Council), of maximum reported use concentrations by product category.

Frequency and concentration of use has generally increased for these ingredients since they were originally reviewed, with some of the increases being quite significant. According to VCRP survey data, the frequency of use of Dimethicone has increased from 1659 reported uses in 1998 to 14,050 reported uses in 2020, and the number of uses reported for Methicone increased from 0 reported in 1998 to 654 uses reported in 2020 (Table 2).[1,9] Although the overall increase in the reported maximum concentration of use of Dimethicone is not substantial (from 80% to 85%), increases in concentration according to exposure type are notable.[1,10,11] For example, increases in maximum use concentrations of Dimethicone for products resulting in dermal contact increased from 30% in 1999 to 85% in 2019, application to the eye area increased from 13% (in eyebrow pencils) in 1999 to 37.8% (in eyeliners) in 2019, incidental ingestion via lipstick formulations increased from 20% in 1999 to 71.3% in 2019, and incidental inhalation increased from 16% (in perfume sprays) in 1999 to 85% (in moisturizing sprays) in 2019, and from 30% in 1999 to 53% in 2019 for face powders.

Of the recently included ingredients, according to 2020 VCRP data, Caprylyl Methicone has the highest overall frequency of use (234), with 43 reported uses in moisturizing formulations.[9] Also, Caprylyl Methicone has the highest reported maximum concentration of use for the newly added ingredients; it is reported to be used at up to 16% in eye lotions.[12] The 8 ingredients which are not reported to be in use, according to VCRP and survey data, are listed in Table 3.

The ingredients named in this report are not restricted from use in any way under the rules governing cosmetic products in the European Union.[13]

Non-Cosmetic

Dimethicone

The allowable concentration of use of Dimethicone as an active ingredient in the formulation of skin protectant drug products for over-the-counter human use is 1 - 30%. [21 CFR § 347.10] Dimethicone has been used as a physical barrier method of eradicating head lice and eggs.[14,15] Dimethicone use is also prevalent in condom lubricants.[3,16] Dimethicone is also used industrially, in various construction sealants, rubber, and paints.[3]

In 2008, at the Joint Expert Committee on Food Additives (JECFA) of the World Health Organization (WHO), the established acceptable daily intake (ADI) level for Dimethicone of 0 - 1.5 mg/kg was withdrawn due to variability in safety data, and was temporarily replaced with 0 - 0.8 mg/kg, while concerns about ocular toxicity resulting from molecular weight and viscosity-dependent absorption and toxicity were evaluated.[17] As of 2011, the original ADI of 0 - 1.5 mg/kg was reinstated.[17]

TOXICOKINETIC STUDIES

Penetration

Caprylyl Methicone

The dermal penetration of Caprylyl Methicone is deemed unlikely due to a low water solubility and log P_{ow}.[6]

Dimethicone

Penetration of Dimethicone (9.5 kg/m·s and 332.5 kg/m·s) was examined in female human abdominal skin and vaginal tissue.[3] Both viscosities were applied in infinite doses for 96 h to the donor side of split-thickness human abdominal skin sections (reference standard) and full-thickness human vaginal tissue mounted in Franz in vitro diffusion cells. (The identification of the vehicle and receptor fluid was not provided.) The dermal flux rate for Dimethicone (332.5 kg/m·s) in abdominal skin was 0.3 ng/cm^2/h, compared to 2 ng/cm^2/h for vaginal tissue; while the flux rates for Dimethicone (9.5 kg/m·s) in abdominal skin were 0.2 ng/cm^2/h and 6 ng/cm^2/h for vaginal tissue. The authors concluded that there was a low penetration rate, which occurred more rapidly in vaginal tissue, for both viscosities.

In a dermal penetration study, the authors sought to determine if Dimethicone interacts with and alters the stratum corneum lipid microstructure.[18] Excised human stratum corneum tissue samples were obtained from the inner thigh of a healthy 50 yr-old woman and the abdomen of a healthy 26 yr-old man. An in vitro model lipid system containing stratum corneum fatty acids was also used to mimic the skin barrier. These tissue samples were rinsed with 0.001% m/m trypsin inhibitor and stored for 48 h in 76% humidity, at ambient temperature, to achieve an approximately 20% hydration level. The hydrated samples were then treated for 20 min in various viscosities of excess Dimethicone (332.5, 475, 950, or 19,000 kg/m·s) at 37 ºC, removed with a cellulose tissue, and analyzed for change using thermal profile, x-ray diffraction, polarized light microscopy, and transmission electron microscopy. All results indicated that Dimethicone did not disturb or interact with the liquid crystalline structure of the upper layer of the epidermis, and hence is not likely to penetrate the skin barrier.

Absorption, Distribution, Metabolism, and Excretion (ADME)

Several acute pharmacokinetic studies in dogs, rats, and a monkey reported minimal gastrointestinal absorption of Dimethicone and up to 99.99% recovery of the administered dose via excretion.[1] In a repeated dose study, beagle dogs were fed 91% Dimethicone at a dose of 300 mg/kg/d for 120 d in the diet. Although one female showed atrophy of the spleen, and another female had slightly reddened rugae near the stomach and mucus in the intestine, Dimethicone was not detected in any organs or considered absorbed.

Animal

Dimethicone

In a study examining dermal absorption and distribution, an occlusive patch containing [^{14}C]Dimethicone (332.5 kg/m·s) was applied to male CD rats (number not provided) for 24 h.[3] After the initial 24-h exposure period, animals were removed from the metabolism cages, the occlusive patch was removed, and the exposure site was washed. The animals were re-wrapped with a non-occlusive bandage and returned to metabolism caging for continued monitoring and collection of biologic samples. The animals were killed 72 h after their initial exposure and the exposure sites were carefully excised. Radioactivity tracing demonstrated that 70% of the administered dose was found on the patch materials, 11.4% was present at the site of application, and none was found in the blood. Minimal amounts were found in the feces (0.01%) and carbon dioxide traps (0.001%).

Human

In human studies, absorption was seen in humans following ingestion of a Dimethicone sample containing low-molecular-weight polymers.[1] Dermal upper back exposure to Dimethicone for 10 d did not increase blood or urine silicone concentrations in men.

Caprylyl Methicone

According to an estimated blood:air partition coefficient of 1.7 x 10^{-4}:1 for human inhalation, systemic circulation of Caprylyl Methicone is not likely.[6] Based on an algorithm, the soluble fraction of Caprylyl Methicone in the blood is << 1%, suggesting the minimal likelihood of this ingredient being excreted in urine as water soluble metabolites.

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

Dermal

The dermal LD_{50} for Dimethicone was > 2000 mg/kg in rats and rabbits.[1] The dermal LD_{50} for Methicone was > 20 ml/kg in rabbits. The dermal LD_{50} for Vinyldimethicone was > 16 ml/kg in rabbits.

C30-45 Alkyl Dimethicone

An acute dermal exposure study with C30-45 Alkyl Dimethicone was performed, in rats, according to the US Toxic Substances Control Act (US TSCA) [40 CFR § 798.1100] Test Guideline (TG).[4] The LD_{50} in rats was reported to be > 2000 mg/kg bw.[4] (No further details, including viscosity, were provided.)

Caprylyl Methicone

In an acute dermal exposure study, performed in accordance with Organization for Economic Cooperation and Development (OECD) TG 402, undiluted Caprylyl Methicone was tested on 5 male and 5 female Wistar rats at a dose of 2000 mg/kg bw.[6] The test substance was spread over approximately 10% of the back area, and covered with an occlusive dressing for 24 h. Test sites were rinsed with water at the end of the application period; animals were examined daily for 14 d, before necropsy. No mortality or signs of systemic toxicity were observed. The dermal LD_{50} of Caprylyl Methicone was determined to be > 2000 mg/kg bw in rats.

Dimethicone

A single, 2008 mg/kg bw dermal application of Dimethicone (332.5 kg/m·s) was made on 5 male and 5 female Sprague Dawley (SD) rats, in accordance with the OECD TG 402.[3] The test substance was spread over approximately 10% of the total body surface and was held in place with a bandage for 24 h. Test sites were rinsed with lukewarm water at the end of the application period; animals were monitored for mortality and clinical signs for 14 d, before necropsy. No mortality or noticeable abnormalities were observed. The dermal LD_{50} in this study was determined to be > 2008 mg/kg bw.

Undiluted Dimethicone (54,150 kg/m·s) was applied to the shaved backs of 5 male and 5 female adult New Zealand White rabbits at a dose of 2000 mg/kg bw.[3] The test site was occluded and Dimethicone was in contact with the skin for 24 h. After exposure, the residual test material was removed with Dimethicone (332.5 kg/m·s)-moistened gauze. The rabbits were frequently observed on the day of treatment, and at least once a day during a 14-d observation period. No signs of systemic toxicity were observed during the study, and no rabbits died during this study. Under the conditions of this study, the acute LD_{50} of Dimethicone in adult male and female rabbits was considered to be > 2000 mg/kg bw.

Oral

Dimethicone, Methicone, and Vinyldimethicone were not acutely toxic following oral exposure.[1] Methicone had an oral LD_{50} of > 64 ml/kg in male albino rats. Vinyldimethicone had an oral LD_{50} of > 16.0 ml/kg in Sprague Dawley rats. Greasy-textured fur was noted in the rats, while one rat had pneumonia and pleuritis observed at necropsy.

Caprylyl Methicone

In accordance with OECD TG 423, 3 female Wistar rats were administered a single dose of 2000 mg/kg bw Caprylyl Methicone, via gavage.[6] No signs of systemic toxicity were observed over the course of a 14-d post-dose observation period. An expected increase in body weight was observed in all animals, none died prior to necropsy, and no gross pathological changes were observed. The acute oral LD_{50} of Caprylyl Methicone was determined as > 2000 mg/kg bw in female rats.

Dimethicone

Five male and 5 female Sprague-Dawley rats were administered a single dose of 2000 mg/kg bw Dimethicone (57,000 kg/m·s) in corn oil by gavage.[3] No overt signs of systemic toxicity were observed over the course of a 14-d post-dose observation period. All of the rats gained weights, no animals died during the study, and no gross necropsy lesions were observed. The acute oral LD_{50} of Dimethicone in male and female rats was determined as > 2000 mg/kg bw.

Inhalation

Two dogs, 7 guinea pigs, and 7 rats were exposed to a "200 fluid" aerosol of Dimethicone at a concentration of 2.12 mg/l for 6 h.[1] Three guinea pigs died during the study, and all necropsied animals had hyperemic lungs with hemorrhagic areas. Vapor exposure to Methicone, at a concentration of 0.78 mg/l for 8h, and Vinyldimethicone, at a near-saturation concentration (no further details provided) for 6 h, did not cause mortality or lesions in rats. Aerosolized Hexyl Methicone was administered by whole-body inhalation exposure to Fischer F344/N rats for 4 h, at varied target doses ranging from 1.0 mg/l - 5.0 mg/l with particles having a mass median aerodynamic diameter (MMAD) of 0.27µm - 0.29µm. All rats exposed to the 5.0 mg/l dose (0.27 µm MMAD) died, while a portion died at the other doses. Lesions at necropsy of the rats who died included dark red or mottled lungs and/or fluid filled trachea. The calculated LC_{50} for both sexes was 1.8 mg/l.

Dimethicone

An acute aerosol inhalation study of Dimethicone (95,000 kg/m·s)was performed in a similar fashion to OECD TG 403.[3] Groups of 5 Wistar rats were exposed for 4 h, nose-only, to solutions of 25% Dimethicone dissolved in petroleum ether, or to two other solvents in separate control groups (control solvents not named). Rats were exposed to mean Dimethicone concentrations of 4315 mg/m^3 at a MMAD of 1.55 µm, or 11,582 mg/m^3 and a MMAD of 0.846 µm. During, and after, the 14-d observation period, no mortality or clinical symptoms were attributed to Dimethicone exposure. The LC_{50} was determined to be > 11,582 mg/m^3.

Dimethicone (9500 kg/m·s) dissolved in dichloromethane was used to perform an acute aerosol inhalation toxicity study, in accordance with OECD TG 403.[3] Groups of 5 Wistar rats were tested with concentrations of either 153.3, 322.0,

445.6, or 694.8 mg/m^3 Dimethicone, with a MMAD up to 1.8 µm. Duration of exposure was not provided; however, according to OECD TG 403, exposure can be up to 6 h (nose-only) in rats. No mortality or toxic effects were observed during the 14-d observation period or at necropsy. The LC_{50} was determined to be > 695 mg/m^3.

Short Term Toxicity Studies

Dermal

No adverse reactions were found in rabbits following short-term dermal dosing with 6% to 25% Dimethicone.[1] Rats were dermally dosed with either 0.04% Dimethicone (18.92 kg/m·s), or a solution containing 5% each of four linear/cyclic dimethylpolysiloxanes for 4 wk. No macroscopic changes were noted. Changes were seen in serum total cholesterol concentrations, and dermal dosing resulted in less silicon accumulation in the fat when compared to oral administration.

Dimethicone

Three groups of 10 New Zealand white rabbits (number per sex not specified) were dermally administered Dimethicone (332.5 kg/m·s) via an occlusive patch for 4 wk (28 d) at doses of 0, 100, 300, or 1000 mg/kg/d.[3] On a daily basis, rabbits were examined for dermal irritation prior to application, and were exposed to the test material for 6 h prior to patch removal. Body weight was measured twice a week, and blood samples were taken for hematology and blood chemistry evaluations on day 29 for males and day 30 for females. No deaths or adverse events related to the treatment occurred. Body weight, hematology, blood chemistry, and gross and microscopic evaluation of selected organs showed no changes that were considered of toxicological significance. The no-observable-adverse-effect-level (NOAEL) for dermal application of Dimethicone in rabbits in this study was therefore considered to be 1000 mg/kg/d.

Oral

Mongrel dogs were fed with up to 3.0 g/kg/d of 83% Dimethicone for 12 wk.[1] The liver of dosed dogs had bile pigment deposits in Kupfer and hepatic cells, which were proportional to the daily dose received.

Caprylyl Methicone

Seven groups of 10 male and 10 female Crl: WI (Han) rats were dosed with 0, 100, 300, or 1000 mg/kg bw/d Caprylyl Methicone, in corn oil, by gavage, for 28 d.[6] Four recovery groups of 5 male and 5 female rats were selected from the control and 1000 mg/kg bw/d group, to be observed for 14 d after exposure. No mortality or clinical abnormalities occurred during observation. An elongated mean activated partial thromboplastin time in the 1000 mg/kg bw/d males became similar to controls at the end of the recovery period. A statistically significant lower red blood cell count in the 300 mg/kg females, an absent pupillary reflex and white stain on the eye of a 100 mg/kg male, slight vacuolation in the adrenal glands of 1 male each from the 100 mg/kg and 1000 mg/kg groups, and 2 males from the 1000 mg/kg/d recovery group, and a statistically significant minimal increase in the liver weights of 300 and 1000 mg/kg females, were all considered unrelated to treatment or toxicologically irrelevant. The reported NOAEL of Caprylyl Methicone was determined to be > 1000 mg/kg bw/d.

Eight groups of 10 male and 10 female Sprague-Dawley rats were dosed with 0, 500, 1000, or 5000 mg/kg bw/d Caprylyl Methicone, via gavage, for 28 d.[5] Two females treated with 500 mg/kg bw, 1 male and 2 females treated with 1000 mg/ kg bw, and 3 males and 1 female treated with 5000 mg/kg bw died prior to sacrifice. The unscheduled animal deaths were attributed to aspiration of the test substance, and not the test substance itself. Besides dark, mottled, and congested lungs, enlarged livers, and sores, alopecia, and rough, stained fur in the posterior regions of animals in the 5000 mg/kg bw group, no statistically significant differences were observed in the laboratory and clinical findings. Statistically significant lower mean organ and body weights were only observed in 5000 mg/kg bw males and females; organ to brain weight ratios of the treated groups were not significantly different from controls. The NOAEL was determined to be 1000 mg/kg bw/d and the no-observed-effect-level (NOEL) was deemed to be 500 mg/kg bw/d.

Dimethicone

In a 28-d oral toxicity study, Dimethicone (9.5 kg/m·s and 332.5 kg/m·s) was administered to groups of 10 CDF-(F344)-CrlBr rats in the diet, at concentrations of 10,000 to 100,000 ppm (1 - 10%).[3] No mortality or adverse clinical signs of toxicity were noted during observation or upon necropsy. Test article related symptoms consisted of dose-related increase in matting of male and female rat fur, increased incidence of corneal opacity and inflammation, and significantly decreased mean triglycerides and low-density-lipoprotein levels (LDL) at higher doses (≥ 2.5%). These symptoms were not regarded as adverse effects and the NOAEL of Dimethicone in the rat diet was determined to be > 100,000 ppm.

Inhalation

A cat, rabbit, guinea pig, 2 rats, and 4 mice were sprayed for 4 h with an atomizer containing 10 ml/kg of a sample of Dimethicone (140 cm^2/s; dynamic viscosity or specific gravity values were not available) for 29 d.[1] During the 6-wk post-dosing observation period, no exposure-related adverse effects were seen in the cat, rabbit, guinea pig, and rats. All 4 mice

died – one after the 20th exposure, and the 3 others during the post-dosing period. The link between treatment and death was uncertain and the authors concluded that Dimethicone inhalation is harmless.

Subchronic Toxicity Studies

Oral

Mice and rats were dosed for 90 d with up to 10% Dimethicone, via diet. [1] *No signs of systemic toxicity were seen during the study or during post-study pathologic examination. Anal leakage of Dimethicone was detected in the high dose groups and in those rats that were fed more viscous Dimethicone. Observations of slight chronic corneal inflammation, opacity, and neovascularization was observed in the eyes of the rats, regardless of dosage, and was regarded as a local ocular effect resulting from contact with the feed. In another rat study, in which animals were fed an antifoam compound containing 0.1%, 0.3%, or 1.0% Dimethicone for 120 d, changes in body weight or spleen weight were observed in the 1.0% Dimethicone dose group.*

Chronic Toxicity Studies

Oral

No significant differences were observed in the organ weights of Wistar rats that were fed 0.3% Dimethicone in the diet for 2 yr, compared to controls.[1] *Upon pathologic examination, pulmonary lesions, changes in the ovaries and uterus, and mild fatty changes in the liver and tubular epithelium of the kidneys was observed in all treated rats. Rats and rabbits which were fed 1% Dimethicone in the diet (50 or 350 cm^2/s; dynamic viscosity or specific gravity values were not available) for up to 1 yr did not exhibit signs of systemic toxicity.*

Dimethicone

Four groups of 30 male and 30 female Fischer 344 were administered Dimethicone (9.5 kg/m·s) in the diet at doses of 0 (control), 100, 300, or 1000 mg/kg bw/d for 12 mo.[3,19] Four groups of 10 males and 10 females from each treatment group were necropsied after 12 mo of Dimethicone administration. The remaining animals (20 male and 20 female rats from each group) were observed for chronic recovery for 12 mo after the 12-mo treatment period. Test article-related toxicological effects in necropsied rats were limited to increased incidence of ocular opacities in ≥ 300 mg/kg bw/d females and 1000 mg/kg bw/d males. Similarly, in the chronic recovery group, there was an increase in eye opacity for all treated male groups, without dose correlation. This result was further supported by microscopic findings of keratitis and corneal dystrophy. The NOEL for systemic toxicity of Dimethicone was determined to be equal to the highest tested dose, 1000 mg/kg bw/d.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY (DART) STUDIES

Dimethicone was tested in numerous oral-dose (using rats) and dermal-dose (using rats, rabbits, monkeys) reproductive and developmental toxicity studies.[1] *In an oral study with rats, 3.3 ml/kg/d Dimethicone was administered directly to the stomach for 6 d. Males treated with 1 of 3 Dimethicone samples (no further details provided) had significantly decreased body weight and/or decreased testes or seminal vesicles weights. No treatment-related adverse findings were noted in pregnant females or fetuses, dosed orally, via diet, and dermally. In an intergenerational study, a motor oil containing an unspecified amount of Dimethicone was applied undiluted in doses of 0.1, 0.4, and 1.5 ml/kg, to the shaved backs of the parental (P_1) and first generation (F_1) of Sprague-Dawley rats, daily for an 8-wk premating period, 3-wk mating period, and throughout gestation and lactation. Mortality was significantly increased on day 0 in the 0.4 ml/kg group, and absolute testes weight was significantly reduced in the adult F_1 male rats of the 1.5 ml/kg group, beginning wk 7, but the relative testes to body weight ratio was not significantly different from controls.*

Caprylyl Methicone

Seven groups of 10 male and 10 female Crl: WI (Han) rats were dosed with 0, 100, 300, or 1000 mg/kg bw/d Caprylyl Methicone, in corn oil, by gavage, for 28 d.[6] The animals were cohoused to facilitate impregnation, after a minimum of 14 d of exposure, for a maximum time period of 14 d. Fertility and conception parameters were not affected and no maternal abnormalities were observed; no changes or differences in fetal or pup body weights, number of live offspring, sex ratios, litter size, and skeletal, visceral, or external malformations were observed. The NOAEL for Caprylyl Methicone maternal toxicity and developmental effects was determined to be > 1000 mg/kg bw/d.

GENOTOXICITY STUDIES

Dimethicone tested negative for genotoxic effects in multiple Ames tests, at up to 5000 µg/plate, bacterial reverse mutation assays, at up to 79% in formulation, micronucleus tests, at up to 5 g/kg, and in mouse cell and Chinese hamster ovary (CHO) assays, at up to 10,000 µg/ml, both with and without metabolic activation.[1]

In Vitro

C30-45 Alkyl Dimethicone

A bacterial reverse mutation assay was performed with C30-45 Alkyl Dimethicone in accordance with OECD TG 471.[4] The test substance was found to be non-mutagenic. (No further details were provided.)

Caprylyl Methicone

In accordance with OECD TG 471, *Salmonella typhimurium* strains TA97s, TA98, TA100, TA102, and TA 1535 were tested with up to 5 mg/plate Caprylyl Methicone (in ethanol), in a bacterial reverse mutation assay, in the presence and absence of metabolic activation.[6] No precipitates or cytotoxicity were observed and the test substance was determined to be non-mutagenic to bacteria, under these study conditions.

Dimethicone

S. typhimurium strains TA98, TA100, TA1535, TA1537, and *Escherichia coli* strains WP2 uvrA and WP2 uvrA (pKM 101) were tested with Dimethicone (57,000 kg/m·s) in a bacterial reverse mutation assay, in the presence and absence of metabolic activation.[3] The assay was performed in two stages, in which a range-finding study, and consequent initial and independent repeat assays were used to evaluate the mutagenic potential of Dimethicone. Based on the toxicity assay, the maximum dose tested was 5000 µg per plate. Although precipitate was observed at ≥ 500 or at ≥ 1500 µg/plate, no appreciable toxicity was observed; Dimethicone was considered non-mutagenic under these study conditions.

In Vivo

Caprylyl Methicone

Groups of 5 ICR mice were intraperitoneally dosed with 0, 1253, 2505, or 5010 mg/kg bw Caprylyl Methicone, or given 80 mg/kg bw of cyclophosphamide (positive control) via gavage, in a mammalian erythrocyte micronucleus test.[5,6] Bone marrow cells were harvested 24, 48, and 72 h after dose exposure. No significant increase in the micronucleated polychromatic erythrocytes (PCEs) was observed in any of the test animals at all harvest times. Caprylyl Methicone was deemed non- genotoxic under the conditions of this study.

CARCINOGENICITY STUDIES

Dimethicone tested negative for carcinogenicity in both an oral (up to 2.5% Dimethicone in diet for 76 wk) and a dermal carcinogenicity study (lifetime application; 50 µl of the test article (motor oil) that contained an unspecified amount of Dimethicone) using mice.[1] One treated mouse in the dermal study had a palpable skin mass at the application site during wk 65, which regressed by wk 67; no application site dermal neoplasms were microscopically confirmed in either treated or control mice.

Dimethicone

The carcinogenic potential of a silicone resin containing 92% Dimethicone and 8% silica (300-1050 cm^2/s; dynamic viscosity or specific gravity values were not provided) was evaluated using groups of 50 male and 50 female F344/DuCrj rats.[20] The rats were given diets containing 0, 1.25, or 5.0% of the test article for 104 wk. Animals were monitored twice daily for signs of toxicity, and body weight was measured alternate weeks. During the study, there were no significant differences in appearance or behavior between the control and treatment groups. Survival rates were also not significantly different between both groups. The relative organ weight percentage for livers in male rats that received 5.0% test article in the diet were significantly lower than those of the livers in male control rats. Lower relative kidney, brain, and heart organ weight percentages were also considered to be statistically significant in treated female rats compared to female control rats. There was a statistically significant, 2 - 18%, increase in the incidence of parafollicular cell (C-cell) adenomas in female rats within the highest dose group (5.0%); however, according to previous carcinogenic assays done by the National Toxicology Program, the naturally occurring incidence of C-cell adenomas ranges from 0 - 34%. The males of the 5.0% dose group experienced a decreased incidence of prostate cancer (8% vs. 22% in controls); however, values for prostatic intraepithelial neoplasias (PINs) were similar across groups. The prostate cancer incidence of the control group was relatively high (compared to historical results elsewhere); thus, the difference between treatment and control groups were considered incidental.

In a long-term toxicity study, 3 groups of 20 male and 20 female F344 rats were observed for oncogenic effects associated with oral administration of Dimethicone (9.5 kg/m·s) at doses of 100, 300, or 1000 mg/kg bw/d for up to 24 mo.[19] Slightly increased incidence of corneal opacity was observed in male rats dosed at 1000 mg/kg bw/d and in female rats dosed at 100 and 1000 mg/kg bw/day, as well as an overall increase in minimal to mild keratitis in all male and female rats (statistical significance not mentioned). A statistically significant increase in the incidence of islet cell adenomas was observed in the 100 mg/kg bw male dose group; however, the lack of an effect in female groups, and high incidence of islet cell adenomas in controls (even when assigned to recover for 12 mo), suggested that that these effects were independent of

Dimethicone exposure. No neoplastic changes were observed and the NOEL for oncogenicity of Dimethicone was determined to be 1000 mg/kg bw/d.

OTHER RELEVANT STUDIES

Immunotoxicity

Dimethicone

Four groups of 20 female A.SW (*H-2^s-T18^b-/SnJ*) mice received a single 0.5-ml intraperitoneal (i.p.) injection of one of the following: phosphate-buffered saline (PBS) as the negative control, pristane (2,6,10,14-tetramethylpentadecane) as the positive control, silicone gel (taken from a mammary implant), or Dimethicone (970 kg/m·s).[21] A pretest bleed was taken via orbital puncture prior to injection, after which blood samples were obtained post-injection once a month for 6 mo. The mice were killed after 6 mo of observation, and peritoneal macrophages were collected by lavage. Additionally, immuno-precipitation, fluorescent antinuclear antibody (FANA) microscopy, macrophage culture, kidney pathology, and enzyme-linked immunosorbent assay (ELISA) immunoglobin analyses were performed. Although Dimethicone-treated mice did not produce lupus-associated antinuclear antibodies (observed only in positive controls) various antibody isotopes were observed within 2 mo of injection. Immunoglobulin M (IgM) levels remained elevated compared to controls, and IgG1 and IgE serum levels were significantly elevated at 4 mo in comparison to 5 - 6 mo for the controls. Macrophages from negative control mice secreted little interleukin-6 (IL-6), a pro-inflammatory cytokine, while pristane-, silicone gel-, and Dimethicone-treated mice spontaneously secreted IL-6 and also produced greater, dose-dependent amounts of IL-6 when cultured with lipopolysaccharide. Suspected silicone droplets and expanded vacuoles within the glomeruli of treated mice kidneys also indicated capacity for systemic accumulation.

DERMAL IRRITATION AND SENSITIZATION STUDIES

Irritation

Most dermal irritation studies using rabbits classified Dimethicone as a minimal irritant.[1] Studies that scored reactions according to the Draize scale reported primary irritation indices of ≤ 2.8(with test samples containing 5% to 100% Dimethicone). Vinyl Dimethicone was not irritating to rabbits following a 4-h exposure.

Animal

C30-45 Alkyl Dimethicone

A skin irritation test using C30-45 Alkyl Dimethicone was performed in rabbits, in accordance with US TSCA [40 CFR § 798.4470].[4] The test substance was determined to be non-irritating. (No further details were provided).

Caprylyl Methicone

In a skin irritation test, performed in accordance with OECD TG 404, 0.5 ml Caprylyl Methicone was applied neat for 4 h under semi-occlusion to a 25 cm^2 patch of closely shaven skin of 3 female New Zealand white rabbits.[6] After patch removal, the exposure sites were washed with water and scored using the Draize scale for up to 72 h. No signs of irritation were observed in any of the animals, and the test substance was deemed non-irritating.

In a dermal toxicity study, also performed in accordance with OECD TG 404, 3 male and 3 female New Zealand white rabbits were exposed to an occlusive application of 97%, undiluted Caprylyl Methicone (dose not specified).[5] No deaths or clinical signs were noted during the study period. Minor erythema was observed in 4 rabbits within 1 h following the contact period, but had subsided within 24 h in 3 of the 4 animals and 48 h for the last animal. Minor edema was apparent in 1 animal within 1 h, but subsided by 24 h. Desquamation developed in 1 rabbit after 7 d of testing; no other signs of irritation were observed, and the test substance was deemed slightly irritating to the skin.

Dimethicone

Three rabbits and 3 guinea pigs were exposed to non-occlusive, daily applications of 0.5 ml of Dimethicone (100 cm^2/s; dynamic viscosity or specific gravity values were not provided) to a 2.5 cm^2 patch of closely shaven skin for 10 d.[22] No erythema or signs of skin irritation or inflammation were noted in the animals.

In an acute dermal toxicity study, undiluted, Dimethicone (57,000 kg/m·s) was applied to the shaved backs of 5 male and 5 female adult New Zealand White rabbits, under occlusion, for 24 h, at a dose of 2000 mg/kg bw.[3] Erythema was observed at the application site in all 10 rabbits, but resolved by the 7th day of observation.

Sensitization

Dimethicone (tested undiluted and at 79%) was not a sensitizer in 4 assays using mice and guinea pigs.[1] It was not a sensitizer at 5.0% in a clinical HRIPT using 83 subjects.

Animal

Caprylyl Methicone

The sensitization potential of Caprylyl Methicone was evaluated with a Buehler test, according to OECD TG 406.[6] During induction, 20 male guinea pigs were patched with 100% Caprylyl Methicone (in acetone) once a week, via 6-h occlusive patches, for 3 wk. After a 2-wk rest period, a one-time, challenge application of 0.75% Caprylyl Methicone (in acetone) held in place by an occlusive dressing for a 6-h exposure period was made. Two groups of 10 guinea pigs served as the negative and positive control groups. The test article was not a sensitizer.

In a guinea pig maximization test (number of animals not specified), intradermal injections of Freund's Complete Adjuvant/saline (1:1), with and without 5% Caprylyl Methicone, did not cause ulceration of the injection sites and was well-tolerated.[5] During topical induction, administration sites treated with 5% Caprylyl Methicone showed minor dermal irritation, however, sites treated with 5% Caprylyl Methicone in mineral oil did not show signs of irritation. Challenge applications were made with 5% Caprylyl Methicone in mineral oil, and were observed at 24 and 48 h after patch removal (occlusion not specified). No dermal reactions were seen in either the test or control groups, and the test substance was deemed a non-sensitizer.

Dimethicone

Five groups of 8 female B6C3F1 mice were tested for contact hypersensitivity to Dimethicone.[23] Dimethicone was determined to be a non-irritant during a primary dermal irritancy study, and was applied undiluted during both the induction and challenge phases. Eight induction applications of either saline, Dimethicone (dose not specified), acetone/olive oil, or 0.5% 1-fluoro-2,4-dinitrobenzene, in acetone: olive oil, were made to a 0.5 cm^2 shaved and debrided region of the upper back. After a 6-d rest period, mice were injected with 0.2 ml of 125-iododeoxyuridine to measure radioisotopic hypersensitivity. Challenge applications were made 7 d after the rest period to the left ear using a cotton swab, and mice were examined for contact hypersensitivity via the mouse ear swelling test (MEST) for 2 d. All mice, except for 8 treated with Dimethicone, were killed after the first MEST; after 7 d, the surviving mice, and an additional 8 mice were tested in a second MEST. No statistically significant hypersensitivity was observed in the mice sensitized with Dimethicone, from the radioisotopic or MEST measurements. Subsequent challenge of previously sensitized mice also did not produce any change in the occurrence of ear swelling, and the test substance was determined a non-sensitizer.

Human

Dimethicone

In a human repeat insult patch test (HRIPT), Dimethicone (11,875 kg/m·s) was tested neat as a negative control, and was used as a vehicle for a 5% (v/v) solution of an unspecified test substance.[3] Sodium lauryl sulfate (0.1% aqueous solution) was used as a positive control. Of the 115 subjects enrolled, 106 completed the study; no subjects withdrew due to adverse reactions to the test substance. Induction consisted of 9 consecutive applications, where 0.2 ml of Dimethicone was applied under a semi-occlusive dressing for 24 h. The test sites were evaluated in the following 48 - 72 h. After the 9th application, there was a 10 to 15-d non-treatment period. Challenge occurred in the sixth week of the study; the substance was applied to an unexposed site for 24 h, and graded after 24 - 48 h. No evidence of sensitization to Dimethicone, as a control or vehicle, was observed.

OCULAR IRRITATION STUDIES

Most ocular irritation studies using rabbits classified Dimethicone, ranging in concentration from 10% to 35%, as a mild to minimal irritant.[1] The most common finding was a conjunctival reaction. However, instillation of 0.005 ml 15% Dimethicone produced minor to moderate conjunctival irritation in all 6 rabbits; the irritation cleared in 5 of the 6 rabbits within 72 h. Additionally, a few studies reported conjunctival reactions, chemosis, and persisting redness, especially when the eyes were unrinsed. Similar to Dimethicone, Methicone and Vinyldimethicone also produced conjunctival reactions.

C30-45 Alkyl Dimethicone

The ocular irritancy potential of C30-45 Alkyl Dimethicone was testedin rabbits, in accordance to US TSCA [40 CFR § 798.4500].[4] Slight conjunctival effects were observed, but resolved within 24 h of exposure. The test substance was determined to be non-irritating. (No further details were provided).

Caprylyl Methicone

In an ocular irritation study, performed in accordance with OECD TG 405, 3 female New Zealand white rabbits were treated with 0.1 ml Caprylyl Methicone in one eye for 24 h (the second eye serving as control).[6] The treated eyes were thoroughly washed with saline after 24 h, and were examined at 1, 24, 48, and 72 h post-application. A 0.01% fluorescein-sodium solution was used to examine the treated eyes for corneal lesions at 24 and 72 h. Dilated blood vessels were observed

in 2 of the 3 animals, as well as colorless eye discharge with moistening of the lids 1 h after instillation. All signs of irritation disappeared within 24 h of treatment, and the test substance was deemed not irritating to the eye.

In a similar study, also performed in accordance with OECD TG 405 (dose not specified), 3 male and 3 female New Zealand white rabbits did not exhibit corneal injury or iritis.[5] Minor conjunctival redness and minor (in 5 animals) to moderate (in 1 animal) ocular discharge occurred in all rabbits. Ocular irritation subsided within 24 h in 5 animals, and 48 h in the last animal. The test substance was deemed slightly irritating to the eye.

Dimethicone

Sixteen adult pigmented rabbits were tested for corneal tolerance of Dimethicone.[24] One eye of each animal was treated (the other eye served as a control) by forming a hanging suture in the lid which allowed 0.7 - 1.0 ml of generically produced, as well as medical-grade, Dimethicone at varying viscosities (485 - 12,125 kg/m·s) to remain on the eye for 3 - 6 h. Medical-grade Dimethicone (970 kg/m·s), which is produced with higher manufacturing, biocompatibility, and safety standards for use in pharmaceuticals and medical devices, was included to assess if it would elicit a variable eye irritation response. The oil was only replaced if the eye cup leaked or if the animal moved. The eyes were examined with fluorescein by slit lamp immediately after treatment, and were either enucleated immediately or 3 - 7 d later. Compared to the control eye, which was treated with a saline balanced salt solution, the eyes treated with Dimethicone exhibited increased epithelial and whole corneal thickness, which persisted for several days and was most noticeable ≥ 3 d post-treatment. Although there appeared to be better ocular tolerance for the medical-grade Dimethicone, it also caused some corneal changes; under light microscopy, all eyes treated with Dimethicone showed various degrees of intracellular epithelial and stromal edema. The authors concluded that both non-medical grade and medical-grade Dimethicone are mildly irritating to the corneal epithelium.

The ocular irritancy of Dimethicone was evaluated in a study using groups of either 3 mice, 3 guinea pigs, or 3 rabbits to test 5 separately-manufactured samples of Dimethicone (100 cm^2/s; dynamic viscosity or specific gravity values unavailable).[22] For the test, a drop of Dimethicone was instilled once daily for 10 d into the lower eyelid of the animals, and conjunctival irritancy and reflex response to light and touch were observed for 15 d. The first sample did not produce inflammation or ocular opacity; however, all tested guinea pigs died by day 8 - 10. The second sample caused inflammation in the eye of one rabbit after 10 d, while 2 guinea pigs and 1 rabbit died. The eyes of animals treated with the second sample were also opaque. No adverse effects were observed in the eyes of the rabbits or guinea pigs treated with 3 remaining samples; the researchers opined that the ocular irritancy and inflammatory effects of silicone fluids may be dependent upon the acidity of the samples.

MUCOUS MEMBRANE IRRITATION STUDIES

A mucoadhesive paste (53% Dimethicone) was introduced (0.5 g) via syringe into the vaginal cavity of 6 albino rabbits.[1] Two control rabbits were dosed with a sodium chloride solution. Tissue was scored according to the Draize scale (maximum score of 8) at 24, 48, and 72 h post dosing. Erythema was noted in 3 rabbits at 24 h, and in one rabbit at 48 h after treatment. None had erythema at 72 h. No edema or signs of toxicity were observed. The irritation score for the paste was 0.22.

Dimethicone

Five samples of Dimethicone (100 cm^2/s; dynamic viscosity or specific gravity values unavailable), each not requiring more than 0.1 ml of 0.05 N alcoholic KOH to neutralize 15 g of the fluid, were tested for irritation of vaginal mucosa.[22] A sample of 0.05 ml of Dimethicone was instilled into the vagina of rats (number of animals not specified) daily for 8 d, the vaginal mucous membrane was observed to determine irritancy, and the effect on leukocyte count was determined. A 77.8 - 88% increase in leukocytes was observed in the vaginal smears of rats treated with two samples of Dimethicone. A similar increase was observed for rats instilled with formaldehyde as the reference irritant. Leukocyte increases in the rats treated with the 3 remaining samples was markedly lower. The authors concluded that 2 of the silicone samples with a higher acidity (0.17) and acid value of 0.3 were more likely to be mucous membrane irritants than the other 3 samples, in which the increase of leukocytes was relatively low (0.05 - 0.10 acidity; acid values were not provided).

CLINICAL STUDIES

Case Reports

Dimethicone

A 23-d old, premature twin male infant suffering with nasal congestion was accidentally sprayed intranasally with diaper rash protectant spray (instead of nasal saline spray), which listed 10% Dimethicone as the only active ingredient.[25] The child went into a choking and coughing spell, and was rushed to the emergency department. After 2 h, he was still in respiratory distress, wherein his oxygen saturation had dropped to 85% and his chest x-ray showed diffuse bilateral infiltrates, suggestive of bilateral chemical pneumonitis. By the 3rd day, he developed an eosinophilia of 31 - 37%, with an

absolute eosinophilic count of 3100 - 4250 per µl. He was treated with frequent saline bronchial lavages and chest physical therapy to remove mucus plugs blocking his endotracheal tube and was weaned off the ventilator by the 7th day after exposure. Referring to the Expert Panel evaluation that Dimethicone is safe for cosmetic use and when inhaled short term,[1] the researchers were of the opinion that Dimethicone did not cause the patient's symptoms. They found that the inactive ingredients of the product were aloe oil extract, caprylic/capric triglyceride, mineral oil, Peruvian balsam oil, shea liquid, and tocopheryl acetate/vitamin E. The authors concluded that the massive dose of mineral oil exposure was the most likely cause for acute pneumonitis, as was the Peruvian balsam oil for eosinophilia.

SUMMARY

According to the *Dictionary*, these 30 methicone ingredients are reported to function in cosmetics as skin conditioning agents, hair conditioning agents, and/or viscosity increasing agents. Of the ingredients in this report, Dimethicone and Methicone have the greatest frequency of use, according to 2020 VCRP data. Reported use for Dimethicone increased from use in 1659 formulations in 1998 to 14,050 in 2020, and reported frequency of use of Methicone increased from no reported uses in 1998 to use in 654 formulations in 2020. The highest concentration of use reported in 2019 was for Dimethicone, at a concentration of 85% in moisturizing products; the maximum concentration of use reported previously for Dimethicone was 80%. Although the overall maximum concentration of use did not increase notably, the maximum concentration of use for several exposure categories did.

Penetration of Dimethicone (9.5 kg/m·s and 332.5 kg/m·s) in human abdominal and vaginal tissue was examined after a 96-h application. A low penetration rate was observed for both viscosities, with more rapid penetration in vaginal tissue. Based on an estimated, low blood: air partition coefficient and an algorithm, the soluble fraction of Caprylyl Methicone is << 1% in the blood, minimizing the possibility of systemic circulation. In a dermal penetration study, the interaction of Dimethicone with the stratum corneum lipid microstructure in healthy excised human tissue was evaluated. All results indicated that Dimethicone did not disturb or interact with the upper layer of epidermis, and is not likely to penetrate the skin barrier. Male rats were exposed to both occlusive and non-occlusive patches of [^{14}C]Dimethicone to observe dermal absorption and excretion over 3 days. Radioactivity tracing demonstrated that 70% of the applied dose remained on the patches, 11.4% of the applied dose was at the site of application, and minimal amounts were found in feces and carbon dioxide traps.

The acute dermal LD_{50} of C30-45 Alkyl Dimethicone was determined to be > 2000 mg/kg bw in rats. In two separate acute dermal studies, undiluted Caprylyl Methicone and Dimethicone (54,150 kg/m·s) were applied, under occlusion, to the shaved backs of 10 Wistar rats and 10 New Zealand white rabbits, respectively, at doses of 2000 mg/kg bw for 24 h. No mortality and signs of toxicity were observed in either study and the acute dermal LD_{50} for each ingredient was determined to be > 2000 mg/kg bw in rats and rabbits, respectively. A single, 2008 mg/kg bw dermal application of Dimethicone did not cause mortality or noticeable abnormalities in 5 male and 5 female Sprague-Dawley rats; under these study conditions the acute dermal LD_{50} was determined to be > 2008 mg/kg bw. Three groups of 10 New Zealand white rabbits were exposed to an occlusive patch of Dimethicone (332.5 kg/m·s) for 28 d at doses up to 1000 mg/kg/d. No deaths or adverse events related to the exposure occurred, and the NOAEL for dermal application in rabbits was determined to be 1000 mg/kg/d.

Three female Wistar rats were administered a single dose of 2000 mg/kg bw Capryl Methicone, via gavage; no mortality or signs of systemic toxicity were observed, and the acute LD_{50} was determined to be > 2000 mg/kg bw. Five male and female Sprague-Dawley rats were administered a single oral dose of 2000 mg/kg bw Dimethicone in corn oil. No toxic effects or gross necropsy lesions were observed, and the acute LD_{50} was determined to be > 2000 mg/kg bw in rats. Caprylyl Methicone was administered in corn oil, via gavage, at doses of 0, 100, 300, or 1000 mg/kg bw/d to groups of 10 male and 10 female Han rats for 28 d. No mortality or clinical abnormalities occurred during observation; statistically significant lower blood cell count in the 300 mg/kg females, slight vacuolation in the adrenal glands of males in the main study, and recovery group, dosed with 1000 mg/kg/d, and minimal increases of the liver weights of females in the 300 and 1000 mg/kg groups, were all considered toxicologically irrelevant. The NOAEL of Caprylyl Methicone was determined to be > 1000 mg/kg bw/d. In another 28-d oral toxicity study of Caprylyl Methicone, groups of 10 male and 10 female Sprague-Dawley rats were orally dosed with 0, 500, 1000, or 5000 mg/kg bw/d, via gavage. Deaths of 2 females in the 500 mg/kg group, 1 male and 2 females in the 1000 mg/kg group, and 3 males and 1 female in the 5000 mg/kg group were attributed to aspiration of the test substance. Congested lungs, enlarged livers, and lower mean organ and body weights in the 5000 mg/kg group were statistically significant, and the NOAEL was determined to be 1000 mg/kg bw/d, while the NOEL was determined to be 500 mg/kg bw/d. In a 28-d oral toxicity study, Dimethicone was administered at up to 10% (100,000 ppm) in the diet of CDF-(F344)-CrlBr rats. Test article related symptoms included matted fur, increased incidence of corneal opacity, and significantly decreased mean triglycerides and LDL levels at higher doses. These symptoms were not considered adverse effects and the NOAEL of Dimethicone was determined > 100,000 ppm. Four groups of 30 male and 30 female Fischer 344 rats were administered Dimethicone (9.5 kg/m·s), in their diet, at doses up to 1000 mg/kg bw/d for 12 mo. Amongst the treated rats, four groups of 10 male and 10 female rats were necropsied after 12 mo, while a remaining 20 male and 20 female

rats per group were observed for recovery for 12 mo after the treatment period. In both necropsied and recovery groups there was an increase in ocular opacity, and the NOEL for systemic toxicity was determined to be 1000 mg/kg bw/d.

Groups of 5 Wistar rats were exposed for 4 h, nose-only, to solutions of 25% Dimethicone (95,000 kg/m·s) dissolved in petroleum ether, or to two other solvents in separate control groups (control solvents not named). No mortality or clinical symptoms were attributed to Dimethicone exposure, and the LC_{50} was determined to be > 11,582 mg/m^3. Dimethicone (9500 kg/m·s) dissolved in dichloromethane was tested for acute inhalation toxicity, at doses up to 694.8 mg/m^3, in Wistar rats. No mortality or toxic effects were observed, and the LC_{50} was determined to be > 695 mg/m^3.

In a reproductive and developmental toxicity study, 7 groups of 10 male and 10 female Han rats were orally dosed with 0, 100, 300, or 1000 mg/kg bw/d Caprylyl Methicone, in corn oil, via gavage for 28 d. Fertility, maternal, birth, and fetal outcomes were not adversely affected; the NOAEL for Caprylyl Methicone was determined to be > 1000 mg/kg bw/d.

Bacterial reverse mutation assays were performed with C30-45 Alkyl Dimethicone and Caprylyl Methicone; the test substances were not found to be non-mutagenic. In a bacterial reverse mutation assay, *S. typhimurium* tester strains TA98, TA100, TA153, TA1537, and *E. coli* strains WP2 uvrA and WP2 uvrA (pKM 101) were tested with Dimethicone (57,000 kg/m·s), at a maximum dose of 5000 µg per plate, in the presence and absence of metabolic activation. Although precipitate was observed at ≥ 500 or ≥ 1500 µg per plate, Dimethicone was considered non-mutagenic under these study conditions. In vivo, Caprylyl Methicone was intravenously administered at up to 5010 mg/kg bw to groups of 5 ICR mice in a micronucleus test; no significant increases in PCEs were observed and the test substance was deemed non-genotoxic.

The carcinogenic potential of a silicone resin containing Dimethicone and silica, was evaluated by feeding 50 male and 50 female F344/DuCrj rats diets containing up to 5.0% of the test article for 104 wk. There was a statistically significant, 2 - 18% increase in the incidence of C-cell adenomas in female rats in the highest dose group, while the male rats in the highest dose group experienced a decreased incidence of prostate cancer compared to the control group. The incidence of prostate cancer in the control group was relatively high, and thus the difference between treatment and control groups was considered incidental.

Three groups of 20 male and 20 female F344 rats were observed for oncogenic effects upon administration of Dimethicone (10 cm^2/s; dynamic viscosity or specific gravity unavailable) at doses of 100, 300, or 1000 mg/kg bw/d for up to 24 mo. Slightly increased incidence of corneal opacity was observed at the maximum dose, as well as a statistically significant increase in islet adenomas among males in the 100 mg/kg bw group. However, the lack of increased islet adenomas in female rats and the high incidence amongst control rats suggested that these effects were independent of Dimethicone exposure. The NOEL for oncogenicity of Dimethicone was determined to be 1000 mg/kg bw/d.

Twenty female A.SW mice received a single 0.5-ml i.p. injection of Dimethicone, while 3 groups of 20 mice were injected with either saline, pristane or silicone gel, to evaluate immunological reactions over 6 mo. Dimethicone-treated mice produced various antibody isotopes within 2 mo of injection, spontaneously secreted and produced greater, dose-dependent amounts of IL-6, and showed silicone droplets and expanded vacuoles within kidney glomeruli, indicating the possibility for systemic accumulation.

A skin irritation test using C30-45 Alkyl Dimethicone (test concentration not specified) was performed in rabbits; the test substance was determined to be non-irritating. Two studies evaluating the dermal irritation potential of a neat, 4-h, occlusive application of Caprylyl Methicone to New Zealand white rabbits were performed; the test substance was deemed non-irritating at a dose of 0.5 ml, while it was deemed slightly irritating at an unspecified dose of 97%, undiluted Caprylyl Methicone. Dimethicone did not cause dermal irritation or inflammation in rabbits and guinea pigs. Caprylyl Methicone was determined to be a non-sensitizer in guinea pigs. Dimethicone did not cause sensitization or irritation in a contact sensitization study of female mice. In an HRIPT, Dimethicone was tested neat (as a negative control), and as used as a vehicle for a 5% solution of an unspecified test substance, in 106 subjects. No evidence of sensitization to Dimethicone, as a control or vehicle, was observed.

The ocular irritancy potential of C30-45 Alkyl Dimethicone was tested in rabbits; slight conjunctivae were observed, but resolved in within 24 h of exposure, and the test substance was deemed non-irritating. Caprylyl Methicone (0.1 ml) was not deemed irritating to rabbit eyes; an unspecified dose of Caprylyl Methicone was considered slightly irritating to rabbit eyes in another study. Sixteen rabbits were exposed for to up to 6 h with 0.7 - 1.0 ml of generic or medical-grade Dimethicone, in one eye, to test for variance in ocular irritancy. All eyes treated with either generic or medical-grade Dimethicone evidenced mild irritation corneal epithelium. In a study using groups of 3 mice, guinea pigs, or rabbits, 5 separately manufactured samples of Dimethicone (100 cm^2/s; dynamic viscosity or specific gravity values unavailable) were instilled into the lower eyelid of the animals once daily for 10 d. All guinea pigs exposed to the first sample died by days 8 - 10, and the second sample caused corneal inflammation in one rabbit after 10 d, and death in another rabbit and 2 guinea pigs. No adverse effects were observed with exposure to the 3 remaining samples. Both Dimethicone samples with positive results had a slightly more acidic profile, suggesting that the ocular irritancy and inflammatory effects of silicone fluids may be acidity-dependent.

The potential for five samples 0.5 ml of Dimethicone (100 cm^2/s; dynamic viscosity or specific gravity values unavailable) to cause vaginal mucosa irritation was tested in rats for 8 d. An ~88% increase in leukocytes was observed in the vaginal smears of rats treated with two Dimethicone samples. A similar increase was observed in rats treated with formaldehyde. The leukocyte increase in the rats treated with the 3 remaining Dimethicone samples was markedly lower. Irritation outcomes for each Dimethicone sample were deemed to be affected by higher acidity and acid values.

A 23-d old, premature twin male infant experienced severe respiratory distress, acute pneumonitis, and eosinophilia as a result of intranasal exposure to a 10% Dimethicone spray. Although Dimethicone was listed as the active ingredient, mineral oil and Peruvian balsam oil were considered to be causative agents for the severe reaction.

DISCUSSION

In accordance with the CIR Procedures & Support to the Expert Panel for Cosmetic Ingredient Safety, the Panel evaluates the conclusions of previously-issued reports approximately every 15 years. In 2003, the Panel published a final report on the safety assessment of 20 dimethicone, methicone, and substituted-methicone polymers, and concluded that the ingredients named in that report are safe as used in cosmetic products. Due to dramatic increases in frequency of use, and increases in concentrations of use for certain exposure types, especially for Dimethicone in products that could result in incidental inhalation, the Panel determined to reopen this safety assessment. In addition to the ingredients previously reviewed, the Panel Clustering and Read Across Working Group considered related polymers for inclusion in this report; the Working Group determined it was appropriate to include 10 additional polymers that have not yet been reviewed, due to chemical similarity and similarity of use.

The Panel noted that Dimethicone is now reported to be used at 85% in moisturizing spray formulations; in the original assessment, the greatest reported maximum use concentration in spray products was 16% in perfumes. Additionally, the Panel noted that some of these polymers are used in powders, which could also possibly be inhaled. Nevertheless, the Panel found that the absence of exposure-related effects from a study reported in the original assessment, in which several species were sprayed with an atomizer containing 10 ml/kg Dimethicone for 29 d, mitigated concern for use of these ingredients in cosmetic products that could be incidentally inhaled. Also, the Panel noted that in aerosol products, 95% – 99% of droplets/particles would not be respirable to any appreciable amount. Furthermore, droplets/particles deposited in the nasopharyngeal or bronchial 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 concentrations at which the ingredient is used, 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.

In addition to concentrations of use, the Panel noted high variability in the viscosity of these ingredients, and that it would be ideal for cosmetic manufacturers to indicate the viscosities at which these ingredients are formulated.

Furthermore, the Panel noted that Dimethicone is now being used at, or above, concentrations at which ocular irritation was observed in studies cited in the original assessment. The Panel discussed the validity of results from an ocular irritation study included in the present assessment, in which test animals died following instillation of 100% Dimethicone (970 kg/m·s) in the eye, for 10 d. The Panel remarked that mortality occurring during an ocular irritation study is very unusual, and toxicologically implausible. Subsequently, the Panel distinguished the difference between instilling 35% pure Dimethicone in the eye, as described in an animal ocular irritation study from the original report, compared to using a cosmetic product containing 37.8% Dimethicone, in which ocular contact is not intended. However, the Panel stated that manufacturers should be cognizant of incidental/accidental exposure to the eye, and specified that products containing the ingredients included in this report must be formulated to be non-irritating to the eye.

The Panel also noted that the potential exists for dermal irritation with the use of products formulated using dimethicone, methicone, and substituted-methicone polymers. The Panel specified that products containing these ingredients must be formulated to be non-irritating.

CONCLUSION

The Expert Panel for Cosmetic Ingredient Safety concluded that the following 30 dimethicone, methicone, and substituted-methicone polymers are safe in cosmetics in the present practices of use and concentration described in this safety assessment when formulated to be non-irritating to the skin and the eye:

Amino Bispropyl Dimethicone
Aminopropyl Dimethicone
Amodimethicone
Amodimethicone Hydroxystearate*
Behenoxy Dimethicone
C20-24 Alkyl Dimethicone
C20-24 Alkyl Methicone*
C24-28 Alkyl Dimethicone*
C24-28 Alkyl Methicone
C26-28 Alkyl Dimethicone
C26-28 Alkyl Methicone*
C30-45 Alkyl Dimethicone
C30-45 Alkyl Methicone
C30-60 Alkyl Dimethicone
C32 Alkyl Dimethicone*
Capryl Dimethicone
Caprylyl Methicone
Cetearyl Methicone
Cetyl Dimethicone
Dimethicone
Dimethoxysilyl Ethylenediaminopropyl Dimethicone
Hexyl Dimethicone
Hexyl Methicone*
Hydroxypropyldimethicone*
Methicone
Stearamidopropyl Dimethicone*
Stearoxy Dimethicone
Stearyl Dimethicone
Stearyl Methicone
Vinyl Dimethicone

**Not reported to be in current use. Were ingredients in this group not in current use to be used in the future, the expectation is that they would be used in product categories and at concentrations comparable to others in this group.*

TABLES

Table 1. Definitions, idealized structures, and functions

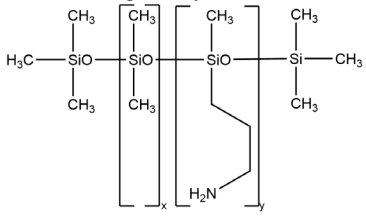
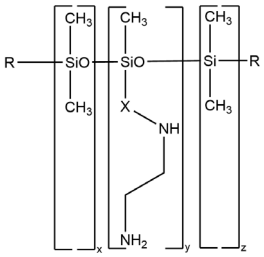
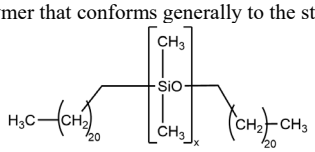
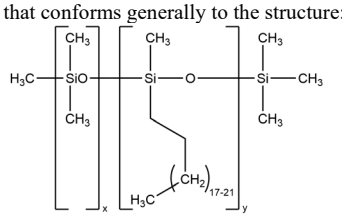
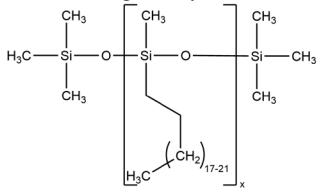
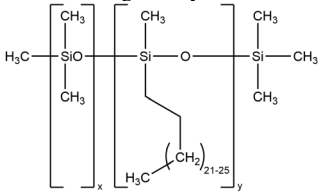
Name & CAS No.	Definition & Structure	Function(s)
Amino Bispropyl Dimethicone 189959-16-8	a complex three-dimensional siloxane polymer formed by the reaction between dimethiconol and 3-(trimethoxysilyl)-*N*-[3-(trimethoxysilyl)propyl]-1-propanamine.	Hair-conditioning agent
Aminopropyl Dimethicone 99363-37-8	the siloxane polymer that conforms generally to the structure: 	Hair-conditioning agent Skin-conditioning agent—miscellaneous
Amodimethicone 106842-44-8 68554-54-1 71750-79-3	a siloxane polymer that contains amino functional groups. It conforms generally to the structure:  where R=OH or CH_3, and X represents the propyl, isopropyl, or isobutyl group.	Hair-conditioning agent
Amodimethicone Hydroxystearate	the salt of Amodimethicone and Hydroxystearic Acid.	Hair-conditioning agent
Behenoxy Dimethicone	a dimethyl siloxane polymer that conforms generally to the structure: 	Skin-conditioning agent—emollient
C20-24 Alkyl Dimethicone 200074-76-6	is the siloxane polymer that conforms generally to the structure: 	Skin-conditioning agent—occlusive Viscosity increasing agent—nonaqueous
C20-24 Alkyl Methicone 200074-77-7	is the siloxane polymer that conforms generally to the structure: 	Skin-conditioning agent – emollient Viscosity increasing agent-- nonaqueous
C24-28 Alkyl Dimethicone 192230-29-8	is the siloxane polymer that conforms generally to the structure: 	Skin-conditioning agent—occlusive Viscosity increasing agent--nonaqueous

Table 1. Definitions, idealized structures, and functions

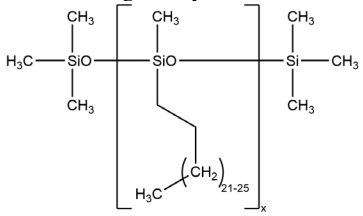
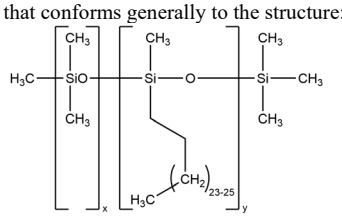
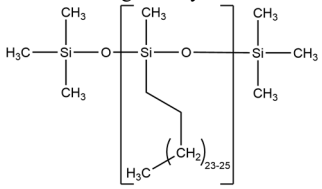
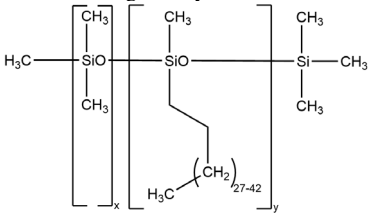
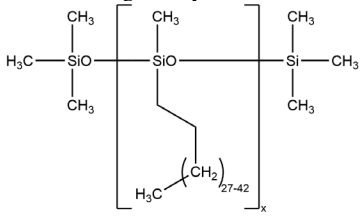
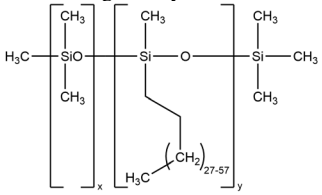
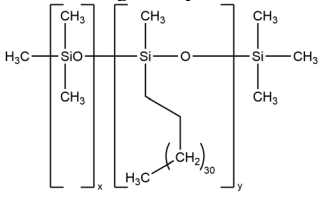
Name & CAS No.	Definition & Structure	Function(s)
C24-28 Alkyl Methicone 189378-12-9	the siloxane polymer that conforms generally to the structure: 	Skin-conditioning agent—emollient Viscosity increasing agent—non-aqueous
C26-28 Alkyl Dimethicone	is the siloxane polymer that conforms generally to the structure: 	Hair-conditioning agent Skin conditioning agent--occlusive
C26-28 Alkyl Methicone 189378-12-9	is the siloxane polymer that conforms generally to the structure: 	Skin-conditioning agent -- occlusive
C30-45 Alkyl Dimethicone	the siloxane polymer that conforms generally to the structure: 	Skin-conditioning agent—occlusive
C30-45 Alkyl Methicone 189378-12-9 246864-88-0	the siloxane polymer that conforms generally to the structure: 	Skin-conditioning agent—occlusive Viscosity increasing agent—non-aqueous
C30-60 Alkyl Dimethicone	the siloxane polymer that conforms generally to the structure: 	Skin-conditioning agent—occlusive Viscosity increasing agent – non-aqueous
C32 Alkyl Dimethicone	is the silicone polymer that conforms generally to the structure: 	Skin- conditioning agent--emollient

Table 1. Definitions, idealized structures, and functions

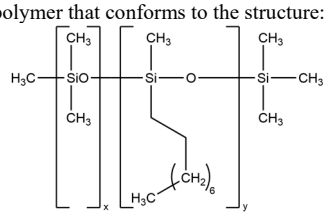
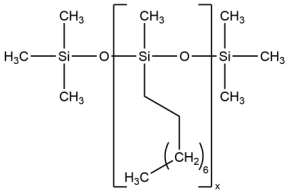
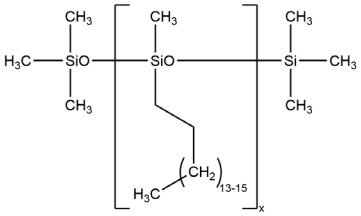
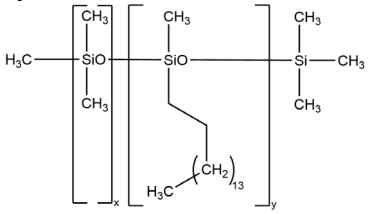
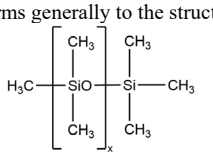
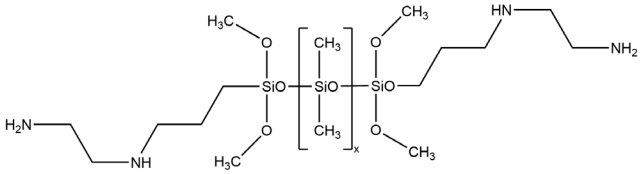
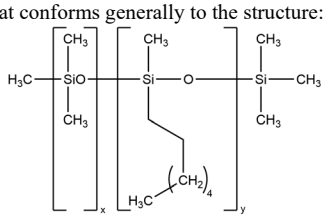
Name & CAS No.	Definition & Structure	Function(s)
Capryl Dimethicone	is a dimethyl siloxane polymer that conforms to the structure: 	Skin-conditioning agent--emollient
Caprylyl Methicone 17955-88-3	is the siloxane polymer that conforms to the structure: 	Skin-conditioning agent--occlusive
Cetearyl Methicone	a siloxane polymer that conforms to the structure: 	Skin-conditioning agent—occlusive
Cetyl Dimethicone 191044-49-2	a dimethyl siloxane polymer that conforms to the structure: 	Antifoaming agent Skin-conditioning agent—emollient and occlusive
Dimethicone 141-62-8 141-63-9 63148-62-9 9006-65-9 9016-00-6 107-52-8	a mixture of fully methylated linear siloxane polymers end blocked with trimethylsiloxy units. It conforms generally to the structure: 	Antifoaming agent Skin protectant Skin-conditioning agent—occlusive Solvent
Dimethoxysilyl Ethylenediaminopropyl Dimethicone 71750-80-6	the siloxane polymer that conforms generally to the structure: 	Hair conditioning agent
Hexyl Dimethicone	the siloxane polymer that conforms generally to the structure: 	Hair conditioning Skin conditioning agents -- miscellaneous

Table 1. Definitions, idealized structures, and functions

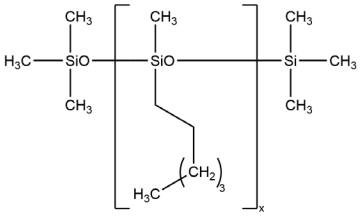
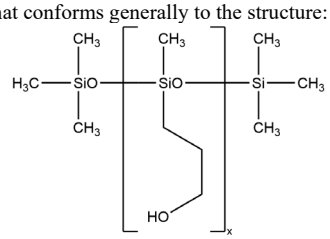
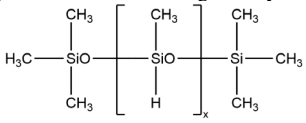
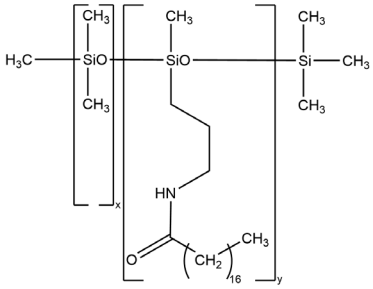
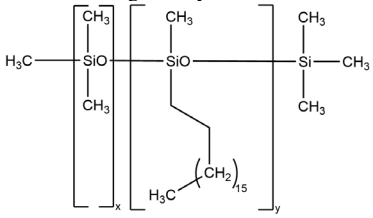
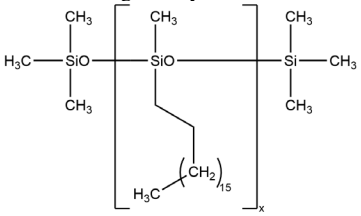
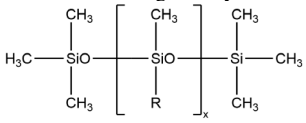
Name & CAS No.	Definition & Structure	Function(s)
Hexyl Methicone 1873-90-1	the siloxane polymer that conforms to the structure: 	Skin-conditioning—emollient
Hydroxypropyldimethicone 102782-61-6	the siloxane polymer that conforms generally to the structure: 	Hair-conditioning Skin-conditioning—miscellaneous
Methicone 63148-57-2 9004-73-3	a linear monomethyl polysiloxane. It conforms generally to the structure: 	Skin-conditioning agent—occlusive Surface modifier
Stearamidopropyl Dimethicone	the siloxane polymer that conforms to the structure: 	Corrosion inhibitor Film former
Stearoxy Dimethicone 68554-53-0	a polymer of dimethylpolysiloxane with some methyl groups replaced by stearoxy groups.	Skin-conditioning agent—emollient
Stearyl Dimethicone 67762-83-8	the siloxane polymer that conforms generally to the formula: 	Skin-conditioning agent—occlusive
Stearyl Methicone	the siloxane polymer that conforms generally to the structure: 	Skin-conditioning agent—occlusive
Vinyl Dimethicone 67762-94-1	a derivative of Dimethicone where some of the methyl groups have been replaced with vinyl groups. The vinyl groups can occur at the ends of the siloxane chain or pendant to the siloxane chain. It conforms generally to the structure:  wherein R is a methyl or vinyl group, and at least one vinyl group is present.	Not reported

Table 2. Current and historical frequency and concentration of use according to duration and exposure

	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	Amino Bispropyl Dimethicone				**Aminopropyl Dimethicone**			
	2020[9]	**1998[1]**	**2019[10]**	**1999[1]**	**2020[9]**	**1998[1]**	**2019[10]**	**1999[1]**
Totals*	**1**	**NR**	**NR**	**NR**	**57**	**NR**	**0.001-3**	**NR**
Duration of Use								
Leave-On	*1*	*NR*	*NR*	*NR*	*36*	*NR*	*0.001-3*	*NR*
Rinse-Off	*NR*	*NR*	*NR*	*NR*	*21*	*NR*	*0.3-0.66*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	NR	NR	NR	NR	1	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	NR	NR	NR	16[a]; 6[b]	NR	0.1-0.5[a]	NR
Incidental Inhalation-Powder	NR	NR	NR	NR	6[b]	NR	NR	NR
Dermal Contact	NR	NR	NR	NR	15	NR	0.001-3	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	Not spray: 0.001	NR
Hair - Non-Coloring	1	NR	NR	NR	36	NR	0.1-0.66	NR
Hair-Coloring	NR	NR	NR	NR	5	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR
	Amodimethicone				**Behenoxy Dimethicone**			
	2020[9]	**1998[1]**	**2019[10]**	**1999[1]**	**2020[9]**	**1998[1]**	**2019[10]**	**1999[1]**
Totals*	**1387**	**166**	**0.0051-5**	**0.0004-3**	**13**	**3**	**0.5**	**2-3**
Duration of Use								
Leave-On	*449*	*29*	*0.0051-4*	*0.0004-0.7*	*12*	*2*	*0.5*	*2*
Rinse-Off	*937*	*137*	*0.06-5*	*0.6-3*	*1*	*1*	*NR*	*3*
Diluted for (Bath) Use	*1*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	1	NR	NR	NR	5	NR	NR	NR
Incidental Ingestion	2	NR	NR	NR	2	NR	NR	NR
Incidental Inhalation-Spray	11; 208[a], 10[b]	3; 9[a]	0.3-2; 0.15-4[a]	0.0004-0.7[a]	4[a]; 1[b]	NR	NR	2[a]; 2[b]
Incidental Inhalation-Powder	1; 10[b]	NR	0.05[c]	NR	1[b]	NR	0.5[c]	2[b]
Dermal Contact	77	1	0.0051-0.49	NR	11	NR	0.5	2-3
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	1240	121	0.06-5	0.0004-3	NR	3	NR	NR
Hair-Coloring	68	44	0.18-1.3	2	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	43	NR	NR	NR	2	NR	NR	NR
Baby Products	2	NR	NR	NR	NR	NR	NR	NR
	C20-24 Alkyl Dimethicone				**C24-28 Alkyl Methicone**			
	2020[9]	**1998[1]**	**2020[12]**	**1999[1]**	**2020[9]**	**1998[1]**	**2019[10]**	**1999[1]**
Totals*	**38**	**NA**	**8**	**NA**	**NR**	**NR**	**NR**	**2**
Duration of Use								
Leave-On	*38*	*NA*	*8*	*NA*	*NR*	*NR*	*NR*	*2*
Rinse-Off	*NR*	*NA*	*NR*	*NA*	*NR*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NA*	*NR*	*NA*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	1	NA	8	NA	NR	NR	NR	NR
Incidental Ingestion	29	NA	NR	NA	NR	NR	NR	2
Incidental Inhalation-Spray	3[a]; 4[b]	NA	NR	NA	NR	NR	NR	NR
Incidental Inhalation-Powder	4[b]	NA	NR	NA	NR	NR	NR	NR
Dermal Contact	9	NA	8	NA	NR	NR	NR	NR
Deodorant (underarm)	NR	NA	NR	NA	NR	NR	NR	NR
Hair - Non-Coloring	NR	NA	NR	NA	NR	NR	NR	NR
Hair-Coloring	NR	NA	NR	NA	NR	NR	NR	NR
Nail	NR	NA	NR	NA	NR	NR	NR	NR
Mucous Membrane	29	NA	NR	NA	NR	NR	NR	2
Baby Products	NR	NA	NR	NA	NR	NR	NR	NR

Table 2. Current and historical frequency and concentration of use according to duration and exposure

	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	C26-28 Alkyl Dimethicone				**C30-45 Alkyl Dimethicone**			
	2020[9]	**1998[1]**	**2020[12]**	**1999[1]**	**2020[9]**	**1998[1]**	**2019[10]**	**1999[1]**
Totals*	**13**	**NA**	**0.8-2.8**	**NA**	**66**	**NR**	**0.16-5.1**	**2**
Duration of Use								
Leave-On	*11*	*NA*	*0.8-2.8*	*NA*	*64*	*NR*	*0.16-5.1*	*2*
Rinse-Off	*2*	*NA*	*NR*	*NA*	*2*	*NR*	*0.5*	*NR*
Diluted for (Bath) Use	*NR*	*NA*	*NR*	*NA*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	10	NA	0.8-2.8	NA	13	NR	0.16-5.1	NR
Incidental Ingestion	1	NA	NR	NA	36	NR	0.4-2.9	NR
Incidental Inhalation-Spray	NR	NA	NR	NA	3[a]; 5[b]	NR	2.3[a]	2[a]
Incidental Inhalation-Powder	NR	NA	NR	NA	5[b]	NR	4; 0.5-4[c]	NR
Dermal Contact	9	NA	2-2.8	NA	24	NR	0.16-5.1	2
Deodorant (underarm)	NR	NA	NR	NA	NR	NR	NR	NR
Hair - Non-Coloring	2	NA	NR	NA	2	NR	0.5-2.3	NR
Hair-Coloring	NR	NA	NR	NA	NR	NR	NR	NR
Nail	NR	NA	NR	NA	NR	NR	NR	NR
Mucous Membrane	1	NA	NR	NA	36	NR	0.4-2.9	NR
Baby Products	NR	NA	NR	NA	NR	NR	NR	NR
	C30-45 Alkyl Methicone				**C30-60 Alkyl Dimethicone**			
	2020[9]	**1998[1]**	**2019[10]**	**1999[1]**	**2020[9]**	**1998[1]**	**2020[12]**	**1999[1]**
Totals*	**71**	**NR**	**0.0054-2.2**	**NR**	**2**	**NA**	**NR**	**NA**
Duration of Use								
Leave-On	*50*	*NR*	*0.0054-2.2*	*NR*	*2*	*NA*	*NR*	*NA*
Rinse-Off	*21*	*NR*	*NR*	*NR*	*NR*	*NA*	*NR*	*NA*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NA*	*NR*	*NA*
Exposure Type								
Eye Area	12	NR	NR	NR	NR	NA	NR	NA
Incidental Ingestion	13	NR	NR	NR	NR	NA	NR	NA
Incidental Inhalation-Spray	7[a]; 5[b]	NR	NR	NR	2[b]	NA	NR	NA
Incidental Inhalation-Powder	5[b]	NR	0.0054-2.2[c]	NR	2[b]	NA	NR	NA
Dermal Contact	52	NR	0.0054-2.2	NR	2	NA	NR	NA
Deodorant (underarm)	NR	NR	NR	NR	NR	NA	NR	NA
Hair - Non-Coloring	3	NR	NR	NR	NR	NA	NR	NA
Hair-Coloring	NR	NR	NR	NR	NR	NA	NR	NA
Nail	2	NR	NR	NR	NR	NA	NR	NA
Mucous Membrane	13	NR	NR	NR	NR	NA	NR	NA
Baby Products	NR	NR	NR	NR	NR	NA	NR	NA
	Capryl Dimethicone				**Caprylyl Methicone**			
	2020[9]	**1998[1]**	**2020[12]**	**1999[1]**	**2020[9]**	**1998[1]**	**2020[12]**	**1999[1]**
Totals*	**NR**	**NR**	**1-5.5**	**NR**	**234**	**NA**	**0.0075-16**	**NA**
Duration of Use								
Leave-On	*NR*	*NR*	*1-5.5*	*NR*	*226*	*NA*	*0.0075-16*	*NA*
Rinse-Off	*NR*	*NR*	*1*	*NR*	*8*	*NA*	*0.22-12*	*NA*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NA*	*NR*	*NA*
Exposure Type								
Eye Area	NR	NR	1.5	NR	51	NA	0.22-16	NA
Incidental Ingestion	NR	NR	NR	NR	20	NA	2.8-7.5	NA
Incidental Inhalation-Spray	NR	NR	NR	NR	1; 63[a]; 38[b]	NA	0.8-6.2	NA
Incidental Inhalation-Powder	NR	NR	1[c]	NR	10; 38[b]	NA	0.014-6[c]; 0.0075-4	NA
Dermal Contact	NR	NR	1-5.5	NR	204	NA	0.0075-16	NA
Deodorant (underarm)	NR	NR	NR	NR	NR	NA	NR	NA
Hair - Non-Coloring	NR	NR	NR	NR	9	NA	0.5-6	NA
Hair-Coloring	NR	NR	NR	NR	NR	NA	NR	NA
Nail	NR	NR	NR	NR	1	NA	NR	NA
Mucous Membrane	NR	NR	NR	NR	20	NA	2.8-7.5	NA
Baby Products	NR	NR	1	NR	NR	NA	NR	NA

Table 2. Current and historical frequency and concentration of use according to duration and exposure

	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	Cetearyl Methicone				**Cetyl Dimethicone**			
	2020[9]	**1998[1]**	**2019[10]**	**1999[1]**	**2020[9]**	**1998[1]**	**2019[10]**	**1999[1]**
Totals*	**45**	**1**	**0.75-1.1**	**0.5-1**	**233**	**27**	**0.001-11.8**	**0.5-10**
Duration of Use								
Leave-On	*45*	*1*	*0.75-1.1*	*0.5-1*	*228*	*26*	*0.1-11.8*	*0.5-10*
Rinse-Off	*NR*	*NR*	*NR*	*NR*	*5*	*1*	*0.001-6*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	2	NR	NR	NR	64	5	1-6	0.5
Incidental Ingestion	NR	1	NR	0.6-1	14	NR	1.1-10	4-5
Incidental Inhalation-Spray	34[a];6[b]	NR	0.75[a]	0.5[b]	38[a]; 6[b]	4[a]; 2[b]	0.5-4[a]	2[a]; 2[b]
Incidental Inhalation-Powder	6[b]	NR	1.1[c]	0.5[b]	19; 6[b]	2; 2[b]	6; 0.1-11.8[c]	0.9-3; 2[b]
Dermal Contact	43	NR	0.9-1.1	0.5	210	24	0.001-11.8	0.9-10
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	2	NR	0.75	NR	7	1	0.5-6	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	1	NR	0.6-1	14	NR	0.001-10	4-5
Baby Products	NR	NR	NR	NR	NR	NR	5	NR
	Dimethicone				**Dimethoxysilyl Ethylenediaminopropyl Dimethicone**			
	2020[9]	**1998[1]**	**2019[10]**	**1999[1]**	**2020[9]**	**1998[1]**	**2019[10]**	**1999[1]**
Totals*	**14,050**	**1659**	**0.0000014-85**	**0.0001-80**	**NR**	**NR**	**0.043-2.1**	**NR**
Duration of Use								
Leave-On	*12,426*	*1333*	*0.002-85*	*0.0001-80*	*NR*	*NR*	*0.043*	*NR*
Rinse-Off	*1616*	*320*	*0.0000014-23.4*	*0.001-10*	*NR*	*NR*	*2.1*	*NR*
Diluted for (Bath) Use	*8*	*6*	*2.5-3*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	1976	111	0.25-37.8	0.3-13	NR	NR	NR	NR
Incidental Ingestion	347	12	0.4-71.3	0.001-20	NR	NR	NR	NR
Incidental Inhalation-Spray	119; 4763[a]; 2430[b]	56; 336[a]; 299[b]	1-85; 0.3-63.5[a]; 1-2.9[b]	0.2-16; 0.3-15[a]; 0.0001-10[b]	NR	NR	0.043[a]	NR
Incidental Inhalation-Powder	482; 2430[b]; 31[c]	87; 299[b]; 7[c]	0.33-53; 1-2.9[b]; 0.5-66.9[c]	0.3-30; 0.0001-10[b]; 2[c]	NR	NR	NR	NR
Dermal Contact	11,377	1313	0.0022-85	0.0001-30	NR	NR	NR	NR
Deodorant (underarm)	33[a]	9[a]	spray: 2-18.6; not spray: 5-40	0.5-23[a]	NR	NR	NR	NR
Hair - Non-Coloring	1522	249	0.0000014-63.5	0.08-80	NR	NR	0.043	NR
Hair-Coloring	291	29	0.00015-3.3	0.5	NR	NR	2.1	NR
Nail	397	36	0.002-75	0.001-3	NR	NR	NR	NR
Mucous Membrane	442	54	0.0022-71.3	0.001-20	NR	NR	NR	NR
Baby Products	34	8	0.21-10	2	NR	NR	NR	NR
	Hexyl Dimethicone				**Methicone**			
	2020[9]	**1998[1]**	**2020[12]**	**1999[1]**	**2020[9]**	**1998[1]**	**2019[10]**	**1999[1]**
Totals*	**NR**	**NA**	**0.17**	**NA**	**654**	**NR**	**0.00014-3.6**	**0.009-5**
Duration of Use								
Leave-On	*NR*	*NA*	*0.17*	*NA*	*635*	*NR*	*0.00014-3.6*	*0.009-5*
Rinse-Off	*NR*	*NA*	*NR*	*NA*	*18*	*NR*	*0.15-0.46*	*0.05-0.3*
Diluted for (Bath) Use	*NR*	*NA*	*NR*	*NA*	*1*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	NR	NA	0.17	NA	166	NR	0.1-3.6	0.02-0.9
Incidental Ingestion	NR	NA	NR	NA	91	NR	0.36	0.06
Incidental Inhalation-Spray	NR	NA	NR	NA	7[a]; 21[b]	NR	NR	0.3[b]
Incidental Inhalation-Powder	NR	NA	NR	NA	92; 21[b]	NR	0.064-1.5; 0.048-1.9[c]	0.08-5; 0.3[b]; 0.3[c]
Dermal Contact	NR	NA	0.17	NA	505	NR	0.00014-3.6	0.01-5
Deodorant (underarm)	NR	NA	NR	NA	NR	NR	spray: 0.25	NR
Hair - Non-Coloring	NR	NA	NR	NA	10	NR	0.46	NR
Hair-Coloring	NR	NA	NR	NA	5	NR	NR	0.3
Nail	NR	NA	NR	NA	24	NR	0.0035-2.5	0.009
Mucous Membrane	NR	NA	NR	NA	95	NR	0.36	0.06
Baby Products	NR	NA	NR	NA	NR	NR	0.46	0.3

Table 2. Current and historical frequency and concentration of use according to duration and exposure

	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	Stearoxy Dimethicone				**Stearyl Dimethicone**			
	2020[9]	**1998[1]**	**2019[10]**	**1999[1]**	**2020[9]**	**1998[1]**	**2019[10]**	**1999[1]**
Totals*	**44**	**21**	**0.8-1.5**	**0.1-3**	**183**	**7**	**0.2-8.3**	**0.8-6**
Duration of Use								
Leave-On	*43*	*20*	*0.8-1.5*	*0.1-3*	*176*	*6*	*0.2-8.3*	*0.8-6*
Rinse-Off	*1*	*1*	*NR*	*0.5*	*7*	*1*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	9	NR	NR	2-3	46	2	3.6-8.3	0.8-6
Incidental Ingestion	10	NR	0.8	3	25	2	0.38-2.6	4-6
Incidental Inhalation-Spray	7[a]; 8[b]	6[a]; 10[b]	NR	0.1; 0.2-3[a]; 2[b]	3; 28[a]; 35[b]	1[a]	0.38[a]	4[b]
Incidental Inhalation-Powder	8[b]	1; 10[b]	NR	2[b]	2; 35[b];	NR	0.2-2.3[c]	4[b]
Dermal Contact	32	21	1.5	0.5-3	149	3	0.2-8.3	1-6
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	not spray:1.2	NR
Hair - Non-Coloring	1	NR	NR	0.1-0.2	9	NR	0.3	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	10	NR	0.8	3	25	2	0.38-2.6	4-6
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR
	Stearyl Methicone				**Vinyl Dimethicone**			
	2020[9]	**1998[1]**	**2019[10]**	**1999[1]**	**2020[9]**	**1998[1]**	**2019[10]**	**1999[1]**
Totals*	**1**	**NR**	**NR**	**NR**	**1**	**NR**	**NR**	**NR**
Duration of Use								
Leave-On	*1*	*NR*	*NR*	*NR*	*1*	*NR*	*NR*	*NR*
Rinse-Off	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	1	NR	NR	NR
Incidental Inhalation-Spray	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Powder	NR	NR	NR	NR	NR	NR	NR	NR
Dermal Contact	1	NR	NR	NR	NR	NR	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	1	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

*Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.

[a] It is possible these products are sprays, but it is not specified whether the reported uses are sprays.

[b] Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories.

[c] It is possible these products are powders, but it is not specified whether the reported uses are powders

NR – no reported use

NA – Ingredient was not included in the original safety assessment.

Table 3. Methicone ingredients not reported to be in use[9-12]

Amodimethicone Hydroxystearate
C20-24 Alkyl Methicone
C24-28 Alkyl Dimethicone
C26-28 Alkyl Methicone
C32 Alkyl Dimethicone
Hexyl Methicone
Hydroxypropyldimethicone
Stearamidopropyl Dimethicone

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Final Report on the Safety Assessment of Stearoxy Dimethicone, Dimethicone, Methicone, Amino Bispropyl Dimethicone, Aminopropyl Dimethicone, Amodimethicone, Amodimethicone Hydroxystearate, Behenoxy Dimethicone, C24–28 Alkyl Methicone, C30–45 Alkyl Methicone, C30–45 Alkyl Dimethicone, Cetearyl Methicone, Cetyl Dimethicone, Dimethoxysilyl Ethylenediaminopropyl Dimethicone, Hexyl Methicone, Hydroxypropyldimethicone, Stearamidopropyl Dimethicone, Stearyl Dimethicone, Stearyl Methicone, and Vinyldimethicone[1]

Dimethicone is a fluid mixture of fully methylated linear siloxane polymers end-blocked with trimethylsiloxy units. Methicone is a linear monomethyl polysiloxane. The other dimethicones and methicones covered in this review are siloxane polymers of Dimethicone and Methicone. Most of these ingredients function as conditioning agents in cosmetic formulations at current concentrations of use of $\leq$15%. Clinical and animal absorption studies reported that Dimethicone was not absorbed following oral or dermal exposure. *Dimethicone, Methicone, and Vinyldimethicone* were not acutely toxic following oral exposure. No adverse reactions were found in rabbits following short-term dermal dosing with 6% to 79% Dimethicone, yet adverse effects were noted with a hand cream formulation containing 1% Dimethicone, suggesting something else in the preparation was toxic. Mice and rats were dosed for 90 days with up to 10% Dimethicone without adverse effect. Dimethicone did not produce adverse effects in acute and short-term inhalation-route studies, Methicone and Vinyldimethicone were negative in acute exposure studies using rats, but Hexyl Methicone was toxic to rats at 5 mg/L delivered in small particle (mean diameter of 0.29 μ) aerosols. Most dermal irritation studies using rabbits classified Dimethicone as a minimal irritant. Dimethicone (tested undiluted and at 79%) was not a sensitizer in four assays using mice and guinea pigs. It was not a sensitizer at 5.0% in a clinical repeated insult patch test using 83 panelists. Most ocular irritation studies using rabbits classified Dimethicone as a mild to minimal irritant. Dimethicone was tested in numerous oral-dose (using rats) and dermal-dose (using rats, rabbits, and monkeys) reproductive and developmental toxicity studies. In a few studies, treated males had significantly decreased body weight and/or decreased testes or seminal vesicles weights. No treatment-related adverse findings were noted in dosed pregnant females or fetuses. Dimethicone was negative in all genotoxicity assays. It was negative in both an oral (tested at 91%) and dermal (tested at an unknown concentration) dose carcinogenicity assay using mice. The Cosmetic Ingredient Review (CIR) Expert Panel considered it unlikely that any of these polymers would be significantly absorbed into the skin due to their large molecular weight. Although adverse effects were noted in one inhalation study with small aerosol particles, the expected particle sizes for cosmetic products would primarily be in the range of 60 to 80 μ, and less than 1% would be under 10 μ, which is an upper limit for respirable particles. Overall, the safety test data support the safety of these ingredients at the concentrations they are known to be used in cosmetic formulations. Accordingly, the CIR Expert Panel was of the opinion that Stearoxy Dimethicone, Dimethicone, Methicone, Amino Bispropyl Dimethicone, Aminopropyl Dimethicone, Amodimethicone, Amodimethicone Hydroxystearate, Behenoxy Dimethicone, C24–28 Alkyl Methicone, C30–45 Alkyl Methicone, C30–45 Alkyl Dimethicone, Cetearyl Methicone, Cetyl Dimethicone, Dimethoxysilyl Ethylenediaminopropyl Dimethicone, Hexyl Methicone, Hydroxypropyldimethicone, Stearamidopropyl Dimethicone, Stearyl Dimethicone, Stearyl Methicone, and Vinyldimethicone are safe as used in cosmetic formulations.

Received 4 December 2003; accepted 18 March 2003.

[1]Reviewed by the Cosmetic Ingredient Review (CIR) Expert Panel. This report was prepared by Bindu Nair, with the assistance of Amy R. Elmore, both former CIR staff.

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INTRODUCTION

This report is a compilation of data relevant to assessing the safety of Stearoxy Dimethicone, Dimethicone, Methicone,

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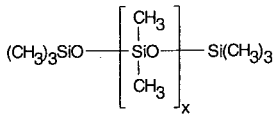
Amino Bispropyl Dimethicone, Aminopropyl Dimethicone, Amodimethicone, Amodimethicone Hydroxystearate, Behenoxy Dimethicone, C24–28 Alkyl Methicone, C30–45 Alkyl Methicone, C30–45 Alkyl Dimethicone, Cetearyl Methicone, Cetyl Dimethicone, Dimethoxysilyl Ethylenediaminopropyl Dimethicone, Hexyl Methicone, Hydroxypropyldimethicone, Stearamidopropyl Dimethicone, Stearyl Dimethicone, Stearyl Methicone, and Vinyldimethicone for use in cosmetic formulations. Almost all of the studies were done on Dimethicone identified under the CAS no. 63148-62-9 and defined as "dimethyl silicones and siloxanes." Heading names are used to identify studies that were done on other ingredients.

CHEMISTRY

Definition and Structure

Stearoxy Dimethicone (CAS no. 68554-53-0) is a polymer of dimethylpolysiloxane end-blocked with stearoxy groups. No structure is available. Synonyms include Dimethylsiloxane·Methylstearoxysiloxane Copolymer; Dimethyl Siloxy Stearoxy Siloxane Polymer; Poly(dimethylsiloxy) Stearoxysiloxane; Siloxanes and Silicones, Dimethyl, (Octadecyloxy)-Terminated; and Stearoxymethylpolysiloxane (Wenninger, Canterbery, and McEwen 2000).

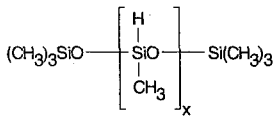
Dimethicone (CAS no. 9006-65-9, 63148-62-9, and 9016-00-6) is a mixture of fully methylated linear siloxane polymers $[-(CH_3)_2SiO-]_x$ end-blocked with trimethylsiloxy units $[-(CH_3)_3SiO-]$. It conforms generally to the formula (Wenninger, Canterbery, and McEwen 2000; Committee on Revision of the United States Pharmacopeial Convention 1995):



Dimethicone

Synonyms include Dimethylpolysiloxane; Dimethyl Silicone; Highly Polymerized Methyl Polysiloxane (1) and (2); Methyl Polysiloxane; Poly[oxy(dimethylsilylene)], α-(trimethylsilyl)-ω-methyl-; Silicone L-45 (Wenninger, Canterbery, and McEwen 2000), and α-(trimethylsilyl)-ω-methylpolydimethylsiloxane poly[oxy(dimethylsilylene)] (Committee on Revision of the United States Pharmacopeial Convention 1995). The Food and Agriculture Organization (FAO) of the World Health Organization (WHO) also lists the following three synonyms: Dimethylsilicone Fluid, Dimethylsilicone Oil, and Poly(dimethylsiloxane) (FAO/WHO 1994).

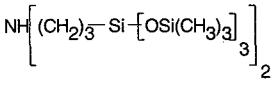
Methicone (CAS no. 9004-73-3) is a linear monomethyl polysiloxane. It conforms generally to the formula (Wenninger, Canterbery, and McEwen 2000):



Methicone

Synonyms include Hydrogen Methyl Polysiloxane, Methyl Hydrogen Polysiloxane, and Poly[oxy(methylsilylene)] (Wenninger, Canterbery, and McEwen 2000).

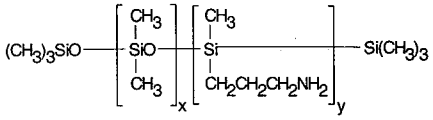
Amino Bispropyl Dimethicone is a substituted siloxane amine that conforms generally to the formula (Wenninger, Canterbery, and McEwen 2000):



Amino Bispropyl Dimethicone

No synonyms for Amino Bispropyl Dimethicone were found.

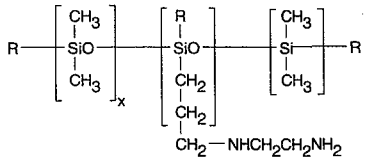
Aminopropyl Dimethicone is a silicone polymer that conforms generally to the formula (Wenninger, Canterbery, and McEwen 2000):



Aminopropyl Dimethicone

No synonyms for Aminopropyl Dimethicone were found.

Amodimethicone is a silicone polymer end blocked with amino functional groups. It conforms generally to the formula (Wenninger, Canterbery, and McEwen 2000):



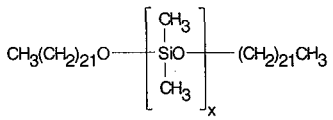
Amodimethicone

where R represents OH or CH3

Synonyms for Amodimethicone include Aminoethylaminopropylsiloxane · Dimethylsiloxane Copolymer Emulsion (Wenninger, Canterbery, and McEwen 2000).

Amodimethicone Hydroxystearate is the salt of Amodimethicone (q.v.) and Hydroxystearic Acid (q.v.) (Wenninger, Canterbery, and McEwen 2000). No structure was available and no synonyms were found.

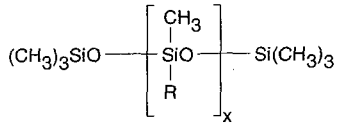
Behenoxy Dimethicone is a dimethyl siloxane polymer that conforms generally to the formula (Wenninger, Canterbery, and McEwen 2000):



Behenoxy Dimethicone

No synonyms for Behenoxy Dimethicone were found.

C24–28 Alkyl Methicone is the silicone polymer that conforms to the formula (Wenninger, Canterbery, and McEwen 2000):

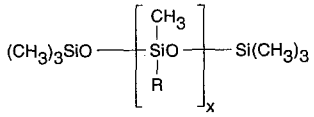


C24-28 Alkyl Methicone

where R represents the C24-28 alkyl group

No synonyms for C24–28 Alkyl Methicone were found.

C30–45 Alkyl Methicone is the silicone polymer that conforms to the formula (Wenninger, Canterbery, and McEwen 2000):

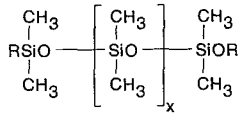


C30-45 Alkyl Methicone

where R represents the C30-45 alkyl group

No synonyms for C30–45 Alkyl Methicone were found.

C30–45 Alkyl Dimethicone is a silicone polymer that conforms generally to the formula (Wenninger, Canterbery, and McEwen 2000):

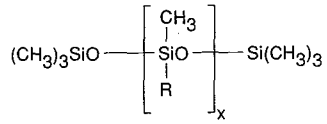


C30-45 Alkyl Dimethicone

where R represents the C30-45 alkyl group

No synonyms for C30–45 Alkyl Dimethicone were found.

Cetearyl Methicone is the silicone polymer that conforms to the formula (Wenninger, Canterbery, and McEwen 2000):

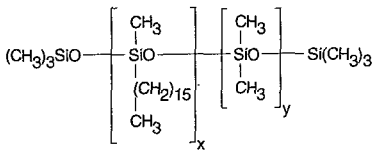


Cetearyl Methicone

where R represents the C16-18 alkyl group

No synonyms for Cetearyl Methicone were found.

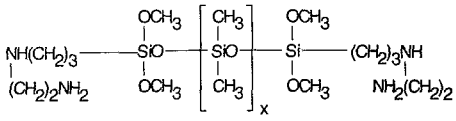
Cetyl Dimethicone is a dimethyl siloxane polymer that conforms to the formula (Wenninger, Canterbery, and McEwen 2000):



Cetyl Dimethicone

No synonyms for Cetyl Dimethicone were found.

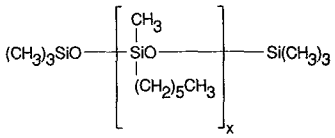
Dimethyoxysilyl Ethylenediaminopropyl Dimethicone (CAS no. 71750-80-6) is the silicone polymer that conforms generally to the formula:



Dimethyoxysilyl Ethylenediaminopropyl Dimethicone

Synonyms include Siloxanes and Silicones, Dimethyl, Mono-[[3-[(2-aminoethyl)amino]propyl]dimethoxysilyl]oxy-terminated (Wenninger, Canterbery, and McEwen 2000).

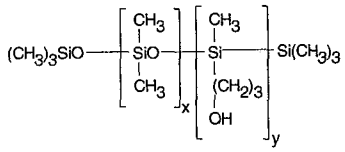
Hexyl Methicone (CAS no. 1873-90-1) is the silicone polymer that conforms to the formula:



Hexyl Methicone

Synonyms for Hexyl Methicone include trisiloxane, 3-Hexyl-1,1,1,3,5,5,5-Heptamethyl- (Pepe, Wenninger, and McEwen 2002), and 1,1,1,3,5,5,5-Heptamethyl-6-Hexyltrisiloxane (IIT Research Institute 1994).

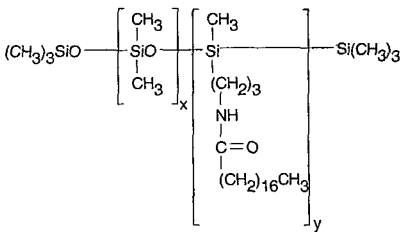
Hydroxypropyldimethicone (CAS no. 102782-61-6) is the silicone polymer that conforms generally to the formula:



Hydroxypropyldimethicone

A synonym is Siloxanes and Silicones, Dimethyl, 3-Hydroxypropyl Methyl (Wenninger, Canterbery, and McEwen 2000).

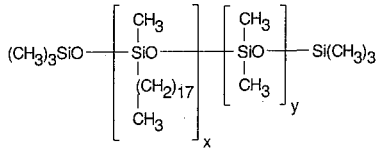
Stearamidopropyl Dimethicone is the silicone polymer that conforms to the formula (Wenninger, Canterbery, and McEwen 2000):



Stearamidopropyl Dimethicone

No synonyms for Stearamidopropyl Dimethicone were found.

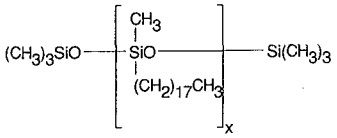
Stearyl Dimethicone is the silicone polymer that conforms generally to the formula (Wenninger, Canterbery, and McEwen 2000):



Stearyl Dimethicone

No synonyms for Stearyl Dimethicone were found.

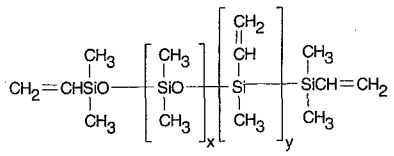
Stearyl Methicone is the silicone polymer that conforms to the formula (Wenninger, Canterbery, and McEwen 2000):



Stearyl Methicone

No synonyms for Stearyl Methicone were found.

Vinyldimethicone is a polymer of dimethylsiloxane containing vinyl functional groups. It conforms generally to the formula (Wenninger, Canterbery, and McEwen 2000):



Vinyldimethicone

The Registry of Toxic Effects of Chemical Substances (RTECS 1998) identifies "vinyl dimethylsiloxy-terminated polydimethylsiloxane" with the CAS no. 68083-19-2.

Physical and Chemical Properties

Dimethicone is a white, almost odorless fluid polymer. The Cosmetic, Toiletry, and Fragrance Association (CTFA) specifications for Dimethicone state that the color and odor are specified by the buyer. Also specified by the buyer are the refractive index at 25°C (within the range of 1.4000 to 1.4035), and the kinematic viscosity (provided that the specified mean viscosity at 25°C is not less than 20 centistokes [cs] and not greater than 60,000 cs, and that the specification limits are not greater than ±5% of the specified mean). It contains 98.5% to 101.1% Dimethicone and the total acid number is 0.01 maximum (Nikitakis and McEwen 1990).

One supplier of Dimethicone noted that 100 and 350 cs fluids are generally used for cosmetics (Dow Corning no date).

The National Formulary specifies that Dimethicone have a nominal viscosity in the discrete range between 20 and 12,500 cs and contain between 97.0% and 103.0% of polydimethylsiloxane. Minimum and maximum viscosity cs values were established for nominal viscosity cs values of 20, 100, 200, 350, 500, 1000, and 12500. The specific gravity ranged from 0.946 for the 20-cs nominal viscosity to 0.975 for the 1000-cs nominal viscosity (specific gravity values were not given for the 12500-cs nominal viscosity). The refractive index ranged from 1.3980 for the 20-cs nominal viscosity to 1.4055 for the 12500-cs nominal viscosity (Committee of Revision of the United States Pharmacopeial Convention 1995).

Method of Manufacture

Stearoxy Dimethicone is produced by the reaction of dichloropolydimethylsiloxane with stearyl alcohol (Goldschmidt Chemical Corp. 1998).

Dimethicone is produced by polymerization/equilibration (Goldschmidt Chemical Corp. 1998).

Cetyl Dimethicone is produced by hydrosilylation of C_{16} alpha-olefins (Goldschmidt Chemical Corp. 1998).

Stearyl Dimethicone is produced by hydrosilylation of C_{18} alpha-olefins (Goldschmidt Chemical Corp. 1998).

Manufacturing methods were not available for other ingredients.

Impurities

One supplier of these ingredients noted that Stearoxy Dimethicone, Dimethicone, Cetyl Dimethicone, and Stearyl Dimethicone contain no antioxidants or preservatives. Heavy metals are at 5 ppm maximum, and D4/D5 cyclomethicone is at less than 1% (Goldschmidt Chemical Corp. 1998).

USE

Cosmetic

The functions of Stearoxy Dimethicone and the related cosmetic ingredients are listed in Table 1. Almost all function as conditioning agents for either the hair or skin; the exceptions are Stearamidopropyl Dimethicone (corrosion inhibitor, film former) and Vinyldimethicone (chemical additive). In addition to being conditioning agents, Dimethicone and Cetyl Dimethicone also function as antifoaming agents. C24–28 Alkyl Methicone and C30–45 Alkyl Methicone are also viscosity-increasing agents—nonaqueous (Pepe, Wenninger, and McEwen 2002). One supplier noted that Stearoxy Dimethicone, Cetyl Dimethicone, and Stearyl Dimethicone are also used as "spreading agents" (Goldschmidt Chemical Corp. 1998).

Seven of the 20 ingredients were reported to the Food and Drug Administration (FDA) as in use in January 1998 (FDA 1998). These seven were used in a total of 1884 formulations (Table 2). Two uses of C14–20 polyalkylmethicone were also reported to the FDA, although this ingredient is not listed in the *International Cosmetic Ingredient Dictionary and Handbook* (Pepe, Wenninger, and McEwen 2002).

Recent data submitted to the Cosmetic Ingredient Review (CIR) from one source indicated use of Stearoxy Dimethicone at ≤3.0%, Dimethicone at ≤15%, Cetyl Dimethicone at ≤3.0%, and Stearyl Dimethicone at ≤5.0% (Goldschmidt Chemical

TABLE 1
Cosmetic function of Dimethicones and Methicones

Ingredient	Function[1]	Used in 1998[2]
Stearoxy Dimethicone	Skin-conditioning agent—emollient; spreading agent[3]	Yes
Dimethicone	Antifoaming agent; skin-conditioning agent—emollient	Yes
Methicone	Skin-conditioning agent—occlusive	
Amino Bispropyl Dimethicone	Hair-conditioning agent	
Aminopropyl Dimethicone	Hair-conditioning agent	
Amodimethicone	Hair-conditioning agent	Yes
Amodimethicone Hydroxystearate	Hair-conditioning agent	
Behenoxy Dimethicone	Skin-conditioning agent—emollient	Yes
C24–28 Alkyl Methicone	Skin-conditioning agent—emollient; viscosity increasing agent—nonaqueous	
C30–45 Alkyl Methicone	Skin-conditioning agent—occlusive; viscosity increasing agent—nonaqueous	
C30–45 Alkyl Dimethicone	Skin-conditioning agent—occlusive	
Cetearyl Methicone	Skin-conditioning agent—occlusive	Yes
Cetyl Dimethicone	Antifoaming agent; skin-conditioning agent—occlusive; spreading agent[3]	Yes
Dimethoxysilyl Ethylenediaminopropyl Dimethicone	Hair-conditioning agent	
Hexyl Methicone	Skin-conditioning agent—emollient	
Hydroxypropyldimethicone	Hair-conditioning agent; skin-conditioning agent—miscellaneous	
Stearamidopropyl Dimethicone	Corrosion inhibitor; film former	
Stearyl Dimethicone	Skin-conditioning agent—occlusive; spreading agent[3]	Yes
Stearyl methicone	Skin-conditioning agent—occlusive	
Vinyldimethicone	Chemical additive	

[1]Pepe, Wenninger, and McEwen 2002.
[2]FDA 1998.
[3]Goldschmidt Chemical Corp. 1998.

Corp. 1998). Concentration of use data provided by the CTFA are given in Table 2 (CTFA 1999).

Current concentrations of use may be compared with historical data from industry reports to FDA in 1984 in which Stearoxy Dimethicone was used at ≤5% (51 uses total), Dimethicone was used predominately at ≤25%, with one use at 25% to 50% (1012 uses total), Methicone was used in two formulations at ≤1% but also in one formulation at >50%, and Amodimethicone was used in nine products at unknown concentrations (FDA 1984).

According to the Ministry of Health, Labor and Welfare (MHLW) in Japan, Stearoxy Dimethicone, Dimethicone, Methicone, Amino Bispropyl Dimethicone, Aminopropyl Dimethicone, Amodimethicone, Amodimethicone Hydroxystearate, Behenoxy Dimethicone, C24–28 Alkyl Methicone, C30–45 Alkyl Methicone, C30–45 Alkyl Dimethicone, Cetearyl Methicone, Cetyl Dimethicone, Dimethoxysilyl Ethylenediaminopropyl Dimethicone, Hexyl Methicone, Hydroxypropyldimethicone, Stearamidopropyl Dimethicone, Stearyl Dimethicone, Stearyl Methicone, and Vinyldimethicone are not restricted in any manner in cosmetic formulations (MHLW 2001).

Stearoxy Dimethicone, Dimethicone, Methicone, Amino Bispropyl Dimethicone, Aminopropyl Dimethicone, Amodimethicone, Amodimethicone Hydroxystearate, Behenoxy Dimethicone, C24–28 Alkyl Methicone, C30–45 Alkyl Methicone, C30–45 Alkyl Dimethicone, Cetearyl Methicone, Cetyl Dimethicone, Dimethoxysilyl Ethylenediaminopropyl Dimethicone, Hexyl Methicone, Hydroxypropyldimethicone, Stearamidopropyl Dimethicone, Stearyl Dimethicone, Stearyl Methicone, and Vinyldimethicone are not listed in Annex II (list of substances that must not form part of the composition of cosmetic products) or Annex III (list of substances that cosmetic products must not contain except subject to the restrictions and conditions laid down) of the *Cosmetics Directive of the European Union* (European Commission, 2003).

TABLE 2
Product formulation data

Product category (number of formulations reported to FDA) (FDA 1998)	Number of formulations containing ingredient (FDA 1998)	Current concentration of use (CTFA 1999)
Stearoxy Dimethicone		
Eye shadow (506)	—	3%
Eye lotion (18)	—	2%
Hair spray (aerosol fixative) (261)	—	0.1%
Tonics, dressings, and other hair-grooming aids (549)	—	0.2%
Foundations (287)	—	0.7%
Lipstick (790)	—	3%
Face powders (250)	1	—
Makeup bases (132)	1	0.9%
Skin cleansing (653)	1	0.5%
Face and neck skin care (excluding shaving) (263)	3	2%
Body and hand skin care (excluding shaving) (796)	7	2%
Moisturizing creams, lotions, powders, and sprays (excluding shaving preparations) (769)	5	2%
Night skin care (188)	1	—
Other skin care preparations (692)	2	—
Suntan gels, creams, and liquids (136)	—	3%
1998 total for Stearoxy Dimethicone	21	
Dimethicone		
Baby lotions, oils, powders, and creams (53)	7	2%
Other baby products (29)	1	2%
Bath oils, tablets, and salts (124)	1	—
Bubble baths (200)	1	—
Other bath preparations (159)	4	—
Eyebrow pencil (91)	1	13%
Eyeliner (514)	6	1%–5%
Eye shadow (506)	55	1%–10%
Eye lotion (18)	5	0.5%–1%
Eye makeup remover (84)	2	4%
Mascara (167)	20	0.3%–4%
Other eye makeup preparations (120)	22	—
Colognes and toilet waters (656)	3	—
Sachets (28)	1	—
Perfumes (28)	—	16%
Other fragrance preparations (148)	30	5%–6%
Hair conditioners (636)	103	0.2%–10%
Hair sprays (aerosol fixatives) (261)	23	0.2%–0.6%
Hair straighteners (63)	1	—
Permanent waves (192)	2	—
Rinses (noncoloring) (40)	4	0.4%–3%
Shampoos (noncoloring) (860)	72	0.08%–4%
Tonics, dressings, and other hair-grooming aids (549)	28	1%–10%
Wave sets (55)	1	—
Other hair preparations (276)	15	10%–80%
Hair dyes and colors (1572)	1	—
Hair tints (54)	28	—

(Continued on next page)

TABLE 2
Product formulation data *(Continued)*

Product category (number of formulations reported to FDA) (FDA 1998)	Number of formulations containing ingredient (FDA 1998)	Current concentration of use (CTFA 1999)
Other hair-coloring preparations (59)	—	0.5%
Blushers (all types) (238)	86	3%–23%
Face powders (250)	87	0.3%–30%
Foundations (287)	122	1%–16%
Lipstick (790)	12	0.6%–20%
Makeup bases (132)	11	4%–23%
Rouges (12)	1	1%
Makeup fixatives (11)	2	24%
Other makeup preparations (135)	14	3%
Basecoats and undercoats (48)	3	0.001%
Cuticle softeners (19)	2	—
Nail creams and lotions (17)	4	0.6%–1%
Nail extenders (<4)	1	0.001%
Nail polish and enamel (80)	16	0.001%–3%
Other manicuring preparations (61)	10	—
Other oral hygiene products (6)	—	0.001%
Bath soaps and detergents (385)	6	0.5%–0.8%
Deodorants (underarm) (250)	9	0.5%–23%
Other personal cleanliness products (291)	30	3%
Aftershave lotion (216)	18	0.5%–2%
Preshave lotions (all types) (14)	1	—
Shaving cream (139)	8	0.5%–1%
Other shaving preparation products (60)	5	3%
Cleansing (653)	43	0.07%–3%
Depilatories (28)	—	0.5%–3%
Face and neck skin care (excluding shaving) (263)	63	0.0001%–10%
Body and hand skin care (excluding shaving) (796)	228	0.5%–10%
Foot powders and sprays (35)	8	—
Moisturizing (769)	200	0.5%—10%
Night skin care (188)	41	1%–2%
Paste masks (mud packs) (255)	13	2%
Skin fresheners (184)	2	0.3%–5%
Other skin care preparations (692)	111	5%
Suntan gels, creams, and liquids (136)	27	1%–15%
Indoor tanning preparations (62)	29	1%–5%
Other suntan preparations (38)	9	4%
1998 total for Dimethicone	1695	
Amodimethicone		
Colognes and toilet waters (656)	1	—
Hair conditioners (636)	67	0.7%–3%
Hair sprays (aerosol fixatives) (261)	2	—
Hair straighteners (63)	2	0.6%
Permanent waves (192)	18	—
Rinses (noncoloring) (40)	1	—
Shampoos (noncoloring) (860)	5	—
Tonics, dressings, and other hair-grooming aids (549)	9	0.0004%–0.7%

(Continued on next page)

TABLE 2
Product formulation data (*Continued*)

Product category (number of formulations reported to FDA) (FDA 1998)	Number of formulations containing ingredient (FDA 1998)	Current concentration of use (CTFA 1999)
Other hair preparations (276)	17	—
Hair dyes and colors (1572)	41	—
Hair bleaches (113)	1	—
Other hair-coloring preparations (59)	1	2%
Hair lighteners with color (6)	1	—
Wave sets (55)	—	0.7%
1998 total for Amodimethicone	166	
Behenoxy Dimethicone		
Foundations (287)	—	2%
Face and neck creams, powders, lotions and sprays (excluding shaving preparations) (263)	—	2%
Paste masks (mud packs) (255)	—	3%
Hair conditioners (636)	1	—
Other hair preparations (276)	2	—
Suntan gels, creams, and liquids (136)	—	2%
1998 total for Behenoxy dimethicone	3	
C14–20 Polyalkylmethicone[a]		
Eyebrow pencil (91)	1	—
Lipstick (790)	1	—
1998 total for C14-20 Polyalkylmethicone	2	
C24–28 Alkyl Dimethicone		
Lipstick (790)	—	2%
1998 total for C24–28 Alkyl Methicone	—	
C30–45 Alkyl Dimethicone		
Suntan gels, creams, and liquids (136)	—	2%
1998 total for C30–45 Alkyl Methicone	—	
Cetearyl Methicone		
Face and neck creams, powders, lotions and sprays (excluding shaving preparations) (263)	—	0.5%
Lipstick (790)	1	0.6%–1%
1998 total for Cetearyl Methicone	1	
Cetyl Dimethicone		
Eye shadow (506)	1	—
Mascara (167)	2	0.5%
Other eye makeup preparations (120)	2	—
Tonics, dressings, and other hair-grooming aids (549)	1	—
Blushers (all types) (238)	5	4%–10%
Face powders (250)	2	0.9%–3%
Foundations (287)	2	6%
Lipstick (790)	—	4%–5%
Makeup bases (132)	4	—
Other makeup preparations (135)	2	4%
Cleansing (653)	1	—
Face and neck skin care (excluding shaving) (263)	1	—
Body and hand skin care (excluding shaving) (796)	1	2%
Moisturizing (769)	2	—

(Continued on next page)

TABLE 2
Product formulation data (*Continued*)

Product category (number of formulations reported to FDA) (FDA 1998)	Number of formulations containing ingredient (FDA 1998)	Current concentration of use (CTFA 1999)
Suntan gels, creams, and liquids (136)	—	2%
Other suntan preparations (38)	1	—
1998 total for Cetyl Dimethicone	27	
Stearyl Dimethicone		
Mascara (167)	2	0.8%
Eye shadow (506)	—	1%–6%
Makeup bases (132)	—	6%
Makeup fixatives (11)	—	5%
Foundations (287)	1	1%–6%
Lipstick (790)	2	4%–6%
Blushers (all types) (238)	—	6%
Moisturizing (769)	1	—
Paste masks (mud packs) (255)	1	—
Other skin preparations (692)	—	4%
Suntan gels, creams, and liquids (136)	—	4%
1998 total for Stearyl Dimethicone	7	
Methicone		
Baby lotions, oils, powder, and creams (53)	—	0.3%
Eyebrow pencil (91)	—	0.2%–0.9%
Eyeliner (514)	—	0.05%–0.8%
Eye shadow (506)	—	0.05%–0.9%
Eye makeup remover (84)	—	0.05%
Mascara (167)	—	0.1%–0.2%
Other eye makeup preparations (120)	—	0.02%
Other hair coloring preparations (59)	—	0.3%
Blushers (all types) (238)	—	0.5%–0.9%
Face powders (250)	—	0.08%–5%
Foundations (287)	—	0.03%–2%
Lipstick (790)	—	0.06%
Makeup bases (132)	—	0.7%
Makeup fixatives (11)	—	0.6%
Other makeup preparations (135)	—	0.01%
Nail polish and enamel (80)	—	0.009%
Body and hand skin care (excluding shaving) (796)	—	0.3%
1998 total for Methicone	0	

[a]C14–20 Polyalkylmethicone is not listed in the *International Cosmetic Ingredient Dictionary and Handbook* (Wenninger, Canterbery, and McEwen 2000).

Noncosmetic

Food

In 1979, the Joint Expert Committee on Food Additives (JECFA) of the WHO established an acceptable daily intake (ADI) level for Dimethicone of 0 to 1.5 mg/kg body weight. The ADI applied, "only to compounds with a relative molecular mass in the range of 200–300" (FAO/WHO 1994).

The Select Committee of GRAS Substances (SCOGS) of the Federation of American Societies for Experimental Biology (FASEB) evaluated the safety of Dimethicone (under the name methylpolysilicones) for food use. The Select Committee was of the opinion:

> The bulk of food grade methylpolysilicones consists of high molecular weight compounds which are not absorbed to any appreciable extent from the intestinal tract. However, these silicones may also contain some low molecular weight (<1000) polymers which might be absorbed. Prudence dictates that food grade specifications should be modified to minimize the presence of absorbable components.

The Select Committee concluded that there was no evidence that demonstrated or suggested grounds to suspect that Dimethicone was hazard to the public when used at levels, "that are now current or that might be reasonably expected in the future." At the time, daily intake was estimated at 0.1 μg/kg/body weight (FASEB 1981).

The FDA has included "siloxanes and silicones, dimethyl . . ." as acceptable defoaming agents in the manufacture of paper and paperboard for use in packaging, transporting, or holding food. The regulation appears in the Code of Federal Regulations (CFR) at 21 CFR §176.210.

Pharmaceutical

The FDA has proposed classifying Dimethicone as Category 1 (recognized as safe and effective) for use as a skin protectant up to 30% in infants, children, and adults with the labeling: *Warning. Not to be applied over puncture wounds, infections, or lacerations* (FDA 1978). The FDA has also proposed Dimethicone as Category 1 in the treatment and prevention of diaper rash (FDA 1990).

At one time, Dimethicone was used in antacid formulations (Locock 1971). Now, simethicone (not contained in this report) is used (Harvey 1990).

GENERAL BIOLOGY

Dimethicone Absorption and Excretion

Oral Delivery—Animal Studies

Dow Corning Corp. (1956) orally administered an antifoam compound containing 28% [^{14}C]-Dimethicone to two lactating dogs (25 g given to ~9-kg animals) and one albino rat (0.58 g given to ~170-g animal, sex not given). No evidence of assimilation was observed in the rat. Traces of siloxanes were found throughout the body of both dogs. It was estimated that 0.0001% of the dose had been absorbed from the gastrointestinal (GI) tract.

The University of Birmingham (1968) reported a study in which four beagle dogs (two of each sex) were fed an antifoam compound (91% Dimethicone) at a dose of 300 mg/kg/day for 120 days. The material was mixed with a small amount of meat and given prior to the main meal to ensure that all of the dose was eaten. Total silicon consumption was between 300 and 500 g. A control group received untreated feed. Urine and feces were collected periodically. At the end of dosing, dogs were fed untreated feed for 5 days and then killed. Blood samples were taken and major organs were weighed and examined for microscopic and histopathologic changes and for silicon content. Average output of urinary silicate was not increased in treated dogs. Fecal silicon output was approximately equal to the amount ingested. Silicon was not detected in any organ. One dosed male had a healed gastric ulcer. The spleen of one dosed female had areas of atrophy with wide fibrous trabeculation. The other treated female had a slightly reddened rugae in an area of the stomach and adherent mucus in the intestine, but was microscopically normal. The antifoam compound was considered not absorbed by beagle dogs.

Dow Corning Corp. (1972a) gave a 41.8-mg/kg oral dose of [^{14}C]-Dimethicone (360 fluid with a specific activity of 0.5 mCi/g) to a male rhesus monkey. The animal was held in a unit that prevented respiratory air from being contaminated with volatile products from feces and urine. Air, feces, and urine were analyzed. Virtually all radioactive label was found in the feces. By 70.5 h after dosing, 65.4% of the dose was recovered in the feces. An additional 27.3% of the dose was recovered over the next hour, with only trace amounts after that. Analysis of toluene extracts of the fecal samples established that Dimethicone was excreted unchanged.

Dow Corning Corp. (1989a) gave male Sprague-Dawley rats a single oral dose of [^{14}C]-Dimethicone fluid (either 35 or 1000 cs, with unspecified specific activity) at either 250 or 2500 mg/kg. In a repeated-dose study, rats were fed 0.5% or 5.0% Dimethicone for 13 days followed by a single oral dose of the radioactive Dimethicone at either 250 or 2500 mg/kg. Plasma, excreta, organs, and tissues were collected at 4, 8, 24, and 48 h post dosing and analyzed for radioactivity via liquid scintillation spectrophotometry. Most of the test material was found in the GI tract at 4 and 8 h and in the feces at 24 and 48 h after administration of [^{14}C]-Dimethicone fluid. Anal leakage was observed with the 35 cs fluid at the 2500-mg/kg dose. Trace activity was detected in the urine and scattered tissue samples until 8 h; no activity was detected in tissues or organs at 48 h. Dimethicone was considered to be rapidly excreted from the GI tract following gavage.

Oral Delivery—Human Studies

In a report from the University of Birmingham (1967a), four subjects were instructed to ingest a capsule containing 376.5 mg silicone (an antifoam product containing 91% Dimethicone) twice a day for 10 days. Two subjects completed the protocol. Daily fecal samples were collected from the two during the last 3 days of the dosing period, and 24-h urine samples were collected from all four during the last 5 days. Fecal analysis detected a silicone output that was slightly greater than the intake. The authors considered that the short sampling time had not established a quanitative balance between oral intake and fecal output. No significant increase in soluble silicate was detected in the urine. In studies with other species, the authors stated that almost 99% and 82.5% of the administered silicone was recovered in the 4-day feces of rats and rabbits, respectively. They concluded that Dimethicone was unlikely to be absorbed from the GI tract of humans, rats, and rabbits.

Dow Corning Corp. (1974) studied the absorption and elimination of silicon contained in two Dimethicone antifoam preparations in human tests. Each of the two samples was given as a single oral dose of 100 mg/kg to six humans or as a single dose (100 mg/kg) of an emulsion (30 mg/kg solids) to five humans. Total and organosoluble urinary silicon output (for 72 h post administration) and organosoluble silicon output in expired

air (8-h value) were measured. The compound that contained <0.22% low-molecular-weight polymers (in 91% Dimethicone) did not produce a significant increase in total or organosoluble urinary silicon. Further, no organosilicon compounds were detected in the expired air. An increase in all three parameters was observed with the second compound, which contained 10% low-molecular-weight polymers (in 93% Dimethicone). The urine contained 1.8% and 3.3% of the administered dose of the compound and emulsion, respectively. The expired air contained approximately 0.25% of the given dose. It was suggested that the increased silicon concentrations found with the second Dimethicone sample represented organosoluble silicon rather than inorganic silicon (silica). Approximately 25% of the urinary silicon was an unidentified form of a soluble organosilicon compound. The exhaled material contained primarily octamethylcyclotetrasiloxane and small amounts of decamethylcyclopentasiloxane.

Dermal Delivery—Human Studies

Hobbs, Fancher, and Calandra (1972) applied a 100 cs Dimethicone fluid (TX-225) once daily (50 mg/kg) to the back of five Caucasian males for 10 days. The material was evenly distributed over the entire back surface and no special covering was required. After 20 h of exposure, the excess material was rinsed off. Daily logs of diet were maintained and subjects were asked to refrain from eating raw leafy vegetables during the study. Subjects provided samples of home drinking water and beer, so that dietary silicon contributions could be quantified.

Absorption was measured as silicon in blood and urine. Baseline concentrations were established for several days (up to 25) prior to dosing. Samples were taken on days 1, 3, 6, 8, and 10 during the dosing period. No significant difference between pretest and test urinary silicon concentrations were found in four subjects. One subject had increased urinary silicon ($p = 0.05$) that was attributed to a large value on day 10, accompanied by large urine output on that day. Another two subjects had consistently greater total urinary silicon concentrations throughout the study compared to other subjects. The finding was attributed to relatively high concentrations of silicon in the subjects' home drinking water, high beer intake, and generally greater urine output. Statistical analysis of group data indicated no significant increase in urine silicon concentrations. No increase in blood silicon concentrations was noted in any subjects. The investigators concluded that there was no evidence of dermal absorption of Dimethicone (Hobbs, Fancher, and Calandra 1972).

Absorption Enhancement by Dimethicone

Two clinical studies investigated the effects of various lipophilic vehicles on the skin penetration of methyl nicotinate. Dimethicone 100 was selected as the standard because it was not expected to exert "specific vehicle effects" due to its high molecular weight (6700 Da). As expected, Dimethicone did not alter drug penetration (Leopold and Lippold 1995; Leopold and Maibach 1996).

ANIMAL TOXICOLOGY

Acute Oral Toxicity

Dimethicone

The acute oral LD_{50} values for various Dimethicone samples, summarized in Table 3, are consistent with the conclusion that Dimethicone is not acutely toxic.

Methicone

Methicone (as L-31) had an oral LD_{50} of >64 ml/kg in male albino rats. No deaths occurred in five rats given that dose (Mellon Institute 1993).

Vinyldimethicone

A substance identified as "vinyl dimethylsiloxy-terminated polydimethylsiloxane" (CAS no. 68083-19-2) had an oral LD_{50} of >16.0 ml/kg in 10 Sprague Dawley rats. Greasy-textured fur was noted. One rat had pneumonia, and pleuritis was observed at necropsy (Myers and Ballantyne 1993).

Short-Term Oral Toxicity

Dimethicone

MacDonald, Lanier, and Deichmann (1960) fed groups of 50 Sprague-Dawley rats (10 of each sex) 1% Dimethicone at one of five viscosities, 30, 350, 1000, 10000, and 60000 cs, for 90 days. A control group received untreated feed. Rats were killed after the dosing period and examined for gross lesions. Feed consumption, weight gain, hematological parameters (total and differential leukocyte counts, hematocrit, and hemoglobin measured on days 45 and 90), organ weights (heart, lungs, liver, spleen, kidneys, and testes), microscopic examination (spleen, kidneys, liver, testes/ovaries, uterus, aorta, stomach, intestines) were similar between dosed and control rats. One rat of the 60,000-cs group had an aggregation of leukocytes in the myocardium of the right ventricle of the heart. Varying degrees of inflammation were noted in the lungs.

In a study at the University of Birmingham (1967b), groups of 20 rats (10 of each sex) were fed 0.1% or 1% of an antifoam preparation containing 91% Dimethicone for 90 days. It was estimated that rats consumed almost 22.5 g of the compound during the dosing period. Rats were then transferred to a control diet and a 24-h urine specimen was collected for silicate content analysis. Rats were killed after 2 weeks of feeding the control diet and were necropsied. Blood samples were taken from the caudal vein and the lungs; any detectable lymphoid tissue was examined microscopically. The liver, kidneys, spleen, testes, and intestine were analyzed for silicone content.

No significant differences were observed in body weight gain, serum parameters (sodium, potassium, serum glutamic oxaloacetic transaminase [SGOT], serum pyruvic glutamic transaminase [SPGT], total protein, albumin, globulin, hemoglobin concentration, packed cell volume [PCV], total white cells, polymorphonuclear leukocytes, eosinophils, lymphocytes, and monocytes), urine-concentrating ability, protein content,

TABLE 3
Acute oral toxicity of Dimethicone

Dimethicone sample	Oral LD_{50}	Reference
	Mice	
35% aqueous dispersion as TX 184A and 184B	>10.0 ml/kg	Hill Top Research 1967
	Rats	
3.26% in a caulking compound	26.85 g/kg	Food and Drug Research Labs 1978
3.26% in a caulking compound	>17.22 g/kg (approximate) Substance blocked airways	Food and Drug Research Labs 1979a
6.9% in rubber adhesive sealant	>8.49 g/kg (approximate) Substance blocked airways	Food and Drug Research Labs 1979b
15% in emulsion	12.3 ml/kg (males) 6.50 ml/kg (females)	Bushy Run Research Center 1984
15.7% in a rubber adhesive sealant	23.12 g/kg (approximate) Substance blocked airways	Food and Drug Research Labs 1980
15.7% in caulking	6.98 g/kg	Food and Drug Research Labs 1981
35.0% in emulsion	>40 ml/kg	Food and Drug Research Labs 1977a
38.0% in emulsion	>40 ml/kg	Food and Drug Research Labs 1977b
50% aqueous dispersion	>10.0 ml/kg	Dow Corning Corp. 1972b
81.8% in a putty	21.2 g/kg	Food and Drug Research Labs 1977c
85.8% in putty	19.9 g/kg	Food and Drug Research Labs 1977d
85.8% in a putty (given as a 75% suspension in 95% ethanol)	31.9 g/kg (discounting ethanol effects)	Food and Drug Research Labs 1977e
XF-1-3753	>10.0 g/kg	Dow Corning Corp. 1970
XF-2-1075	>15.4 g/kg	Dow Corning Corp. 1975
X2-1133 heat-transfer fluid	≥15.4 g/kg	Dow Corning Corp. 1977
X2-1162 heat-transfer fluid	≥15.4 g/kg	Dow Corning Corp. 1978a
Heat-transfer fluid	≥15.4 g/kg	Dow Corning Corp. 1978b
Trade compound (>90% Dimethicone)	>17 g/kg	Springborn Labs 1991
	Guinea pigs	
Two 35% aqueous dispersions	>30.0 g/kg	Dow Corning Corp. 1949
Two 35% aqueous emulsions	>10.0 g/kg	Dow Corning Corp. 1950

silicate concentration, or organ weight. Male rats of the 1% group weighed significantly more ($p < 0.05$) than controls at the time of necropsy. No changes were noted at microscopic examination. Silicone was not detected in the spleen, kidneys, liver, testes, or intestine (University of Birmingham 1967b).

Atlas Chemical Industries (1969) fed an antifoam compound containing 95% Dimethicone to groups of six dogs (three of each sex) at concentrations of 120, 380, or 1200 mg/kg/day for 90 days. Body weight gain, serum chemistry parameters (urea, nitrogen, glucose, sodium, potassium, chloride, cholesterol, alkaline phosphatase, and SGOT), hematology parameters (PCV, hemoglobin, sedimentation rate, leukocyte count, differential count, and plasma prothrombin time [PTT]), urinary parameters, and gross and microscopic examination of tissues and organs were similar to controls groups.

Dow Corning Corp. (1972c) described Dimethicone fluids that contain low-molecular-weight linear and cyclic dimethylpolysiloxanes as "ubiquitous trace components" and conducted a study of the effects of a 4-week oral exposure to 20-cs Dimethicone fluid using rats. The study measured changes in organ weight, thyroid function, and tissue elemental silicon accumulation. Rats were fed either the 20 cs fluid containing not more than 0.04% linear/cyclic dimethylpolysiloxanes (where number of Si atoms ≤ 6) or a "spiked" solution containing 5% each of four linear/cyclic dimethylpolysiloxanes. Controls were sham-dosed. No changes were noted with respect to final body weights or organ weights. Whole body oxygen consumption was not altered by treatment. Changes were seen in serum total cholesterol concentrations, but were not consistent with regard to compound, sex, or route of administration. The authors observed that females accumulated more organosiloxane-derived silicone in depot fat than males. Administration of cyclic compounds resulted in greater fat silicone concentrations in fat compared to administration of linear compounds.

Dow Corning Corp. (1989b) investigated silicon oil as a low-calorie alternative to traditional edible oils. Groups of 30 CD-1 mice (15 of each sex) were fed diets containing 5% and 10% Dimethicone fluid for 90 days. A control group received

untreated feed. Mice were killed at the end of dosing and major organs were collected, weighed, and examined for microscopic lesions. No signs of toxicity, changes in behavior, or mortality were seen in any group. Mean body weights were comparable between treated and control mice. Treated mice consumed significantly more feed; the increased intake was considered to compensate for the non-nutritive components of the diet. Anal leakage was observed in treated mice and was greatest in females of the 10% group, but stool consistency was similar to controls. Organ weights were similar and no microscopic lesions were observed.

At the Dow Corning Corp. (1989c), groups of 40 Sprague-Dawley rats (20 of each sex) were fed 1%, 5%, or 10% Dimethicone at one of three viscosities, 35, 350, and 1,000 cs (total of nine treatment groups) for 90 days. Two control groups received untreated feed. Blood samples were obtained by cardiac puncture from 20 rats of each group (10 of each sex) and urine was collected from 10 of these 20 rats (5 of each sex) at the end of the study. All rats were killed and major organs were collected, weighed, and examined for microscopic lesions.

No signs of toxicity or changes in behavior were observed. One control female and two treated male rats were moribund and were killed. The authors did not consider the deaths treatment related. Slight-to-marked anal leakage was observed in rats of the 10% group; leakage decreased with increasing viscosity. Slight leakage was also observed in rats of the 5% group. Stool consistency was similar to controls. Although occasionally body weight increase was significantly greater in treated male rats, most of the mean body weight data was comparable between treated and control groups. Treated rats consumed more feed and, as in the mouse study, the finding was considered a compensatory response to the non-nutritive components of the diet.

Changes in blood, clinical chemistry, bone marrow, or urinary parameters were observed occasionally but were not considered biologically significant. Some mean absolute and relative organ weights were significantly different between treated and controls, but the findings were not considered of biological or toxicological significance.

Treatment-related changes were observed in the eyes (corneal opacities and neovascularization). Some rats also had mineralization of the cornea. Mild chronic inflammation of the cornea was observed microscopically. The ocular findings were not dose dependent and could have resulted from direct irritation from the Dimethicone fluid in the feed. Three lymphomas were observed in treated males (two lymphocytic lymphomas in the 10%, 1000-cs group, and one undifferentiated lymphoma in the 1%, 35-cs group). The neoplasms were not considered treatment related because the incidence was within that of the historical control and the incidence was not duplicated in the follow-up study (described below) using a larger group of rats (Dow Corning Corp. 1989c).

Because of the lymphomas seen in the study described above, male rats were selected for further study (Dow Corning Corp. 1989d). Groups of 100 were fed 10% Dimethicone fluid at one of three viscosities (35, 350, and 1000 cs) for 90 days. Two control groups received untreated feed. At the end of dosing all rats were killed, major organs and blood were collected and examined for microscopic and hematologic changes. No overt signs of toxicity or behavioral changes were observed. Two treated rats were killed; one was moribund. A statistically significant difference in mean body weight was observed between rats of the 35-cs group and one control group, but was not considered treatment related. Like earlier studies, treated rats had significantly greater mean feed consumption. No significant changes were observed in hematology parameters or at necropsy and histopathologic examination.

Subchronic Oral Toxicity

Dimethicone

Child, Paquin, and Deichmann (1951) reported a study in which groups of two mongrel dogs were fed Dimethicone (83% in an antifoam compound) at 0.3, 1.0, or 3.0 g/kg/day in ground horse meat 5 days per week for 3 months. A control group was fed untreated horse meat. Afterwards, dogs were fed the Dimethicone in commercial dog food for another 3 months. Dogs were killed at the end of the study; organs and tissues were weighed and examined for microscopic lesions. Both dogs of the 3.0-g/kg group had a thin layer of viscid, gray material covering the intestinal tract and enlarged lymphoid aggregates of the small intestine. The liver of dosed dogs had pigment deposits that were revealed to be bile; quantities deposited in the Kupffer and hepatic cells were directly related to the daily dosing. The authors concluded that the antifoam compound would be harmless should traces be absorbed by humans "from time to time."

Dow Corning Corp. (1954a) fed an antifoam compound (83% Dimethicone) in an emulsion to rats at concentrations of 0.1%, 0.3%, and 1.0% for 120 days. No adverse effect was noted in growth, appearance, behavior, mortality, hematologic parameters, or blood urea nitrogen (BUN). An increase in the spleen and liver weight was noted in rats of the 1.0% group.

Chronic Oral Toxicity

Dimethicone

Rowe, Spencer, and Bass (1950) fed 0.3% (by weight) Dimethicone antifoam compound to groups of 50 Wistar rats (25 of each sex) for 2 years. A control group received untreated feed. Rats were killed at the end of the study. Gross appearance, behavior, growth, and survival were comparable between treated and control animals. Treated rats had greater weight gains compared to controls. No significant differences were observed in the weights of the heart, liver, kidneys, spleen, and testes. BUN and hepatic lipid values were comparable. At microscopic examination, pulmonary lesions, changes in the ovaries and uterus, and mild fatty changes in the liver and tubular epithelium of the kidneys were observed in all treated rats.

Carson, Weinberg, and Oser (1966) fed Dimethicone, as it appeared in a fluid (50 or 350 cs) or in an antifoam compound, as 1% of the diet to groups of rats (for 1 year) and rabbits (for 8 months). The number of animals was not stated. Control groups received untreated feed. Feed and water were available ad libitum. Blood and urine samples were taken periodically. Necropsy was done at the end of dosing. No adverse effects were observed. At the same time, additional groups of rats and rabbits received Dimethicone plus 0.8% cholesterol. The control group for this portion of the study received the cholesterol-supplemented feed. Adverse effects were observed in animals fed cholesterol (both with and without Dimethicone) compared to basal controls. The changes were attributed to the cholesterol.

Acute Dermal Toxicity

Dimethicone

Bushy Run Research Center (1984) reported that a commercial emulsion containing 15% Dimethicone had a dermal LD_{50} of approximately 16.0 ml/kg in rabbits. At that dose, Dimethicone killed 2/5 males and 2/5 females. A Dimethicone dose of 8.0 ml/kg killed 1/5 males and 0/5 females.

Hazleton France (1988a) applied a colorless slightly viscous liquid containing Dimethicone (2008 mg/kg; 2.07 ml/kg volume applied) to the clipped skin of 10 Sprague-Dawley rats (5 of each sex). The exposure area was approximately 10% of the total body surface. The concentration of Dimethicone in the liquid was unreported. The site was covered for 24 h of exposure and then rinsed with water. Observations were made at 15 min, 1 h, 2 h, 4 h, and then once daily for 14 days. Necropsy was done at the end of the study. No adverse reactions were noted. The dermal LD_{50} was >2008 mg/kg.

Springborn Labs (1991) applied a trade mixture (containing >90% Dimethicone) in a single dermal application (2000 mg/kg) to a group of 10 rabbits (5 of each sex). Rabbits were killed on day 15 and necropsied. Decreased feed consumption, diarrhea, mucoid/soft stool, and application site dermal irritation were observed. No changes were noted at necropsy. The acute dermal LD_{50} was >2000 mg/kg.

Methicone

Methicone (as L-31) had a dermal LD_{50} of >20 ml/kg in albino rabbits. The dose was the maximum amount of fluid that could be kept in contact with the skin under impervious covering. At that dose (24-h contact), none of four rabbits died and no irritation was noted (Mellon Institute 1993).

Vinyldimethicone

A substance identified as "vinyl dimethylsiloxy-terminated polydimethylsiloxane" (CAS no. 68083-19-2) had a dermal LD_{50} of >16.0 ml/kg in New Zealand white rabbits. The rabbits (five of each sex) had received a 24-h occlusive exposure to the single dose and were observed for 14 days. Erythema and edema were noted, but no signs of systemic effects were observed. No gross lesions were noted at necropsy (Myers and Ballantyne 1993).

Short-Term Dermal Toxicity

Dimethicone

Dow Corning Corp. (1969) reported that three formulations intended for application to the feet, containing 6%, 11%, or 25% Dimethicone, were applied daily (2000 mg/kg) to clipped sites on male rabbits for 7 days. A control group was treated with a formulation containing 22% Dimethicone. Another control group was left untreated. Rabbits were killed at the end of the study and observed for gross lesions. No adverse reactions, effects on body weights, or pathologic changes were noted.

As described earlier, Dow Corning Corp. (1972c) conducted a study of the effects of a 4-week oral exposure to 20-cs Dimethicone fluid using rats. Rats also were dermally dosed with either the 20 cs fluid containing not more than 0.04% linear/cyclic dimethylpolysiloxanes (where number of Si atoms $\leq$ 6) or a "spiked" solution containing 5% each of four linear/cyclic dimethylpolysiloxanes. Controls were sham-dosed. The study measured changes in organ weight, thyroid function, and tissue elemental silicon accumulation. No changes were noted with respect to final body weights or organ weights. Whole body oxygen consumption was not altered by treatment. Changes were seen in serum total cholesterol concentrations, but were not consistent with regard to compound, sex, or route of administration. Dermal dosing resulted in less silicon accumulation in the fat than did oral administration.

Acute Inhalation Toxicity

Dimethicone

Hazleton Labs (1953) exposed two dogs, seven guinea pigs, and seven rats to a "200 fluid" aerosol (containing unspecified concentration of Dimethicone) at a concentration of 2.12 mg/L for 6 h. No particle size was reported. Three guinea pigs died during the study. At the end of dosing, almost all of the animals were killed for necropsy and collection of tissues. One dog was observed for an additional month before it was killed. Hyperventilation, excitability, and salivation were noted during exposure. All animals killed immediately after dosing had hyperemic lungs with hemorrhagic areas. At microscopic examination edema, hemorrhage, and mild interstitial irritation of the lungs were found. The dog killed 1 month later had small areas of dark coloration of the lungs, but microscopic findings were similar to those found in animals that had been immediately killed. The authors concluded that this fluid produced only minimal signs of toxicity and was essentially nontoxic.

Methicone

Methicone (as L-31) generated as a concentrated vapor caused no mortality when six female albino rats were exposed for 8 h. The calculated concentration was 0.78 mg/L. Rats appeared normal throughout the subsequent 2-week observation

period and no remarkable lesions were noted at necropsy. No further details were given (Mellon Institute 1993).

Hexyl Methicone

Aerosolized Hexyl Methicone was administered by whole-body inhalation exposure to groups of 10 Fischer F344/N rats (5 of each sex) for a 4-h exposure. The initial target dose was 5.0 mg/L (5.08 mg/L achieved) with particles having a mass median aerodynamic diameter (MMAD) of 0.27 μm. All exposed rats died within 24 h. A second exposure was done using a 2.0 mg/ml dose with an MMAD of 0.29 μm. Four males died within 2 h of exposure; the remaining six rats survived the 14-day observation period. A third exposure was then conducted with a targeted dose of 1.0 mg/L (0.95 mg/L achieved), with an MMAD of 0.27 μm. Two males died immediately after the exposure; the remaining rats survived through the observation period. Dyspnea and decreased activity or hypoactivity were clinically observed in surviving rats immediately after exposure. Lesions at necropsy of rats that died included dark red or mottled lungs and/or fluid filled trachea; no unusual findings were noted at necropsy of rats that had survived the observation period. The calculated LC_{50} was 1.12 mg/L for males, between 2.0 and 5.0 mg/L for females, and 1.8 mg/L for the combined sexes (IIT Research Institute 1994).

Vinyldimethicone

Sprague Dawley rats were placed in a sealed chamber and exposed for 6 h to a near-saturation vapor of a substance identified as "vinyl dimethylsiloxy-terminated polydimethylsiloxane" (CAS no. 68083-19-2). No particle size was reported. Rats were observed for 14 days after exposure. No deaths or gross lesions were observed. No further details were provided (Myers and Ballantyne 1993).

Short-Term Dermal Toxicity

Dimethicone

A cat, rabbit, guinea pig, two rats, and four mice were sprayed for 4 hours with an atomizer containing 10 ml/kg of a Dimethicone sample. The sample contained approximately 110 siloxane units and its viscosity was 140 cs at 20°C. No particle size was reported; but the atomizer output was described as a thick fog that settled rapidly on the animals and the cage. The treatment was repeated 29 days later. The cat, rabbit, guinea pig, and rats had no adverse effects from the exposure. Weight gain was normal during the exposure and 6-week postdosing observation periods, the urine was free from protein, and the blood had no changes in hemoglobin content or in erythrocyte and leukocyte counts. All four mice died. The first died after 20 exposures and the others died during the postdosing period. None were examined microscopically. The authors stated that there was a relatively high mortality rate in mice in the laboratory at the time and that the link between the treatment and deaths was not certain. Overall, the authors concluded that inhalation of silicone oil was harmless (Gloxhuber and Hecht 1955).

Vaginal Irritation

Dimethicone

A mucoadhesive paste (53% Dimethicone) was introduced (0.5 g) via syringe into the vaginal cavity of six albino rabbits. Two control rabbits were dosed with a sodium chloride solution. Tissue was scored according to the Draize scale (maximum score of 8) at 24, 48, and 72 h post dosing. Erythema was noted in three rabbits at 24 h, and in one rabbit at 48 h after treatment. None had erythema at 72 h. No edema or signs of toxicity were observed. The irritation score for the paste was 0.22 (Toxikon Corp. 1991).

Dermal Irritation

Dimethicone

Hazleton Labs (1975) reported a preliminary skin irritation study using six adult albino rabbits (species/sex not stated). A Dimethicone fluid (0.5 ml) was applied for 24 h under occlusive patches to an intact and abraded site (clipped of hair) on each of two rabbits. Sites were scored for erythema and edema at the time of patch removal (24 h) and again 48 h later. The maximum score was 8.0. The authors reported a primary irritation index (PII) of 6.54 and concluded that the material was a severe irritatnt to rabbit skin.

CTFA (1977a) reported no reactions when a Dimethicone sample (100%) was applied in a 24-h patch to the clipped backs of eight rabbits, four with abraded backs.

Dow Corning Corp. (1978a) evaluated intact and abraded sites on rabbits exposed to three heat-transfer fluids (for industrial use) at 24 and 72 h (presumably on a 0–8 scale). The protocol used to test was not reported. The three fluids had PII scores of 0.1, 0.0, and 0.0, respectively (Dow Corning Corp. 1977, 1978a, 1978b). Based on unreported findings, the investigators stated that one fluid, "may be absorbed through the skin in acutely toxic amounts" and recommended dermal absorption toxicity testing.

The Bushy Run Research Center (1984) reported that a 4-h occlusive exposure to 0.5 ml of a commercial emulsion (15% Dimethicone) produced moderate erythema in all six rabbits tested and minor-to-moderate edema in four. The erythema persisted in most of the rabbits for 10 days (rabbits were observed for 21 days). Desquamation developed within 7 days. One rabbit died on day 21; the death was not considered treatment related.

Hazleton France (1989) applied AK 350 (containing an unreported amount of Dimethicone) for 4 h on each of two sites on six New Zealand white rabbits. No irritation was reported at the 1 h scoring or the 72 h scoring.

Springborn Labs (1991) reported a study in which a trade mixture (containing >90% Dimethicone) were applied for 4 h on each of two sites on six New Zealand white rabbits. Slight-to-well-defined erythema and very slight edema was observed at almost all test sites at the 1-h scoring. The irritation diminished with time and had cleared by the 72 h scoring (last scoring). The calculated PII was 0.40. The maximum score was 8.0.

Vinyldimethicone

A substance identified as "vinyl dimethylsiloxy-terminated polydimethylsiloxane" (CAS no. 68083-19-2) was applied in a 4-h occlusive patch (0.5-ml dose) to the clipped, intact dorsal skin of six New Zealand white rabbits (2 to 3.5 kg, sex not given). Sites were scored using the Draize scale for 7 days. The PII was 0.0 (maximum possible = 8.0). No irritation was observed (Myers and Ballantyne 1993).

Cumulative Dermal Irritation

Dimethicone

Dow Corning Corp. (1949) applied two mold release emulsions each containing 35% Dimethicone (Type P and XE-18) in 10 applications over 14 days to the external ears and shaved abdomen of rabbits. The number of rabbits used and actual exposure time were not reported. No reactions were observed in the pinna, but both emulsions produced slight "simple" irritation to the abdomen. In a follow-up study, Dow Corning Corp. (1950) reported that another two 35% aqueous emulsions, tested under similar conditions, produced similar reactions.

Dow Corning Corp. (1953) reported that Dimethicone (as XF-409) applied to the intact skin of the external ear or abdomen of rabbits (number not stated) for a total of 10 applications produced very slight hyperemia after prolonged contact for several days.

Dow Corning Corp. (1954b) reported four irritation studies in which Dimethicone 200 fluid, tested at 99 parts (as XF1-3753) and as a 50% aqueous dispersion (as XEF-4-3561) was applied to three sites: the intact external ear (10 applications), the intact abdomen (10 applications), and abraded abdomen (3 applications) on an unspecified number of rabbits. Exposure time was not reported. The authors concluded that Dimethicone did not produce irritation in these studies.

Gloxhuber and Hecht (1955) painted a rabbit's external ear once daily for 60 consecutive working days with a Dimethicone sample. The sample contained approximately 110 siloxane units and its viscosity was 140 cs at 20°C. No changes were noted compared to the untreated pinna.

These same authors painted the ears of three rabbits twice daily with a 40% Dimethicone emulsion (60 cs at 20°C). One rabbit died on day 10; the death was not considered treatment related. The other two rabbits were painted 60 and 100 times, respectively, without adverse effect (Gloxhuber and Hecht 1955).

Hill Top Research (1967) applied two 35% Dimethicone aqueous dispersions (TX-184A and TX-184B) for an unspecified amount of time to two rabbits. Sites were evaluated for 15 days. No irritation was observed.

Dow Corning Corp. (1975) reported that when tested as a hydraulic fluid (99.7% as XF-21075), Dimethicone produced no reaction in the external ear, hyperemia after the sixth application to the intact abdomen that became moderate with slight edema after the ninth application, and slight hyperemia after the first application to the abraded abdomen.

CTFA (1977b) reported that Dimethicone (100%), applied to the clipped skin of three male Hartley guinea pigs once a day for 3 consecutive days (it was not stated whether or not the site was covered), produced no reaction.

Irritation Barrier

Dimethicone

A cream containing 10% Dimethicone was investigated as a barrier against dermal irritation. The cream was applied to one side of the clipped back of female guinea pigs. Plastic syringe reservoirs containing the irritants toluene, mineral oil, sodium hydroxide, and sodium lauryl sulfate (SLS) were applied for exposure times of 2 or 24 h. Each irritant was tested on three guinea pigs. Punch biopsies were taken from the test site and were examined for pathologic changes. The cream did not significantly protect against irritation by toluene or sodium hydroxide. It did protect against SLS-induced irritation when the SLS had been applied in a hydrophobic phase, but not when a water solution was used. The cream protected against mineral oil-induced skin changes (Mahmoud, Lachapelle, and van Neste 1984).

Dermal Sensitization

Dimethicone

Dow Corning Corp. (1985) applied a gel containing 79% Dimethicone (Q7-2167/68) to the clipped and depilated backs of 10 male Hartley albino guinea pigs. Four 48-h occlusive patches (0.1 ml) were applied in 10 days. At the third application, 0.2 ml Freund's complete adjuvant (FCA) was injected intradermally near the test site. Sites were evaluated at the time of patch removal. Following a 10-day nontreatment period, guinea pigs were challenged at an unexposed site. Challenge reactions were evaluated at 24, 48, and 72 h postapplication. Positive- and negative-control groups (five guinea pigs in each group) were maintained. Hyperemia and edema were each scored on 0–4 scales. Observations during induction were not reported. No reactions were observed at challenge.

Hazleton France (1989) tested a trade mixture (containing >90% Dimethicone) using the Magnusson-Kligman protocol. On induction day 1, groups of 20 Dunkin-Hartley guinea pigs (10 of each sex) received three series of two injections consisting of (1) FCA alone, (2) a 50% *w/w* solution of the test article alone, and (3) FCA plus test article. Because pretesting established that the test article was not an irritant, an SLS patch was applied on day 8. A 48-h occlusive patch of the test material as supplied was applied on day 9. Following an 11-day nontreatment period, a 24-h patch of the test article was applied to a previously unexposed site. Challenge sites were evaluated 24 and 48 h after patch removal. A control group was treated with water. No reactions were observed at challenge.

National Institute of Environmental Health Sciences (1990) reported a study in which Dimethicone fluid was applied (20 μl) to shaved and dermabraded dorsal sites on sixteen female B6C3F$_1$ mice daily for 8 days. Seven days later, mice were

challenged on the dorsal and ventral sides of the left external ear. A hypersensitivity reaction was measured by both the radioisotopic incorporation assay ([^{125}I]-Iododeoxyuridine (IUDR) was injected into the tail vein of all mice the day before challenge) and the mouse ear swelling test (MEST). Following the MEST test, all mice were killed except for eight of the Dimethicone group. The challenged and untreated external ears of killed mice were biopsied and counted in a gamma counter. Seven days later, the eight remaining mice were joined with another group of eight mice that had been treated with saline for 5 days. All of these mice were challenged with an application of Dimethicone on the left external ear and again analyzed by the MEST assay for 2 days. The authors concluded that Dimethicone did not produce a contact hypersensitivity reaction.

Dow Corning Corp. (1991) tested a Dimethicone liquid (Q7-2867) following a modified split-adjuvant protocol. The liquid (0.2 ml) was applied under gauze to 10 male Hartley guinea pigs. Four 48-h occlusive patches were applied in 10 days. FCA was injected at the third application and application of the fourth patch occurred 72 h later. Following a 12-day nontreatment period, a 24-h challenge patch was applied to an unexposed site. Challenge reactions were evaluated at 24, 48, and 72 h post application. Two negative-control groups (saline and alcohol), one positive-control group, and a vehicle-control group were maintained. No irritation was noted during induction, and the Dimethicone liquid did not produce any reactions at challenge.

Ocular Toxicity

Dimethicone

Dow Corning Corp. (1953) reported that Dimethicone (as XF-409) produced very slight pain and irritation for a few hours after instillation into rabbit eyes (number not stated) regardless of whether the eye was subsequently rinsed or unrinsed.

Dow Corning Corp. (1954b) tested Dimethicone as 200 fluid in four studies using rabbits. Dimethicone was reported to produce a slight conjunctival irritation that subsided in 24 h when tested undiluted in rinsed and unrinsed eyes.

Another study (Dow Corning Corp. 1957a) observed essentially no irritation when electrical-grade silicone fluid was tested undiluted, although slight pain and conjunctivitis, which subsided in 24 h, were noted when the electrical-grade silicone fluid was instilled as a 10% solution in propylene glycol. Treated and untreated electrical-grade fluid instilled as a single dose or daily for 5 days produced conjunctival irritation that was slow to heal; the irritation was more severe following repeated exposure (Dow Corning Corp. 1957b).

Dow Corning Corp. (1959) reported very slight but definite conjunctival irritation in another repeated-dose study using rabbits, but details were not available.

Dow Corning Corp. (1968) stated that Dimethicone at 10% and 29% in trade formulations produced essentially no irritation. Slight conjunctivitis or iritis was noted with 35%, but lesions had cleared in 24 h.

Dow Corning Corp. (1970) stated that Dimethicone (as XF-1-3753) produced a very slight conjunctival reponse in a rabbit that subsided within 24 h.

Dow Corning Corp. (1972b) stated that Dimethicone, as a 50% aqueous dispersion (XEF-4-3561), produced slight conjunctivitis in rabbits at 1 h; the conjunctivitis cleared by 24 h.

Dow Corning Corp. (1975) stated that Dimethicone (as XF 2-1075) produced essentially no response when tested in rinsed and unrinsed rabbit eyes.

Hazleton Labs (1975) reported that although Dimethicone (50% in SM2080) was a mild irritant to rabbit eyes following a 2- or 4-s rinsing, it was a severe irritant to unrinsed eyes.

CTFA (1977c) reported that Dimethicone produced a conjunctival reaction when instilled into one conjunctival sac of each of three rabbits. The total score was 4.7 (maximum 110). It was considered a "minimal irritant."

Dow Corning Corp. (1977, 1978a, 1978b) tested three heat-transfer fluids (containing Dimethicone) on six rabbits. The protocol used was not reported but the conjunctiva, cornea, and iris were observed 24 h, 48 h, 72 h, and 7 days after exposure. Two fluids produced no reaction (Dow Corning Corp. 1978a, 1978b), the third produced conjunctival redness in all rabbits and conjunctival chemosis in two rabbits at the 24-h observation (Dow Corning Corp. 1977). The chemosis had cleared by 48 h, whereas the redness persisted through the 72-h scoring, but cleared by day 7. The cornea and iris were not affected.

The Bushy Run Research Center (1984) reported that a 0.1-ml dose of a trade mixture (15% Dimethicone) produced moderate corneal injury, iritis, and conjunctival irritation in all of the six rabbits. A 0.01-ml dose produced moderate conjunctival irritation in all rabbits and moderate iritis in two. A 0.005-ml dose produced minor to moderate conjunctival irritation in all rabbits that cleared in five of six rabbits by 72 h.

Hazleton France (1989) reported that Dimethicone (a major component of trade mixture) was a slight irritant when instilled into one eye of six rabbits followed by a 72-h observation period.

Springborn Labs (1991) instilled 0.1 ml of a trade mixture (containing >90% Dimethicone) into one eye of each of six rabbits, followed by a 7-day observation period. The authors concluded that Dimethicone was a nonirritant based on the European Commission evaluation criteria.

Five 35% aqueous emulsions tested separately produced slight conjunctivitis in rabbits that cleared within 2 days with no corneal damage, although one emulsion produced "immediate and painful irritation" when first instilled (Dow Corning Corp. 1950).

Methicone

Three undiluted methicone oils were each instilled (0.1 ml) into one conjunctival sac of each of two albino rabbits (sex, species, body weights were not given). The contralateral eye served as the control. One dosed eye was rinsed 20 s after exposure with tap water for one min; the other dosed eye was not rinsed. Eyes were examined by a hand slit lamp at 1 and 4 h, and

at 1, 2, and 3 days. None of the three oils produced corneal injury; DF 1040 produced minimal congestion of the iris at 1 h; and all produced mild conjunctival redness that lasted up to 2 days (Dupont De Nemours & Co. 1966).

Vinyldimethicone

A substance identified as "vinyl dimethylsiloxy-terminated polydimethylsiloxane" (CAS no. 68083-19-2) was instilled (0.1 ml undiluted) into the lower conjunctival sac of one eye of six New Zealand rabbits. Eyes were scored for 7 days using the Draize scale. Minor conjunctivitis was noted; the conjunctivitis cleared within 1 to 2 days. The maximum mean score was 6.0 (Myers and Ballantyne 1993).

REPRODUCTIVE AND DEVELOPMENTAL TOXICOLOGY

Oral

Dimethicone

The Food and Drug Research Labs (1966) tested Dimethicone-containing fluids in oral studies to investigate possible atrophic changes in rat seminal vesicles. The test material was administered directly into the stomach of 10 male Sprague-Dawley rats at a dose of 3.3 ml/kg/day for 6 days. A control group received saline. Feed and water were available ad libitum. Rats were killed at the end of dosing and necropsy was performed. Final body weight and the weight of the seminal vesicles were measured. A Dimethicone sample (TX-158F) produced a significant reduction in the average seminal vesicle to body weight ratio but not in absolute organ weight. Two other Dimethicone samples had no adverse effect.

Atlas Chemical Industries (1970) reported a study in which a medical grade antifoam compound (93% Dimethicone) was given orally to pregnant Wistar rats on gestational days (GDs) 6 to 15 at doses of 0.38, 1.20, and 3.80 g/kg/day. The highest dose was selected to represent 70 times the recommended clinical dose for the treatment of intestinal gas and 1000 times that recommended to treat peptic ulcers. A control group received tap water. Rats were examined by laparotomy on GD 20 at which time fetuses were removed from the uterus. Dams were killed and the ovaries were examined for corpora lutea. The authors concluded that Dimethicone at any dose did not induce significant differences in fetal viability at laparotomy, resorptions, average weight, and gross external, soft tissue, and skeletal anomalies.

Siddiqui (1994) fed an antifoam compound (food-grade Dimethicone) to time-mated New Zealand white rabbits at concentrations of 0%, 0.5%, 1.0%, and 2.5% on GDs 6 to 19. Females were observed daily for clinical signs of toxicity. On gravid day 29, confirmed-pregnant females (20 to 22 per group) were evaluated for gestational outcome. Each live fetus was examined for external, visceral, and skeletal malformations. No overt signs of toxicity in the dams, and no statistically significant differences in feed consumption were observed between treated and control rabbits. No adverse effects were noted in mean maternal body weight or liver weight. The incidence of resorptions among the total fetal population was not altered by feeding the antifoam compound. Male and female pup weights were not affected by the maternal treatment. No significant treatment related adverse effects in the incidence of external, visceral, or skeletal abnormalities were observed.

Dermal

Dimethicone

Kennedy et al. (1976) applied 200 mg/kg Dimethicone (medical grade fluid, 350 cs; suspended in either corn oil or sesame oil in a 1:5 ratio) to the shaved backs of groups of 15 pregnant rabbits on GDs 6 to 18. Other groups received subcutaneous injections of 20, 200, or 1000 mg/kg Dimethicone (diluted in sesame oil, or undiluted at the highest dose). Vehicle control groups were treated with corn oil or sesame oil. Litters were delivered by cesarean section on day 29. The uterus and other genital organs of each dam were inspected. Implantation sites and live and dead pups were counted. Live pups were incubated for 24 h and then killed. Dead pups and two thirds of those killed were cleared and stained for skeletal examination. The remaining pups were necropsied. The investigators considered that the vehicles, corn, and sesame oil had an effect on the incidence of resorptions. No treatment-related fetal abnormalities were found. The incidence of talipes varus in the 200-mg/kg group was at or above the upper limit for historical controls, but the abnormality was not detected at the 1000 mg/kg dose.

Following the same protocol, these authors applied Dimethicone (225 fluid, 10 cs) suspended in corn oil (1:5) (200 mg/kg) to the shaven backs of groups of 15 pregnant rabbits on GDs 6 to 18. Treatment did not affect maternal body weight, weight gains, number of implantation or resorption sites, or viable fetuses. Umbilical hernia was noted in one pup each of the treated and control group; one treated pup had talipes varus. No other abnormalities were observed and 24-h survival was comparable between treated and control pups (Kennedy et al. 1976).

In a study by an unknown author, retrieved from the National Technical Information Service (NTIS 1987a), motor oil containing an unspecified amount of Dimethicone was applied undiluted to the shaved backs of the parental (P_1) and first (F_1) generation of Sprague-Dawley rats, 7 days a week for an 8 week premating period, 3-week mating period, and throughout gestation and lactation. Doses applied were 0.1, 0.4, and 1.5 ml/kg. Twenty pregnant P_1 females from each dose group underwent natural parturition; the remaining 20 were killed on GD 13 and the uteri content was examined for implants. A single male and female were selected from each F_1 litter to produce the F_2 generation; dermal treatment began one day after weaning. All F_1 females were allowed a natural parturition. P_1 and F_1 males were killed at the end of mating. F_2 rats were not treated and were killed at weaning.

No statistically significant difference was detected in the mortality or survival rates in F_1 litters on day 0 (parturition). However, mortality after day 0 was significantly decreased in the

0.4- and 1.5-ml/kg groups. In contrast, mortality in the F_2 litter was significantly increased in the 0.4-ml/kg group on day 0. Body weights and weight gains were significantly reduced in adult F_1 male rats of the 1.5-ml/kg group beginning on week 7 and continuing throughout the mating period. Absolute testes weight was also significantly reduced in these males, but the relative testes to body weight ratio was not significantly different from controls.

Gestating dam body weights were significantly increased in the 0.1- and 0.4-ml/kg group compared to sham controls. No significant differences were noted in F_1 or F_2 litter body weight or body weight gains. External appearance and microscopic features of the F_1 and F_2 skeletal systems were comparable to controls. Mild dermal irritation was observed in P_1 and F_1 rats. Mild epidermal acanthosis was observed in P_1 and F_1 rats of the 1.5-ml/kg group. According to the authors, the motor oil did not induce any significant alterations in the reproductive performance of either the P_1 or F_1 generation (NTIS 1987a).

In a study by an unknown author, retrieved from the National Technical Information Service (NTIS 1987b), motor oil containing an unknown concentration of Dimethicone was applied undiluted (1.5 ml/kg) to the shaved back of 20 timed-pregnant Sprague-Dawley rats on GDs 6 to 15. A sham-control was maintained. No deaths occurred during the study. Mean dam and litter body weight, pup viability, incidence of external, soft tissue, and skeletal abnormalities were comparable between treated and control animals.

GENOTOXICITY

Dimethicone

Mutagenicity studies done on Dimethicone are summarized in Table 4. Dimethicone, tested pure or in a trade mixture, was not mutagenic in either in vitro studies using bacterial or mammalian cells, or in vivo studies using mammalian systems.

CARCINOGENICITY

Oral

Dimethicone

Cutler et al. (1974) fed an antifoam compound containing 91% Dimethicone at 0.25% and 2.5% to groups of 100 outbred mice (50 of each sex) for 76 weeks. Another group received a single subcutaneous injection of the test material (0.2 ml) into the left flank. Silicone exposure was calculated to be 520 and 5200 mg/kg/day for the 0.25% and 2.5% oral dose groups, respectively, and 201 mg for the subcutaneous injection group. A control group for the oral-dose study was fed untreated feed and a control group for the injection study received an injection of liquid paraffin. Mice were killed at 80 weeks and necropsied.

Microscopic examination was done on any organ that appeared abnormal and sections from the lungs, heart, stomach, small intestine, spleen, liver, and kidneys from 20 mice of each group were examined. The liver, kidneys, spleen, and perirenal fat of five mice that had been subcutaneously injected were analyzed for silicon. Ten mice of the 2.5% oral dose group were analyzed for whole-body silicon content.

Survival to week 80 was significantly ($p < 0.05$) less than controls for female mice fed 2.5% silicone (however, four had died from cage flooding, and the parameter was not significant when these deaths were excluded) and male mice injected with silicone (however, mice had been killed after the appearance of subcutaneous fibromas). A significantly greater percentage of males injected with silicone developed injection site cysts, had hair loss; a smaller proportion had silicone deposits in the urinary bladder.

Males of the 0.25% diet group had increased incidence of superficial ulceration of the stomach and females of this group had an increased incidence of lymphoid hyperplasia. Neither change was noted in the 2.5% diet group and thus was not considered treatment related. A reduced incidence of uterine atrophy was noted in the females of the 2.5% dietary group. No increase in the number of malignant or benign neoplasms was observed in mice that received silicone in the feed or by injection, compared to controls. In some instances, the incidence of certain benign neoplasms was lower in dosed mice, compared to controls. Analysis of tissue failed to detect silicone in samples obtained from orally dosed or subcutaneously injected mice (Cutler et al. 1974).

Dermal

Dimethicone

In a study by an unknown author, retrieved from the National Technical Information Service (NTIS 1987c), a motor oil containing an unspecified amount of Dimethicone was applied undiluted (50 μl) to the shaved skin of 50 male C3H/HeN mice, twice weekly for life. The sites were not covered and the test material was not mechanically spread after its application. A sham-control group had 120 male mice. The study was terminated when the survival rate for each group reached $\leq$10%. Mice were necropsied, and tissue samples of the application site and stomach were prepared for microscopic examination.

Five control mice died accidentally during the study and were excluded from statistical analysis. The median life span was 79.5 weeks for treated mice and 79.0 weeks for control mice. Mean time-to-death and mortality rates were comparable between treated and control mice. At certain observations, treated mice had significantly greater mean body weight and body weight gains compared to control mice. The differences were not considered treatment related or of biological significance. The final effective number (number of mice alive at week 60 plus the number of dead mice with neoplasms prior to week 60) was 44 treated mice and 91 control mice.

No application site dermal neoplasms were microscopically confirmed in treated or control mice. Ulceration at the application site was observed in 8.0% of treated mice compared to 2.6% of control mice. One treated mouse had a palpable skin mass at the application site during week 65, which regressed by week 67. Epidermal hyperplasia at the application site was more evident

TABLE 4
Genotoxicity testing on Dimethicone

Test	Protocol and Dimethicone dose*	Results	Reference
Bacterial cell			
Ames assay: *Salmonella typhimurium* TA98, TA100, TA1535, TA1537, TA1538	Dimethicone (pure) tested at 33.3, 100, 333.3, 1000, 3333.3, and 10000 μg/plate ± S9	Negative	SRI International 1980
Ames assay: *S. typhimurium* TA98, TA100, TA1535, TA1537, TA1538	Dimethicone (fluid at 100 and 1000 cs) tested at 0.5, 5, 100, and 500 μg/plate ± S9	Negative	Dow Corning Corp 1978c
Ames assay: *S. typhimurium* TA98, TA100, TA1535, TA1537	Dimethicone mixture (unknown conc) tested at 50, 158, 500, 1580, and 5000 μg/plate ± S9	Negative	NTIS 1988
S. typhimurium TA98, TA100, TA1535, TA1537, TA 1538	Trade mixture (to contain >90% Dimethicone) tested at 1, 5, 10, 50, 100 μl/plate ± S9	Negative	Hazleton France 1988b
S. typhimurium TA98, TA100, TA1535, TA1537 and *Escherchia coli* WP2	Surfactant containing 3 wt.% Dimethicone was tested in ethanol at 100, 333, 1000, 3333, and 5000 μg/plate ± S9	Negative	Microbiological Associates 1994
Bacterial reverse mutation: *S. typhimurium* TA98, TA100, TA1535, TA1537 and *E. coli* WP2	Ethanol extractions of CU-7439 (<0.1% Dimethicone) tested at 312.5, 625, 1250, 2500, and 5000 μg/plate ± S9	Negative	Dow Corning Corp 1989e
Bacterial reverse mutation	X2-5169 (10% Dimethicone)	Negative	Dow Corning Corp 1986a
Bacterial reverse mutation	X2-3379 (28% Dimethicone)	Negative	Dow Corning Corp 1990a
Bacterial reverse mutation	X3-9626 (49% Dimethicone)	Negative	Dow Corning Corp 1986b
Bacterial reverse mutation	X2-3320 (59% Dimethicone)	Negative	Dow Corning Corp 1990b
Bacterial reverse mutation	Q7-2159A gel (79% Dimethicone)	Negative	Dow Corning Corp 1986c
Bacterial reverse mutation	Q7-2867	Negative	Dow Corning Corp 1990c
Mammalian cell line			
BALB/C-3T3 mouse cell transformation assay	Q7-2159A gel (79% Dimethicone) tested at 500, 1000, and 2000 μg/ml ± S9	Negative	Dow Corning Corp 1986d
BALB/C-3T3 mouse cell transformation assay	Q7-2167/68 gel (79% Dimethicone) tested at 1250, 2500, 5000, and 10000 μg/ml ± S9	Negative	Dow Corning Corp 1989f
Chinese hamster ovary (CHO) chromosome aberration assay	Q7-2167/68 gel (79% Dimethicone) tested at 625, 1250, 2500, 5000, and 10000 μg/ml ± S9	Negative	Dow Corning Corp 1989g
CHO/HGPRT forward mutation assay	Q7-2159A gel (79% Dimethicone) tested at 31.3, 62.5, 125, 250, 500, and 1000 μg/ml ± S9	Negative	Dow Corning Corp 1986e
CHO/HGPRT forward mutation assay	Q7-2167/68 gel (79% Dimethicone) tested at 312.5, 625, 1250, 2500, 5000, and 10000 μg/ml ± S9	Negative	Dow Corning Corp 1989h

(Continued on next page)

TABLE 4
Genotoxicity testing on Dimethicone *(Continued)*

Test	Protocol and Dimethicone dose*	Results	Reference
Mammalian system			
Micronucleus test using Swiss/Webster mice	Ten mice (5 of each sex) received a single intraperitoneal injection of an extract of Q7-2159A gel (79% Dimethicone) in tissue culture fluid (dose 5 g/kg)—peripheral blood samples were taken at 24, 48, and 72 h post dosing. Micronuclei per 1000 polychromatic erythrocytes counted	Negative	Dow Corning Corp 1986f
Micronucleus test using CD-1 mice	Groups of 10 mice (5 of each sex) received a single intraperitoneal injection of an extract of Q7-2167/68 gel (79% Dimethicone) in ethanol (sterile water dilutions of the ethanol extract were made to obtain doses** of 1.25, 2.0, and 2.5 g/kg)—peripheral blood samples were taken at 24, 48, and 72 h post dosing. Micronuclei counted	Negative	Dow Corning Corp 1989i

*All studies used CAS no. 63148-62-9 to identify dimethyl silicones and siloxanes except for SRI International (1980), which used CAS no. 9006-65-9; all studies maintained appropriate positive- and negative-control groups; S9 activation prepared from an adult male rat liver; HGPRT (hypoxanthine guanine phosphoribosyl transferase) locus.
**Linear dimethylsiloxane at doses of 0.005, 0.008, and 0.01 g/kg; dimethyl cyclics at 0.01 to 0.02 g/kg.

in treated mice (17/50) than in control mice (1/115), suggesting to the author slight dermal irritation (NTIS 1987c).

CLINICAL ASSESSMENT OF SAFETY

Oral

Dimethicone

Bio-Research Labs (1985a) tested 350 cs Dimethicone fluid as a food additive. In a preliminary study, six men received the additive as 1% of the diet for 5 days (15 g), followed by a 2-day "washout" period. Subjects then received the additive as 2% of the diet for another 5 days (30 g), followed by another washout period. Blood, urine, and fecal samples were collected to assess absorption of selected nutrients. No anal leakage or major GI disturbances were reported. An increased frequency of bowel movements was reported. No changes in protein, carbohydrates, or vitamin A, D, or E were observed.

Bio-Research Labs (1985b) conducted a subsequent study in which seven male subjects received the additive in ascending doses of 2%, 3%, 4%, and 5% of the diet by weight for five consecutive 3-day periods. After this phase of the study, a bolus dose was given. One subject was withdrawn due to inability to produce a fecal specimen until day 6. Three subjects were placed on control diets on day 10 after 3 days at the 3% dose because they experienced anal leakage. Another subject experienced leakage after the first day on the 4% diet; the next day (day 11), this subject, as well as the remaining two subjects, were all placed on the control diet. On day 14, all subjects received a bolus dose of 30 g of the additive (equal to the 2% daily intake dose) and the control diet was continued for another two days. No anal leakage was observed following the bolus.

Subjects experienced flatulence during the study but no other significant discomfort. An increase in the frequency of bowel movements was noted. No significant changes in vitamin K absorption, as estimated by serum prothrombin time and partial thromboplastin time values, were observed. A decrease in mean platelet count was noted following introduction of the test material, but the count returned to baseline values post study. An increase in the percentage of neutrophil count, accompanied by a decrease in the percentage of lymphocyte count with a slight decease in total white blood cell count, was observed post study. Post study mean SGOT, SGPT, and BUN were decreased 14% to 16% from prestudy values. Post study mean values for alkaline phosphatase increased 8%, and total serum bilirubin

increased 54% (this increase was almost entirely accounted for by one subject). Weight loss of 2.7 to 5 kg was observed in three subjects. The significance of the clinical findings was not known (Bio-Research Labs 1985b).

Dermal Irritation

Dimethicone

Dimethicone, applied in a 24-h occlusive patch to the forearm, produced no irritation in 54 men (CTFA 1981).

Dermal Sensitization

Dimethicone

Hill Top Research (1984) conducted a repeated-insult patch test (RIPT) with a solution containing 5.0% *w/v* active Dimethicone in cyclomethicone. During induction, 10 24-h patches containing 0.3 ml of the test material were applied to the same site on the arm of 103 Caucasian subjects. Twenty subjects were withdrawn before study termination due to noncompliance unrelated to the test material. Subjects were challenged at an unexposed site. Sites were scored on a scale of 0 to 5. Patch application was either terminated or moved to another site if any reaction >1 was observed. The protocol was followed except for isolated instances of site scorings being conducted later than prescribed. Reactions were all ≤1. The investigators concluded that the test substance was neither an irritant nor a sensitizer.

Therapeutic

Dimethicone

Johnson (1976) tested a cream consisting of 2.5% Dimethicone in a hydrophilic base as an alternative to steroid creams in the treatment of allergic contact dermatitis. The cream contained no pharmacologically active ingredient. Participants included 56 patients with cutaneous disease considered "likely to respond" to an inactive cream, as well as 19 patients who were considered "not likely to respond." The panel consisted of 47 males and 28 females ranging in age from less than 2 years to 78 years old. Patients (or their parents/caregivers) were instructed to apply the cream to the affected area(s) four times per day for 14 days as well as after the affected areas had been washed. Panelists were instructed to avoid other therapy for the cutaneous disease.

The cutaneous disease characterized by dryness, roughness, scaling, and cracking of the skin were either cleared or improved by the therapy (46 of the 56 "likely responders"). Symptomatic relief and lessened discomfort was noted in some of the 19 "unlikely responders." The nonactive cream was considered a viable alternative in the treatment of cutaneous disease that did not require steroid therapy (Johnson 1976).

SUMMARY

Dimethicone is a fluid mixture of fully methylated linear siloxane polymers end-blocked with trimethylsiloxy units. Methicone is a linear monomethyl polysiloxane. The other dimethicones and methicones covered in this review are siloxane polymers of Dimethicone and Methicone. Most of the data reviewed in this report are studies of Dimethicone.

Almost all of the 20 ingredients function as conditioning agents in cosmetic formulations. FDA reported seven of the ingredients used in 1998 in a total of 1884 formulations; CTFA reported 10 uses. The highest current concentration of use was 15%.

Dimethicone has both food and over-the-counter topical drug use. Its use in foods is limited by molecular weight.

Clinical and animal absorption studies generally reported that Dimethicone was not absorbed following oral or dermal exposure, although some absorption was seen in humans following ingestion of a Dimethicone sample containing low-molecular-weight polymers.

Dimethicone, Methicone, and Vinyldimethicone were not acutely toxic following oral exposure. Mice and rats were dosed for 90 days with up to 10% Dimethicone without adverse effect. Changes in body weight or spleen weight were observed in some rat studies. Anal leakage was noted when Dimethicone fluids of low viscosity were used. Bile deposits in the Kupffer and hepatic cells were observed in dogs dosed with 3 g/kg/day for 6 months.

The dermal LD_{50} for Dimethicone was >2 g/kg in rats and rabbits. The dermal LD_{50} for Methicone was >20 ml/kg in rabbits. The dermal LD_{50} for Vinyldimethicone was >16 ml/kg in rabbits. No adverse reactions were found in rabbits following short-term dermal dosing with 6% to 79% Dimethicone. Adverse effects were noted with a hand cream formulation containing 1% Dimethicone (the other components of the cream were not disclosed).

Only limited inhalation toxicity data were available. A "200 fluid" did produce adverse effects in one study. Methicone and Vinyldimethicone were negative in acute exposure studies using rats. Hexyl Methicone did produce toxic effects in Fischer F344/N rats—the LC_{50} was 1.8 mg/L.

Most dermal irritation studies using rabbits classified Dimethicone as a minimal irritant. Studies that scored reactions according to the Draize scale reported PIIs of ≤2.8 (with test samples containing 5% to 100% Dimethicone).

Dimethicone (tested undiluted and at 79%) was not a sensitizer in four assays using mice and guinea pigs. It was not a sensitizer at 5.0% in a clinical RIPT using 83 panelists. Vinyldimethicone was not irritating to rabbits following a 4-h exposure.

Most ocular irritation studies using rabbits classified Dimethicone as a mild to minimal irritant. The most common finding was a conjunctival reaction. However, a few studies reported severe reactions. Similar to Dimethicone, Methicone and Vinyldimethicone also produced conjunctival reactions.

Dimethicone was tested in numerous oral-dose (using rats) and dermal-dose (using rats, rabbits, monkeys) reproductive and developmental toxicity studies. In a few studies, treated males had significantly decreased body weight and/or decreased testes or seminal vesicles weights.

No treatment-related adverse findings were noted in dosed pregnant females or fetuses.

Dimethicone was negative in all mutagenicity assays. It was negative in both an oral (tested at 91%) and dermal (tested an unknown concentration) dose carcinogenicity assay using mice.

DISCUSSION

The CIR Expert Panel considered it unlikely that any of these polymers would be significantly absorbed into the skin due to the large molecular weight of these polymers. Inhalation exposure, however, was of concern given the limited inhalation toxicity findings in the report. It was noted, however, that only a few of these ingredients are used in aerosol formulations and at a very low concentration. In addition, the Panel was informed that particles from cosmetic formulations containing these ingredients would not likely be inhaled. In particular, it was stated that expected particle sizes would primarily be in the range of 60 to 80 microns, and less than 1% would be under 10 microns, which is an upper limit for respirable particles. The Panel expects that the manufacture process for cosmetic formulations in which these ingredients are found and which may be inhaled would continue to produce particle size distributions that are not significantly respirable.

Overall, the safety test data in the report support the safety of these ingredients at the concentrations that they are known to be used in cosmetic formulations. Accordingly, the CIR Expert Panel was of the opinion that Stearoxy Dimethicone, Dimethicone, Methicone, Amino Bispropyl Dimethicone, Aminopropyl Dimethicone, Amodimethicone, Amodimethicone Hydroxystearate, Behenoxy Dimethicone, C24–28 Alkyl Methicone, C30–45 Alkyl Methicone, C30–45 Alkyl Dimethicone, Cetearyl Methicone, Cetyl Dimethicone, Dimethoxysilyl Ethylenediaminopropyl Dimethicone, Hexyl Methicone, Hydroxypropyldimethicone, Stearamidopropyl Dimethicone, Stearyl Dimethicone, Stearyl Methicone, and Vinyldimethicone may be used safely in cosmetic formulations.

CONCLUSION

Based on the available data, the CIR Panel concludes that Stearoxy Dimethicone, Dimethicone, Methicone, Amino Bispropyl Dimethicone, Aminopropyl Dimethicone, Amodimethicone, Amodimethicone Hydroxystearate, Behenoxy Dimethicone, C24–28 Alkyl Methicone, C30–45 Alkyl Methicone, C30-45 Alkyl Dimethicone, Cetearyl Methicone, Cetyl Dimethicone, Dimethoxysilyl Ethylenediaminopropyl Dimethicone, Hexyl Methicone, Hydroxypropyldimethicone, Stearamidopropyl Dimethicone, Stearyl Dimethicone, Stearyl Methicone, and Vinyldimethicone are safe as used in cosmetic products.

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2020 VCRP Frequency of Use Data

CATEGORY	CAS_ NUMBER	MAINTERM	CPIS_ COUNT
Amino Bispropyl Dimethicone Total: 1			
05I - Other Hair Preparations	999002112	AMINO BISPROPYL DIMETHICONE	1
Aminopropyl Dimethicone Total: 57			
03G - Other Eye Makeup Preparations	977185264	AMINOPROPYL DIMETHICONE	1
05A - Hair Conditioner	977185264	AMINOPROPYL DIMETHICONE	11
05F - Shampoos (non-coloring)	977185264	AMINOPROPYL DIMETHICONE	5
05G - Tonics, Dressings, and Other Hair Grooming Aids	977185264	AMINOPROPYL DIMETHICONE	12
05I - Other Hair Preparations	977185264	AMINOPROPYL DIMETHICONE	8
06C - Hair Rinses (coloring)	977185264	AMINOPROPYL DIMETHICONE	1
06H - Other Hair Coloring Preparation	977185264	AMINOPROPYL DIMETHICONE	4
07C - Foundations	977185264	AMINOPROPYL DIMETHICONE	4
07F - Makeup Bases	977185264	AMINOPROPYL DIMETHICONE	1
12C - Face and Neck (exc shave)	977185264	AMINOPROPYL DIMETHICONE	6
12F - Moisturizing	977185264	AMINOPROPYL DIMETHICONE	3
12G - Night	977185264	AMINOPROPYL DIMETHICONE	1
Amodimethicone; Total: 1387			
01C - Other Baby Products	977091647	AMODIMETHICONE	2
02B - Bubble Baths	977091647	AMODIMETHICONE	1
03G - Other Eye Makeup Preparations	977091647	AMODIMETHICONE	1
05A - Hair Conditioner	977091647	AMODIMETHICONE	593
05B - Hair Spray (aerosol fixatives)	977091647	AMODIMETHICONE	4
05C - Hair Straighteners	977091647	AMODIMETHICONE	14
05D - Permanent Waves	977091647	AMODIMETHICONE	1
05E - Rinses (non-coloring)	977091647	AMODIMETHICONE	16
05F - Shampoos (non-coloring)	977091647	AMODIMETHICONE	205
05G - Tonics, Dressings, and Other Hair Grooming Aids	977091647	AMODIMETHICONE	204
05I - Other Hair Preparations	977091647	AMODIMETHICONE	203
06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	977091647	AMODIMETHICONE	13
06B - Hair Tints	977091647	AMODIMETHICONE	1
06C - Hair Rinses (coloring)	977091647	AMODIMETHICONE	25
06D - Hair Shampoos (coloring)	977091647	AMODIMETHICONE	6
06E - Hair Color Sprays (aerosol)	977091647	AMODIMETHICONE	7
06G - Hair Bleaches	977091647	AMODIMETHICONE	3

06H - Other Hair Coloring Preparation	977091647	AMODIMETHICONE	13
07B - Face Powders	977091647	AMODIMETHICONE	1
07C - Foundations	977091647	AMODIMETHICONE	2
07E - Lipstick	977091647	AMODIMETHICONE	2
07F - Makeup Bases	977091647	AMODIMETHICONE	3
07I - Other Makeup Preparations	977091647	AMODIMETHICONE	2
10A - Bath Soaps and Detergents	977091647	AMODIMETHICONE	24
10E - Other Personal Cleanliness Products	977091647	AMODIMETHICONE	16
11A - Aftershave Lotion	977091647	AMODIMETHICONE	1
11B - Beard Softeners	977091647	AMODIMETHICONE	1
11E - Shaving Cream	977091647	AMODIMETHICONE	1
12A - Cleansing	977091647	AMODIMETHICONE	5
12C - Face and Neck (exc shave)	977091647	AMODIMETHICONE	10
12F - Moisturizing	977091647	AMODIMETHICONE	3
12G - Night	977091647	AMODIMETHICONE	1
12H - Paste Masks (mud packs)	977091647	AMODIMETHICONE	1
12J - Other Skin Care Preps	977091647	AMODIMETHICONE	2
Behenoxy Dimethicone; Total: 13			
03D - Eye Lotion	977136745	BEHENOXY DIMETHICONE	5
07E - Lipstick	977136745	BEHENOXY DIMETHICONE	2
12A - Cleansing	977136745	BEHENOXY DIMETHICONE	1
12C - Face and Neck (exc shave)	977136745	BEHENOXY DIMETHICONE	1
12F - Moisturizing	977136745	BEHENOXY DIMETHICONE	3
13A - Suntan Gels, Creams, and Liquids	977136745	BEHENOXY DIMETHICONE	1
C20-24 Alkyl Dimethicone; Total 38			
03D – Eye Lotion	200074766	C20-24 ALKYL DIMETHICONE	1
07E - Lipstick	200074766	C20-24 ALKYL DIMETHICONE	29
07F – Makeup Bases	200074766	C20-24 ALKYL DIMETHICONE	1
12C- Face and Neck (exc shave)	200074766	C20-24 ALKYL DIMETHICONE	4
12F- Moisturizing	200074766	C20-24 ALKYL DIMETHICONE	2
12G- Night	200074766	C20-24 ALKYL DIMETHICONE	1
C26-28 Alkyl Dimethicone Total: 13			
03C – Eye Shadow	999001806	C26-28 ALKYL DIMETHICONE	9
03F - Mascara	999001806	C26-28 ALKYL DIMETHICONE	1
05A – Hair Conditioner	999001806	C26-28 ALKYL DIMETHICONE	2
07E - Lipstick	999001806	C26-28 ALKYL DIMETHICONE	1
C30-45 Alkyl Dimethicone Total: 66			

03A - Eyebrow Pencil	170831386	C30-45 ALKYL DIMETHICONE	1
03B - Eyeliner	170831386	C30-45 ALKYL DIMETHICONE	1
03C - Eye Shadow	170831386	C30-45 ALKYL DIMETHICONE	6
03D - Eye Lotion	170831386	C30-45 ALKYL DIMETHICONE	1
03F - Mascara	170831386	C30-45 ALKYL DIMETHICONE	4
05A - Hair Conditioner	170831386	C30-45 ALKYL DIMETHICONE	2
07A - Blushers (all types)	170831386	C30-45 ALKYL DIMETHICONE	3
07E - Lipstick	170831386	C30-45 ALKYL DIMETHICONE	36
07I - Other Makeup Preparations	170831386	C30-45 ALKYL DIMETHICONE	4
12C - Face and Neck (exc shave)	170831386	C30-45 ALKYL DIMETHICONE	5
12F - Moisturizing	170831386	C30-45 ALKYL DIMETHICONE	1
12J - Other Skin Care Preps	170831386	C30-45 ALKYL DIMETHICONE	2
C30-45 Alkyl Methicone Total: 71			
03A - Eyebrow Pencil	977144016	C30-45 ALKYL METHICONE	3
03B - Eyeliner	977144016	C30-45 ALKYL METHICONE	4
03C - Eye Shadow	977144016	C30-45 ALKYL METHICONE	1
03D - Eye Lotion	977144016	C30-45 ALKYL METHICONE	2
03E - Eye Makeup Remover	977144016	C30-45 ALKYL METHICONE	1
03F - Mascara	977144016	C30-45 ALKYL METHICONE	1
05G - Tonics, Dressings, and Other Hair Grooming Aids	977144016	C30-45 ALKYL METHICONE	3
07A - Blushers (all types)	977144016	C30-45 ALKYL METHICONE	1
07C - Foundations	977144016	C30-45 ALKYL METHICONE	5
07D - Leg and Body Paints	977144016	C30-45 ALKYL METHICONE	3
07E - Lipstick	977144016	C30-45 ALKYL METHICONE	13
07F - Makeup Bases	977144016	C30-45 ALKYL METHICONE	1
07I - Other Makeup Preparations	977144016	C30-45 ALKYL METHICONE	1
08G - Other Manicuring Preparations	977144016	C30-45 ALKYL METHICONE	2
12B - Depilatories	977144016	C30-45 ALKYL METHICONE	20
12C - Face and Neck (exc shave)	977144016	C30-45 ALKYL METHICONE	3
12D - Body and Hand (exc shave)	977144016	C30-45 ALKYL METHICONE	2
12F - Moisturizing	977144016	C30-45 ALKYL METHICONE	3
12J - Other Skin Care Preps	977144016	C30-45 ALKYL METHICONE	1
13A - Suntan Gels, Creams, and Liquids	977144016	C30-45 ALKYL METHICONE	1
C30-60 Alkyl Dimethicone; Total: 2			
12C- Face and Neck (exc shave)	999003123	C30-60 ALKYL DIMETHICONE	2
Caprylyl Methicone; Total 234			
03A0 - Eyebrow Pencil	17955883	CAPRYLYL METHICONE	4
03B- Eueliner	17955883	CAPRYLYL METHICONE	18
03C – Eye Shadow	17955883	CAPRYLYL METHICONE	11
03D- Eye Lotion	17955883	CAPRYLYL METHICONE	3

03G – Other Eye Makeup Preparations	17955883	CAPRYLYL METHICONE	15
05A – Hair Conditioner	17955883	CAPRYLYL METHICONE	2
05B – Hair Spray (aerosol fixatives)	17955883	CAPRYLYL METHICONE	1
05F- Shampoos (non-coloring)	17955883	CAPRYLYL METHICONE	1
05G - Tonics, Dressings, and Other Hair Grooming Aids	17955883	CAPRYLYL METHICONE	4
05I- Other Hair Preparations	17955883	CAPRYLYL METHICONE	1
07B – Face Powders	17955883	CAPRYLYL METHICONE	10
07C - Foundations	17955883	CAPRYLYL METHICONE	13
07E - Lipstick	17955883	CAPRYLYL METHICONE	20
07F – Makeup Bases	17955883	CAPRYLYL METHICONE	1
07G - Rouges	17955883	CAPRYLYL METHICONE	1
07H – Makeup Fixatives	17955883	CAPRYLYL METHICONE	3
07I – Other Makeup Preparations	17955883	CAPRYLYL METHICONE	12
08C – Nail Creams and Lotions	17955883	CAPRYLYL METHICONE	1
11A – Aftershave Lotion	17955883	CAPRYLYL METHICONE	1
11G – Other Shaving Preparation Products	17955883	CAPRYLYL METHICONE	1
12A- Cleansing	17955883	CAPRYLYL METHICONE	3
12C – Face and Neck (exc shave)	17955883	CAPRYLYL METHICONE	29
12D – Body and Hand (exc shave)	17955883	CAPRYLYL METHICONE	9
12F - Moisturizing	17955883	CAPRYLYL METHICONE	43
12G - Night	17955883	CAPRYLYL METHICONE	12
12H – Paste Masks (mud packs)	17955883	CAPRYLYL METHICONE	1
12I – Skin Fresheners	17955883	CAPRYLYL METHICONE	1
12J – Other Skin Care Preps	17955883	CAPRYLYL METHICONE	10
13A – Suntan Gels, Creams, and Liquids	17955883	CAPRYLYL METHICONE	2
13B – Indoor Tanning Preparations	17955883	CAPRYLYL METHICONE	1
Cetearyl Methicone; Total: 46			
03D - Eye Lotion	977183359	CETEARYL METHICONE	2
05G - Tonics, Dressings, and Other Hair Grooming Aids	977183359	CETEARYL METHICONE	2
07A - Blushers (all types)	977183359	CETEARYL METHICONE	1
07I - Other Makeup Preparations	977183359	CETEARYL METHICONE	1
12C - Face and Neck (exc shave)	977183359	CETEARYL METHICONE	5
12D - Body and Hand (exc shave)	977183359	CETEARYL METHICONE	1
12F - Moisturizing	977183359	CETEARYL METHICONE	32
12J - Other Skin Care Preps	977183359	CETEARYL METHICONE	1
Cetyl Dimethicone; Total: 233			
03B - Eyeliner	977114263	CETYL DIMETHICONE	5
03C - Eye Shadow	977114263	CETYL DIMETHICONE	42
03D - Eye Lotion	977114263	CETYL DIMETHICONE	2
03F - Mascara	977114263	CETYL DIMETHICONE	2

03G - Other Eye Makeup Preparations	977114263	CETYL DIMETHICONE	13
05A - Hair Conditioner	977114263	CETYL DIMETHICONE	2
05G - Tonics, Dressings, and Other Hair Grooming Aids	977114263	CETYL DIMETHICONE	4
05I - Other Hair Preparations	977114263	CETYL DIMETHICONE	1
07A - Blushers (all types)	977114263	CETYL DIMETHICONE	20
07B - Face Powders	977114263	CETYL DIMETHICONE	19
07C - Foundations	977114263	CETYL DIMETHICONE	37
07E - Lipstick	977114263	CETYL DIMETHICONE	14
07F - Makeup Bases	977114263	CETYL DIMETHICONE	7
07G - Rouges	977114263	CETYL DIMETHICONE	2
07H - Makeup Fixatives	977114263	CETYL DIMETHICONE	2
07I - Other Makeup Preparations	977114263	CETYL DIMETHICONE	11
11A - Aftershave Lotion	977114263	CETYL DIMETHICONE	3
12A - Cleansing	977114263	CETYL DIMETHICONE	2
12C - Face and Neck (exc shave)	977114263	CETYL DIMETHICONE	6
12F - Moisturizing	977114263	CETYL DIMETHICONE	27
12G - Night	977114263	CETYL DIMETHICONE	2
12H - Paste Masks (mud packs)	977114263	CETYL DIMETHICONE	1
12J - Other Skin Care Preps	977114263	CETYL DIMETHICONE	4
13A - Suntan Gels, Creams, and Liquids	977114263	CETYL DIMETHICONE	5
Dimethicone; Total: 14,050			
01B - Baby Lotions, Oils, Powders, and Creams	9006659	DIMETHICONE	31
01C - Other Baby Products	9006659	DIMETHICONE	3
02A - Bath Oils, Tablets, and Salts	9006659	DIMETHICONE	4
02D - Other Bath Preparations	9006659	DIMETHICONE	4
03A - Eyebrow Pencil	9006659	DIMETHICONE	18
03B - Eyeliner	9006659	DIMETHICONE	130
03C - Eye Shadow	9006659	DIMETHICONE	1217
03D - Eye Lotion	9006659	DIMETHICONE	249
03E - Eye Makeup Remover	9006659	DIMETHICONE	12
03F - Mascara	9006659	DIMETHICONE	116
03G - Other Eye Makeup Preparations	9006659	DIMETHICONE	234
04A - Cologne and Toilet waters	9006659	DIMETHICONE	10
04B - Perfumes	9006659	DIMETHICONE	5
04C - Powders (dusting and talcum, excluding aftershave talc)	9006659	DIMETHICONE	14
04E - Other Fragrance Preparation	9006659	DIMETHICONE	79
05A - Hair Conditioner	9006659	DIMETHICONE	580
05B - Hair Spray (aerosol fixatives)	9006659	DIMETHICONE	25
05C - Hair Straighteners	9006659	DIMETHICONE	21
05D - Permanent Waves	9006659	DIMETHICONE	5

05E - Rinses (non-coloring)	9006659	DIMETHICONE	28
05F - Shampoos (non-coloring)	9006659	DIMETHICONE	285
05G - Tonics, Dressings, and Other Hair Grooming Aids	9006659	DIMETHICONE	336
05H - Wave Sets	9006659	DIMETHICONE	6
05I - Other Hair Preparations	9006659	DIMETHICONE	236
06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	9006659	DIMETHICONE	215
06B - Hair Tints	9006659	DIMETHICONE	3
06C - Hair Rinses (coloring)	9006659	DIMETHICONE	23
06D - Hair Shampoos (coloring)	9006659	DIMETHICONE	5
06G - Hair Bleaches	9006659	DIMETHICONE	4
06H - Other Hair Coloring Preparation	9006659	DIMETHICONE	41
07A - Blushers (all types)	9006659	DIMETHICONE	354
07B - Face Powders	9006659	DIMETHICONE	468
07C - Foundations	9006659	DIMETHICONE	417
07D - Leg and Body Paints	9006659	DIMETHICONE	21
07E - Lipstick	9006659	DIMETHICONE	342
07F - Makeup Bases	9006659	DIMETHICONE	94
07G - Rouges	9006659	DIMETHICONE	27
07H - Makeup Fixatives	9006659	DIMETHICONE	13
07I - Other Makeup Preparations	9006659	DIMETHICONE	226
08A - Basecoats and Undercoats	9006659	DIMETHICONE	36
08B - Cuticle Softeners	9006659	DIMETHICONE	5
08C - Nail Creams and Lotions	9006659	DIMETHICONE	6
08E - Nail Polish and Enamel	9006659	DIMETHICONE	313
08F - Nail Polish and Enamel Removers	9006659	DIMETHICONE	2
08G - Other Manicuring Preparations	9006659	DIMETHICONE	35
09A - Dentifrices	9006659	DIMETHICONE	2
09B - Mouthwashes and Breath Fresheners	9006659	DIMETHICONE	1
09C - Other Oral Hygiene Products	9006659	DIMETHICONE	2
10A - Bath Soaps and Detergents	9006659	DIMETHICONE	36
10B - Deodorants (underarm)	9006659	DIMETHICONE	33
10E - Other Personal Cleanliness Products	9006659	DIMETHICONE	51
11A - Aftershave Lotion	9006659	DIMETHICONE	92
11B - Beard Softeners	9006659	DIMETHICONE	1
11D - Preshave Lotions (all types)	9006659	DIMETHICONE	1
11E - Shaving Cream	9006659	DIMETHICONE	15
11G - Other Shaving Preparation Products	9006659	DIMETHICONE	15
12A - Cleansing	9006659	DIMETHICONE	142

12B - Depilatories	9006659	DIMETHICONE	4
12C - Face and Neck (exc shave)	9006659	DIMETHICONE	1103
12D - Body and Hand (exc shave)	9006659	DIMETHICONE	1319
12E - Foot Powders and Sprays	9006659	DIMETHICONE	8
12F - Moisturizing	9006659	DIMETHICONE	3899
12G - Night	9006659	DIMETHICONE	334
12H - Paste Masks (mud packs)	9006659	DIMETHICONE	117
12I - Skin Fresheners	9006659	DIMETHICONE	16
12J - Other Skin Care Preps	9006659	DIMETHICONE	384
13A - Suntan Gels, Creams, and Liquids	9006659	DIMETHICONE	46
13B - Indoor Tanning Preparations	9006659	DIMETHICONE	117
13C - Other Suntan Preparations	9006659	DIMETHICONE	14
Methicone; Total: 654			
02A - Bath Oils, Tablets, and Salts	9004733	METHICONE	1
03A - Eyebrow Pencil	9004733	METHICONE	3
03B - Eyeliner	9004733	METHICONE	15
03C - Eye Shadow	9004733	METHICONE	97
03D - Eye Lotion	9004733	METHICONE	6
03F - Mascara	9004733	METHICONE	19
03G - Other Eye Makeup Preparations	9004733	METHICONE	26
04C - Powders (dusting and talcum, excluding aftershave talc)	9004733	METHICONE	7
05A - Hair Conditioner	9004733	METHICONE	4
05C - Hair Straighteners	9004733	METHICONE	4
05D - Permanent Waves	9004733	METHICONE	1
05F - Shampoos (non-coloring)	9004733	METHICONE	1
06H - Other Hair Coloring Preparation	9004733	METHICONE	5
07A - Blushers (all types)	9004733	METHICONE	58
07B - Face Powders	9004733	METHICONE	85
07C - Foundations	9004733	METHICONE	109
07D - Leg and Body Paints	9004733	METHICONE	1
07E - Lipstick	9004733	METHICONE	91
07F - Makeup Bases	9004733	METHICONE	18
07G - Rouges	9004733	METHICONE	6
07I - Other Makeup Preparations	9004733	METHICONE	38
08A - Basecoats and Undercoats	9004733	METHICONE	2
08E - Nail Polish and Enamel	9004733	METHICONE	21
08G - Other Manicuring Preparations	9004733	METHICONE	1
10A - Bath Soaps and Detergents	9004733	METHICONE	3
12C - Face and Neck (exc shave)	9004733	METHICONE	21
12F - Moisturizing	9004733	METHICONE	6
12J - Other Skin Care Preps	9004733	METHICONE	4

13A - Suntan Gels, Creams, and Liquids	9004733	METHICONE	1
Stearoxy Dimethicone; Total: 44			
03C - Eye Shadow	68554530	STEAROXY DIMETHICONE	7
03F - Mascara	68554530	STEAROXY DIMETHICONE	1
03G - Other Eye Makeup Preparations	68554530	STEAROXY DIMETHICONE	1
05I - Other Hair Preparations	68554530	STEAROXY DIMETHICONE	1
07A - Blushers (all types)	68554530	STEAROXY DIMETHICONE	3
07E - Lipstick	68554530	STEAROXY DIMETHICONE	10
07G - Rouges	68554530	STEAROXY DIMETHICONE	1
07I - Other Makeup Preparations	68554530	STEAROXY DIMETHICONE	2
12A - Cleansing	68554530	STEAROXY DIMETHICONE	1
12C - Face and Neck (exc shave)	68554530	STEAROXY DIMETHICONE	2
12D - Body and Hand (exc shave)	68554530	STEAROXY DIMETHICONE	6
12F - Moisturizing	68554530	STEAROXY DIMETHICONE	7
12J - Other Skin Care Preps	68554530	STEAROXY DIMETHICONE	2
Stearyl Dimethicone; Total: 183			
03A - Eyebrow Pencil	977094464	STEARYL DIMETHICONE	3
03B - Eyeliner	977094464	STEARYL DIMETHICONE	20
03C - Eye Shadow	977094464	STEARYL DIMETHICONE	20
03D - Eye Lotion	977094464	STEARYL DIMETHICONE	2
03G - Other Eye Makeup Preparations	977094464	STEARYL DIMETHICONE	1
04B - Perfumes	977094464	STEARYL DIMETHICONE	1
04E - Other Fragrance Preparation	977094464	STEARYL DIMETHICONE	2
05A - Hair Conditioner	977094464	STEARYL DIMETHICONE	5
05G - Tonics, Dressings, and Other Hair Grooming Aids	977094464	STEARYL DIMETHICONE	1
05I - Other Hair Preparations	977094464	STEARYL DIMETHICONE	3
07A - Blushers (all types)	977094464	STEARYL DIMETHICONE	14
07B - Face Powders	977094464	STEARYL DIMETHICONE	2
07C - Foundations	977094464	STEARYL DIMETHICONE	6
07E - Lipstick	977094464	STEARYL DIMETHICONE	25
07G - Rouges	977094464	STEARYL DIMETHICONE	1
07I - Other Makeup Preparations	977094464	STEARYL DIMETHICONE	8
12C - Face and Neck (exc shave)	977094464	STEARYL DIMETHICONE	9
12D - Body and Hand (exc shave)	977094464	STEARYL DIMETHICONE	26
12F - Moisturizing	977094464	STEARYL DIMETHICONE	12
12G - Night	977094464	STEARYL DIMETHICONE	6
12H - Paste Masks (mud packs)	977094464	STEARYL DIMETHICONE	2
12J - Other Skin Care Preps	977094464	STEARYL DIMETHICONE	5
13A - Suntan Gels, Creams, and Liquids	977094464	STEARYL DIMETHICONE	3
13B - Indoor Tanning Preparations	977094464	STEARYL DIMETHICONE	6
Stearyl Methicone; Total: 1			

07I - Other Makeup Preparations	977130247	STEARYL METHICONE	1
Vinyl Dimethicone; Total: 1			
07E - Lipstick	999002828	VINYL DIMETHICONE	1

Concentration of Use by FDA Product Category – Dimethicone Additions*

Capryl Dimethicone
C20-24 Alkyl Dimethicone
C24-28 Alkyl Dimethicone
C26-28 Alkyl Dimethicone
C30-60 Alkyl Dimethicone
C32 Alkyl Dimethicone
Caprylyl Methicone
C20-24 Alkyl Methicone
C26-28 Alkyl Methicone

Ingredient	Product Category	Maximum Concentration of Use
Capryl Dimethicone	Other baby products	1%
Capryl Dimethicone	Other eye makeup preparations	1.5%
Capryl Dimethicone	Skin cleansing products (cold creams, cleansing lotions, liquids and pads)	1%
Capryl Dimethicone	Face and neck products Not spray	1%
Capryl Dimethicone	Other skin care preparations	5.5%
C20-24 Alkyl Dimethicone	Eyeliners	8%
C26-28 Alkyl Dimethicone	Eye shadows	2.8%
C26-28 Alkyl Dimethicone	Mascaras	0.8%
C26-28 Alkyl Dimethicone	Blushers	2%
C26-28 Alkyl Dimethicone	Makeup bases	2.8%
Caprylyl Methicone	Eyebrow pencils	4.1%
Caprylyl Methicone	Eyeliners	1.8-2.8%
Caprylyl Methicone	Eye shadows	4.1-6.6%
Caprylyl Methicone	Eye lotions	1.5-16%
Caprylyl Methicone	Eye makeup removers	0.22-12%
Caprylyl Methicone	Other fragrance preparations	6.2%
Caprylyl Methicone	Hair conditioners	0.5-6%
Caprylyl Methicone	Hair sprays Pump sprays	0.8%
Caprylyl Methicone	Face powders	0.0075-4%
Caprylyl Methicone	Foundations	0.038-4.6%
Caprylyl Methicone	Lipstick	2.8-7.5%
Caprylyl Methicone	Makeup bases	0.0075-7.5%
Caprylyl Methicone	Makeup fixatives	2%
Caprylyl Methicone	Other makeup preparations	4.8%
Caprylyl Methicone	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.3%
Caprylyl Methicone	Face and neck products Not spray	0.014-6%
Caprylyl Methicone	Body and hand products Not spray	2.2-5%
Caprylyl Methicone	Moisturizing products Not spray	4-8%

Caprylyl Methicone	Night products Not spray	1.9-4%
Caprylyl Methicone	Other skin care preparations	1.5-4%
Caprylyl Methicone	Suntan products Not spray	1%

*Ingredients found only in the title of the table were included in the concentration of use survey, but no uses were reported.

Information collected in 2020
Table prepared October 7, 2020

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

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

DATE: July 9, 2020

SUBJECT: Tentative Report: Safety Assessment of Dimethicone, Methicone, and Substituted Methicone Polymers as Used in Cosmetics (Release Date: June 22, 2020)

The Personal Care Products Council respectfully submits the following comments on the tentative report, Safety Assessment of Dimethicone, Methicone, and Substituted Methicone Polymers as Used in Cosmetics.

Key Issues

Studies from a NICNAS assessment on Silsoft 034 (LTD/1211) (the *Dictionary* lists Silsoft 034 fluid as a trade name for Caprylyl Methicone) should be added to this report.

Carcinogenicity; Summary - During the June 2020 meeting, the Expert Panel for Cosmetic Ingredient Safety determined that Simethicone (a mixture of Dimethicone and Silica) should not be added to the report because of the presence of Silica. Does the Expert Panel still consider that the oral study on a silicone resin containing 92% Dimethicone and 8% silica (used as an antifoaming agent in food) (reference 16) is appropriate for this report?

Additional Considerations

Introduction - The Introduction should also indicate that summary information was obtained from NICNAS assessments.

Non-Cosmetic Use - It should be made clear that it is Dimethicone with Silica (Simethicone) that is taken orally as an anti-flatulent agent.

Subchronic, old report summary - Please indicate the media, e.g., diet, in which the Dimethicone was provided to rats.

Subchronic - If the 90-day dietary study of Dimethicone in rats was presented in the original report (reference 1) why is it also presented in non-italicized text in this report?

Immunotoxicity - Please clarify if the lupus-associated antinuclear antibodies were observed just in the positive control group (pristane) or if they were also observed in the negative control group (PBS treated).

Dermal Irritation; Mucous Membrane Irritation; Summary - The descriptions of reference 18 in both the Dermal and Mucous Membrane Irritation section state that 5 different samples of Dimethicone were tested. The results for only two samples are stated. What were the results for the other 3 samples?

Ocular Irritation, old report summary - Since the Discussion relies on information from the old report that is not currently in this summary, perhaps more details about the lowest concentration associated with eye irritation should be added to this summary.

Summary - In the Summary, please also state that in the dermal ADME study in rats, 70% of the dose was in the patch materials.

It should be noted that the silicone resin tested in the carcinogenicity study also contained silica.

In the case report of the infant, it is not clear that they actually "determined" that the other substances were the causative agents as no other experiments were described. Perhaps "determined" should be changed to "considered to be".

Discussion - Please indicate that the mortality was observed in rabbits treated ocularly for 10 days. Please make it clear that the study testing 37.8% pure Dimethicone was included in the original report.

Table 1 - The CAS No. 67762-94-1 associated with Vinyl Dimethicone in the *Dictionary* needs to be added to Table 1. Joanne Nikitakis used CAS to look up the CAS number 53529-60-5 currently associated with Vinyl Dimethicone in Table 1. CAS said that this number has been deleted. The result from the CAS search is copied below.
Display from REGISTRY

ANSWER 1 © 2020 ACS on STN
CAS Registry Number
67762-94-1 REGISTRY
Deleted Registry Number
53529-60-5