GREEN CHEMISTRY & COMMERCE COUNCIL

SPECIFICATION FOR GREEN CHEMISTRY ALTERNATIVES TO SILICONE CHEMISTRY FOR COSMETICS & PERSONAL CARE PRODUCTS

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ABSTRACT

Sparked by recent regulatory and market drivers to restrict the use of cyclic siloxanes, this GC3 member-developed document is designed to spur innovation by articulating clear criteria for safer, more sustainable alternatives.

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Introduction

The Green Chemistry & Commerce Council (GC3) envisions a global economy where all chemicals, materials and products are safe and sustainable at creation, disposal, and reuse. Green chemistry has been defined as the design of chemical products and processes that reduce or eliminate the use or generation of hazardous substances throughout the lifecycle of products (Anastas, P. T.; Warner, J. C. Green Chemistry: Theory and Practice, Oxford University Press: New York, 1998). The GC3 drives large scale commercial adoption of safer, sustainable, high-performing chemical solutions by: fostering value chain collaboration, cultivating first-movers, convening industry decision-makers to secure major commitments and creating a supportive policy environment.

The GC3 undertakes collaborative projects to advance safer, more sustainable solutions that address market needs. Chemical suppliers and cosmetic and personal care product manufacturers within the GC3 membership expressed an interest in working collaboratively to create a specifications document to inform the development of safer, more sustainable alternatives to silicone chemistry ingredients for cosmetic and personal care products.

The GC3 makes no statement on the environmental impact of cyclic siloxanes or silicones in general and recognizes the uncertainties and inconsistencies in their environmental assessment and regulation. Regulatory restrictions of some of these ingredients have resulted in a market need for alternatives to these widely utilized components. This specifications document addresses the market need to identify alternatives to silicone chemistries, and, consistent with the mission of the GC3, these alternatives should be safer, more sustainable chemistries.

Background

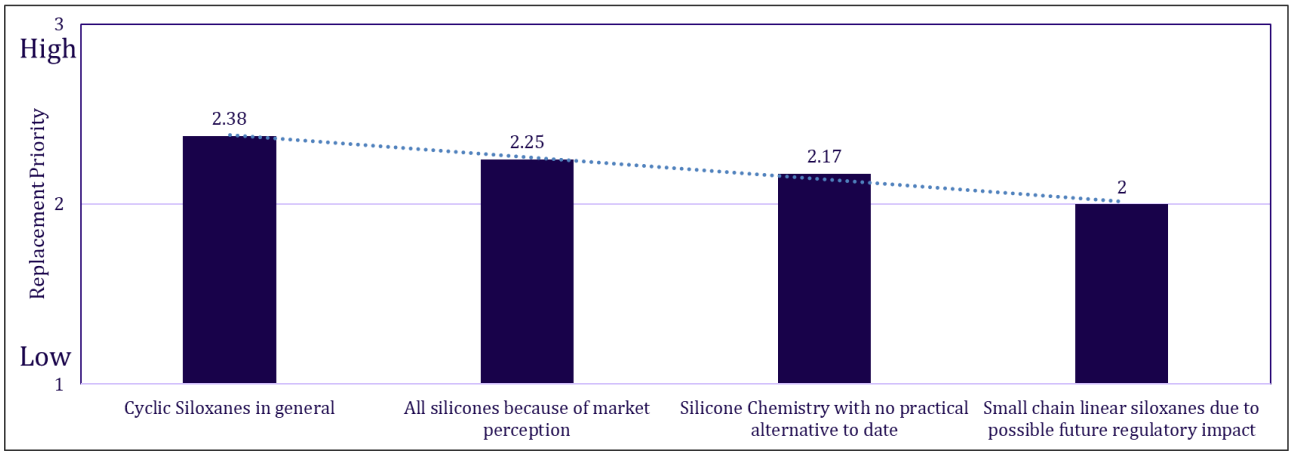
Cyclic siloxanes Octamethylcyclotetrasiloxane (D4), Decamethylcyclopentasiloxane (D5) and Dodecamethylcyclohexasiloxane (D6) are listed on the European Union (EU) Regulation on Registration, Evaluation and Authorisation of Chemicals (REACH) Candidate List for Substances of Very High Concern (SVHC) due to existing or predicted properties consistent with the criteria for persistent, bioaccumulative and toxic (PBT) and/or very persistent and very bioaccumulative (vPvB).

In January 2018, the European Commission published Regulation (EU) 2018/35 restricting the use of D4 and D5 with a maximum concentration not to exceed 0.1% by weight of either substance in wash-off cosmetic products as defined in Article 2(1)(a) of Regulation (EC) No 1223/2009. The regulation came into force effective February 1, 2020 restricting the use of D4 and D5 in wash-off cosmetics products.

In 2019, the European Chemicals Agency (ECHA) issued a proposal to include D6 within the scope of the wash-off cosmetics products restriction and to extend the restriction for D4, D5, and D6 to include leave-on cosmetic products and other direct consumer and professional uses. As of October 2020, this proposal has not been adopted; however, the ECHA Secretariat of Committee for Risk Assessment (RAC) and Committee for Socio-Economic Analysis (SEAC) have issued opinions in support of the restriction. As recently as April 2021, ECHA proposed including D4, D5 and D6 to the REACH Authorisation List which would expand the market impact beyond the cosmetics and personal care products sector.

To assess silicone chemistry replacement priorities, GC3 conducted a survey of cosmetic and personal care product manufacturers. Despite survey outreach including publication in *Happi* and *Cosmetics & Toiletries,* there were only 20 survey respondents including 13 manufacturers representing the targeted cosmetic and personal care sector. As shown in Figure 1, manufacturers generally prioritize cyclic siloxane replacements; however, alternatives for all silicone chemistries were also significant considerations.

Figure 1 Silicone replacement priorities from GC3 survey



Purpose and Scope

This specifications document is intended to support the development and evaluation of new ingredients as safer, more sustainable alternatives to silicone chemistries for cosmetic and personal care product applications. The scope of work is inclusive of all silicone chemistry relevant to cosmetics and personal care products.

- Chemical manufacturers (startups and global corporations alike) could utilize this document to better understand the priorities and expectations of the cosmetic and personal care product manufacturers for silicone chemistry replacements.

  - Performance attributes defined in Table 1 demonstrate current applications and functions of silicone chemistries in the sector.
  - Safety and environmental attributes listed in Table 2 provide guidance to support the development of a testing strategy to assess safer alternatives.
  - Appendix 1 provides suggested test methods and alternative approaches to assess safety and environmental parameters.
- Formulators of cosmetic and personal care products may share this document with suppliers to encourage innovation and development of ingredients as alternatives to silicone chemistry.

Recommended Chemical Information Data Set

Proposed chemical alternatives for silicone chemistries used in cosmetics and personal care products should have sufficient chemical information available including:

1. Chemical identity including CAS number
2. Physical form
3. Molecular weight
4. Particle size (if solid)
5. Solubility
6. pH
7. Partition coefficient (Log Kow)
8. Vapor pressure (volatile liquids)
9. Homogeneity and stability
10. Viscosity
11. Refractive Index
12. Characterization and purity of the chemical, including isomer composition whenever relevant for safety assessment
13. Characterization of the impurities or accompanying contaminants, including residual monomers/oligomers if relevant.

Substances Restricted or Prohibited in Personal Care or Cosmetic Products

The following sources may be helpful in understanding restrictions on ingredients used in personal care and cosmetic products; however, this list continues to evolve, and innovators are encouraged to seek the most current resources.

Regulation 1223/2009/EC on Cosmetic Product of the European Parliament and of the Council, as amended, is a valuable source of reference for substances restricted or prohibited in cosmetic products in Europe.

- Annex II List of substances prohibited in cosmetic products
- Annex III List of restricted substances in cosmetic products

The U.S. Food and Drug Administration has regulations that specifically prohibit or restrict the use of certain ingredients in cosmetics:

- US Code of Federal Regulations, Title 21, Chapter I, Subchapter G, Part 700, Subpart B. Requirements for Certain Cosmetic Products

Findings from independent reviews conducted by the Cosmetic Ingredient Review Expert Panel are publicly available on its website, www.cir-safety.org, including lists such as:

- Safe with qualifications
- Unsafe
- Use not supported

Performance Attributes

For the purposes of this document, *a performance attribute is defined as the capability to meet the desired function(s) in the given application*.

In the cosmetics and personal care sector, it is common for suppliers and manufacturers to have their own respective performance test methods, and similarly, each formulator defines their own acceptable criteria. Therefore, test methods and acceptable criteria are not specified in this document.

To identify performance attributes, GC3 combined subject matter expertise with survey responses from cosmetic and personal care product manufacturers to identify the silicone chemistries used in various applications and their associated function(s).

Table 1 provides the application and function for each type of silicone chemistry identified. The table is segmented into two tiers recognizing that cyclic siloxanes (Tier I) have current regulatory drivers for replacement as compared to the other silicone chemistries (Tier II).

Applications specified in Table 1 are further clarified below:

- Eye Makeup Preparations includes eye shadows, eye liners, etc.
- Hair Coloring Preparations includes dyes, tints, rinses, shampoos-coloring, sprays, lighteners, bleaches, etc.
- Hair Preparations (non-coloring) includes shampoos, conditioners, fixatives and styling aids, straighteners, tonics, etc.
- Makeup Preparations (Not Eye) includes blushers, powders, foundations, lip care, etc.
- Manicuring Preparations includes polishes, basecoats, cuticle softeners, polish removers, etc.
- Personal Cleanliness includes bath soap, shower gels and deodorants.
- Skin Care Preparations includes creams, lotions, powders, and sprays.

Table 1 Performance Attributes

Silicone Chemistry	Silicone Chemical Class	Product Category	Application(s)	Functions(s)
Tier I				
Cyclohexasiloxane (D6)	Cyclic Siloxane	Moisturizer	Skin Care Preparations	Carrier
				Sensory Enhancer
		Serum (Hair)	Hair Preparations (Non-Coloring)	Decrease Greasiness
				Heat Protectant
		Sunscreen	Skin Care Preparations	Lubricity
Cyclopentasiloxane (D5)	Cyclic Siloxane	Anti-Perspirants and Deodorants	Personal Cleanliness	Anti-Staining
				AP Salt Delivery
				Emollient
		Foundation	Makeup Preparations (Not Eye)	Carrier
		Moisturizer	Skin Care Preparations	Carrier
				Sensory Enhancer
		Serum (Hair)	Hair Preparations (Non-Coloring)	Anti-Frizzing Agent
				Slip Agent
				Smoothing Agent
Cyclopentasiloxane (D5) (and) Dimethiconol or Dimethicone	Silicone Gum Blends	Anti-Perspirants and Deodorants	Personal Cleanliness	Anti-Billowing
		Hair Conditioner	Hair Preparations (Non-Coloring)	Combability Agent
				Conditioning Agent/Sensory Enhancer
				Damage Repair/ Prevention/Protection
		Serum (Hair)	Hair Preparations (Non-Coloring)	Anti-Frizzing Agent
				Heat Protectant
Cyclotetrasiloxane	Cyclic Siloxane	Foundation	Makeup Preparations	Carrier

Silicone Chemistry	Silicone Chemical Class	Product Category	Application(s)	Functions(s)
(D4)			(Not Eye)	
		Lotion/Moisturizer (Face, Neck, Body, Hand)	Skin Care Preparations	Carrier
Tier II				
Amodimethicone	Amino-Functional Silicone (Fluids and Emulsions)	Hair Conditioner	Hair Preparations (Non-Coloring)	Color Retention
				Conditioning Agent/Sensory Enhancer
			Hair Coloring Preparations	Damage Repair/ Prevention/Protection
		Serum (Hair)	Hair Preparations (Non-Coloring)	Conditioning Agent/Sensory Enhancer
Dimethicone	Dimethicone, Very Low Viscosity (<5 cst)	Lotion/Moisturizer (Face, Neck, Body, Hand)	Skin Care Preparations	Carrier
				Sensory Enhancer
	Dimethicone, Low Viscosity (5 to 50 cst)	Lotion/Moisturizer (Face, Neck, Body, Hand)	Skin Care Preparations	Emollient
				Sensory Enhancer
	Dimethicone, Medium Viscosity (50 to 1000 cst)	Lotion/Moisturizer (Face, Neck, Body, Hand)	Skin Care Preparations	Anti-Soaping Agent
				Cushion
				Sensory Enhancer
				Skin Protectant
	Dimethicone, High Viscosity (60,000 to 600,000 cst)	Hair Conditioner	Hair Preparations (Non-Coloring)	Hair Conditioning Agent
				Sensory Enhancer
Dimethicone (and) Dimethiconol	Silicone Gum Blends	Anti-Perspirants and Deodorants	Personal Cleanliness	Emollient
		Lotion/Moisturizer (Face, Neck, Body, Hand)	Skin Care Preparations	Emollient
				Skin Protecting Agent
				Slip Agent
Dimethicone/Vinyl Dimethicone Crosspolymer	Silicone Elastomer Blends	Lotion/Moisturizer (Face, Neck, Body, Hand)	Skin Care Preparations	Optical Blurring (Mattifying, Imperfection Masking)
				Sensory Enhancer
Hexamethyldisiloxane (HMDSO)	Linear Siloxane	Nail Polish	Manicuring Preparations	Fast Drying Agent
PEG Dimethicone	Silicone Emulsifier	Foundation	Makeup Preparations	Emulsifying Agent

Silicone Chemistry	Silicone Chemical Class	Product Category	Application(s)	Functions(s)
		Lotion/Moisturizer (Face, Neck, Body, Hand)	Skin Care Preparations	Emulsifying Agent
Phenyl Trimethicone	Phenyl-Functional Silicone	Serum (Hair)	Hair Preparations (Non-Coloring)	Shine
		Lipstick	Makeup Preparations (Not Eye)	Gloss
				Pigment Dispersant
				Slip Agent
		Sunscreen	Skin Care Preparations	Carrier
				Emollient
Silicone Elastomers	Silicone Elastomer Blends	Foundation	Makeup Preparations	Sensory Enhancer
		Lotion/Moisturizer (Face, Neck, Body, Hand)	Skin Care Preparations	Optical Blurring (Mattifying, Imperfection Masking)
				Sensory Enhancer
		Serum (Hair)	Hair Preparations (Non-Coloring)	Cushion
	Silicone Elastomer Powders	Lotion/Moisturizer (Face, Neck, Body, Hand)	Skin Care Preparations	Optical Blurring (Mattifying, Imperfection Masking)
				Sensory Enhancer
Trimethylsiloxysilicate	Silicone Resins	Foundation	Makeup Preparations (Not Eye)	Film Forming Agent
Trisiloxane	Linear Siloxane	Lotion/Moisturizer (Face, Neck, Body, Hand)	Skin Care Preparations	Cushion
				Sensory Enhancer
		Serum (Hair)	Hair Preparations (Non-Coloring)	Carrier
				Dry Feel (Hair)

Safety and Environmental Attributes

The human health (safety) and environmental attributes identified in Figure 2 and the associated test methods in Appendix 1 are intended to provide guidance to manufacturers developing silicone chemistry alternatives. In Appendix I, suggested test methods are accompanied by alternative approaches (i.e., modeling) to consider when methods or test data are not available. In cases where testing is not feasible, use of read-across and comparison with authoritative lists may be appropriate.

The attributes presented here do not represent a minimum or comprehensive list, and similarly, criteria limitations for the attributes are not provided; companies have the discretion to manage internal expectations accordingly which may be more stringent than a consensus-based criteria approach could provide.

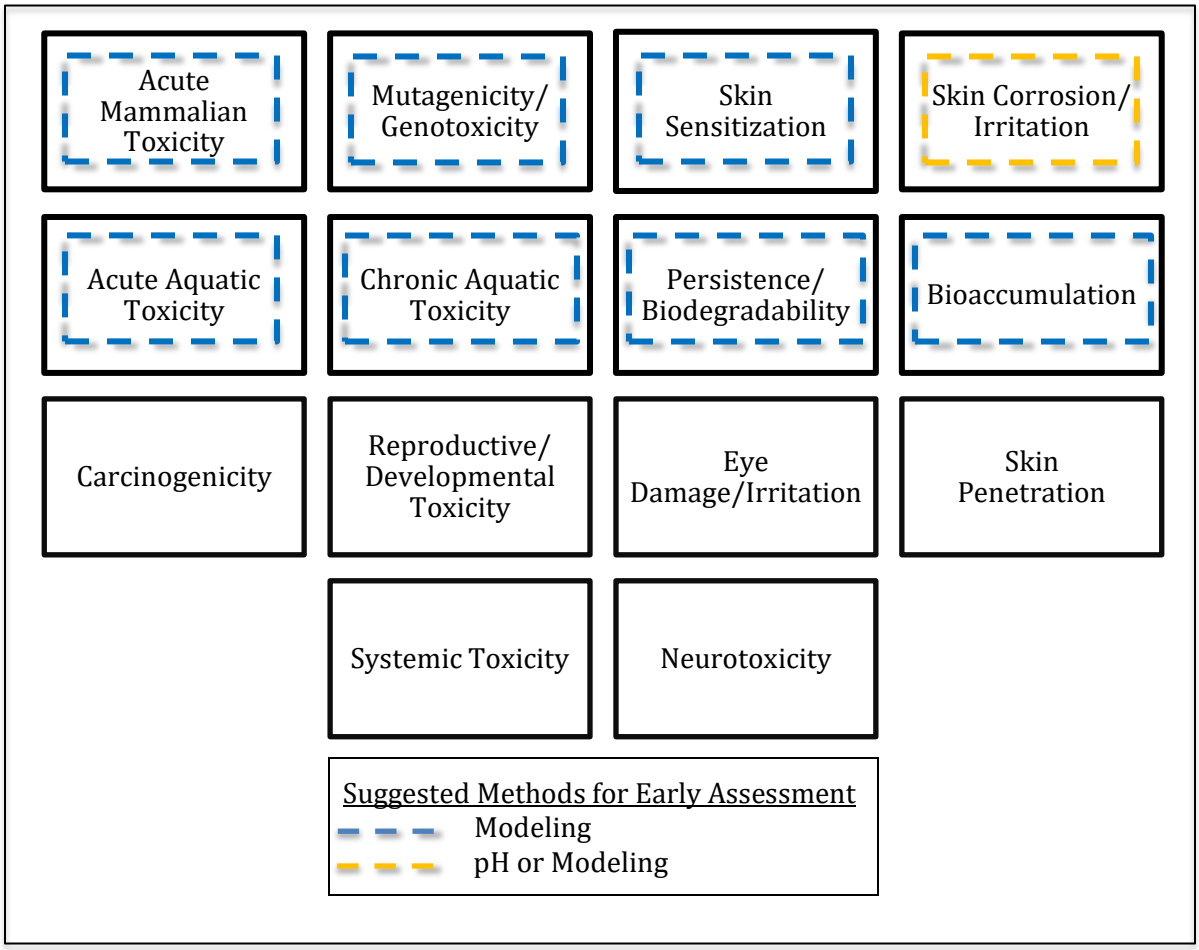
Figure 2 illustrates the suggested 14 safety and environmental attributes to consider when evaluating new ingredients as potential alternatives to silicone chemistries for cosmetic and personal care products. Eight attributes (acute mammalian toxicity, mutagenicity/genotoxicity, skin sensitization, skin corrosion/irritation, acute aquatic toxicity, chronic aquatic toxicity, persistence/biodegradability, and bioaccumulation) are recommended for early assessment through no to low-cost modeling which could provide guidance in the early stages of laboratory analysis with formulators. Modeling tools including ToxTree, EpiSuite and OECD QSAR Toolbox are available at no cost. For additional support in modeling or testing, scientific consulting companies may provide services for a fee.

The early assessment does not replace thorough evaluation of all 14 attributes which should subsequently be completed. Modeling, read-across, and non-animal testing are also available for some of the non-early assessment attributes. Since testing is an expensive and time-consuming process, a testing strategy should be developed with input from the formulator to assess the safety and environmental risks associated with silicone chemistry alternatives economically and in a reasonable timeframe.

Animal testing for cosmetics is banned in many countries and some U.S. states; therefore, the test methodology should be carefully considered before selection to prevent ingredients that are blocked for usage.

Informational resources including the U.S. Environmental Protection Agency Safer Choice Program, European Chemicals Agency, Globally Harmonized Classification and Labelling (GHS), and the Cosmetic Ingredient Review were utilized as a basis for identifying the safety and environmental attributes. The OECD Guidance on Key Considerations for the Identification and Selection of Safer Chemical Alternatives released in March 2021 was utilized for comparison to assure general consistency.

Figure 2 Suggested safety and environmental attributes



Acknowledgements

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List of Figures and Tables

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OECD, 2017 (Mutagenicity/Genotoxcity)
https://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=ENV-JM-MONO(2016)33/rev1&doclanguage=en

OECD, 2019 (Skin Corrosion/Irritation)

https://www.oecd-ilibrary.org/docserver/9789264264618-en.pdf?expires=1586349495&id=id&accname=guest&checksum=4FEADB9CEA1E5814052B62685A4FD9BC

US EPA OPPTS. 2012.
EPA's Safer Choice Program Master Criteria for Safer ingredients. Version 2.1. September 2012.

Appendix 1. Suggested Test Methods for Safety and Environmental Attributes[1]

[1] This table should only be read top-down as separate columns. No inference can be made reading the table from left to right.

Suggested test methods are provided below for safety and environmental attributes. In cases where test data are not available, modeling or use of read-across may be appropriate.

It should be noted that there are no validated OECD test methods for respiratory sensitization and most asthmagens are classified based on occupational human data. Additionally, several in silico methods are available, however, caution should be used when interpretating these results.

Animal testing for cosmetics is banned in many countries and some U.S. states; therefore, test methodology should be carefully considered before selection to prevent ingredients that are blocked for usage.

Attribute	OECD Test Methods	US EPA OPPTS Methods	Other Methods/Criteria	Alternative Approaches & Methods to Consider when Methods or Test Data are Unavailable
HUMAN HEALTH ENDPOINTS				
Acute Mammalian Toxicity	OECD Test Guideline 420: Acute Oral Toxicity-Fixed Dose Method	OPPTS Harmonized Guidelines 870.110: Acute Oral Toxicity	In silico, OECD QSAR Toolbox	Intentionally blank
	OECD Test Guideline 423: Acute Oral Toxicity - Acute Toxic Class Method	OPPTS Harmonized Guideline 870.1200: Acute dermal toxicity		
	OECD Test Guideline 425: Acute Oral Toxicity - Up and Down Procedure	OPPTS Harmonized Guideline 870.1300: Acute inhalation toxicity		
	OECD Test Guideline 402: Acute Dermal Toxicity			
	OECD Test Guideline 403: Acute Inhalation Toxicity			

Attribute	OECD Test Methods	US EPA OPPTS Methods	Other Methods/Criteria	Alternative Approaches & Methods to Consider when Methods or Test Data are Unavailable
Carcinogenicity	OECD Test Guideline 451: Carcinogenicity Studies	OPPTS Harmonized Guideline 870.4200	NTP 2 Year Study Protocol: Specifications for the conduct of studies to evaluate the toxic and carcinogenic potential of chemical, biological, and physical agents in laboratory animals for the National Toxicology Program	Most chemicals will not have carcinogenicity studies. In cases where data gaps exist for carcinogenicity, one may use mutagenicity/ genotoxicity and chronic toxicity studies to inform this endpoint.
	OECD Test Guideline 453: Combined Chronic Toxicity/Carcinogenicity Studies	OPPTS Harmonized Guidelines 870.4300: Combined chronic toxicity/carcinogenicity	Carcinogenicity specific lists: IARC, ACGIH, NTP, EU CLP Annex VI	
			In silico, OECD QSAR Toolbox	
			In silico, US EPA OncoLogic	
Mutagenicity/ Genotoxicity	In vitro: OECD Test Guideline 471: Bacterial Reverse Mutation Test	OPPTS Harmonized Guideline 870.5100 Bacterial Reverse Mutation Test	Test results from OECD Test Guideline 486: Unscheduled DNA Synthesis (UDS) Test with Mammalian Liver Cells in vivo may also be considered when evaluating this endpoint. However, it should be noted this test has some limitations which makes the results less reliable compared to other *in vivo* studies.	Many chemicals do not have in vivo studies. Companies may have specific in-house approaches for determining whether there are sufficient data to classify a substance as a hazard or no hazard for this endpoint.
	In vitro: OECD Test Guideline 473: In vitro Mammalian Chromosome Aberration Test	OPPTS Harmonized Guideline 870.5375 In vitro Mammalian Chromosome Aberration Test	In silico, Expert-rule program: Toxtree (In vitro mutagenicity (Ames test))	
	In vitro: OECD Test Guideline 476: In vitro Mammalian Cell Gene Mutation Test	OPPTS Harmonized Guideline 870.5395 Mammalian Erythrocyte Micronucleus Test	In silico, Expert-rule program: Derek Nexus (in vitro mutagenicity)	
	In vitro: OECD Test Guideline 487: In vitro mammalian cell micronucleus test	OPPTS Harmonized Guideline 870.5385 Mammalian Bone Marrow Chromosome	In silico, Statistical program: Vega (Mutagenicity (Ames Test) Consensus Model)	

Attribute	OECD Test Methods	US EPA OPPTS Methods	Other Methods/Criteria	Alternative Approaches & Methods to Consider when Methods or Test Data are Unavailable
	In vitro: OECD Test Guideline 490: In vitro gene mutation assays using the Thymidine Kinase gene	OPPTS Harmonized Guideline 870.5300 In vitro Mammalian Cell Gene Mutation Test	In silico, Statistical program: T.E.S.T (Mutagenicity)	
	In vivo: OECD Test Guideline 474 (OPPTS 870.5395): Mammalian Erythrocyte Micronucleus Test	OPPTS Harmonized Guideline 870.5380 Mammalian Spermatogonial Chromosome Aberration Test	In silico, Statistical program: Leadscope (Genetox Suite > Gene Mutation > Microbial in vitro)	
	In vivo: OECD Test Guideline 475: Mammalian Bone Marrow Chromosome			
	In vivo: OECD Test Guideline 483: Mammalian Spermatogonial Chromosome Aberration Test			
	In vivo: OECD Test Guideline 478: Rodent dominant lethal test		In silico, OECD QSAR Toolbox	
	In vivo: OECD Test Guideline 488: Transgenic rodent somatic and germ cell gene mutation assays			
	In vivo: OECD Test Guideline 489: In vivo mammalian alkaline comet assay			
Reproductive Toxicity/ Developmental Toxicity	In vivo: OECD Guidelines 421: Reproduction/Developmental Toxicity Screening Test	Intentionally blank	Repeated Dose studies, 28-day and 90-day, where relevant parameters are assessed (e.g., reproductive and accessory sex organs, semen analysis, estrous cycle) can also inform this endpoint. Methods include OECD 408, 409, 411, 413, 407, 410, and 412).	Intentionally blank
	In vivo: OECD Guidelines 422: Combined Repeated Dose Toxicity Study with Repro/Dev Toxicity Screening test		In vitro embryotoxicity tests and in vitro organ and cell cultures may also be used.	

Attribute	OECD Test Methods	US EPA OPPTS Methods	Other Methods/Criteria	Alternative Approaches & Methods to Consider when Methods or Test Data are Unavailable
	In vivo: OECD Test Guideline 414: Prenatal developmental toxicity study		Well-developed and justified reverse toxicokinetic models may be used to support in vitro test results to estimate exposures needed to achieve bioactive blood concentrations (OECD, p. 492)	
	In vivo: OECD Test Guideline 415: One-generation Reproductive Toxicity		ICH Guideline S5A: Detection of Toxicity to Reproduction for Medicinal Products	
	In vivo: OECD Test Guideline 443: One-generation Extended Reproductive Toxicity		ICH Guideline S5B: Toxicity to Male Fertility	
	In vivo: OECD Test Guideline 416: Two-generation Reproductive Toxicity		NTP One generational study: http://ntp.niehs.nih.gov/testing/types/mog/index.html	
	In vivo: OECD Test Guideline 426: Developmental Neurotoxicity Study		Reproductive Assessment by Continuous Breeding (RACB) protocol (e.g. Chapin and Sloane 1997)	
	In vitro: OECD Test Guideline 455: Performance based test guideline for stably transfected transactivation in vitro assays to detect estrogen receptor agonists		In silico, OECD QSAR Toolbox	
	In vitro: OECD Test Guideline 457: BG1Luc Estrogen Receptor Transactivation Test			
	In vitro: OECD Test Guideline 456: H295R Steroidgenesis Assay			

Attribute	OECD Test Methods	US EPA OPPTS Methods	Other Methods/Criteria	Alternative Approaches & Methods to Consider when Methods or Test Data are Unavailable
Skin Sensitization	In vivo: OECD Test Guideline 406: Skin Sensitization Guinea Pig Maximization Test (GPMT) or Buehler	OPPTS Harmonized Guideline 870.2600: Skin Sensitization	In vivo: Human repeated insult patch test (RIPT) Note: While the RIPT is not an OECD Test Guideline method, this method is considered a gold standard for evaluating this endpoint.	Intentionally blank
	In vivo: OECD Test Guideline 429: Mouse Local Lymph Node (LLNA) Assay		In silico, Expert-rule program: ToxTree (skin sensitization reactivity domains)	
	In vitro: OECD Test Guideline 442C: Direct Peptide Reactivity Assay (DPRA)		In silico, Expert-rule program: Derek Nexus	
	In vitro: OECD Test Guideline 442D: ARE-Nrf2 Luciferase (KeratinoSens™)		In silico, OECD QSAR Toolbox	
	In vitro: OECD Test Guideline 442E: h-CLAT, U-SENS™, or IL-8 Luc			
Skin Corrosion/ Irritation	In vivo: OECD Test Guideline 404: Acute Dermal Irritation/Corrosion	OPPTS Harmonized Guideline 870.2600: Skin Sensitization	In vivo: Human patch test	Intentionally blank
	In vitro: OECD Test Guideline 435: Membrane Barrier Test, Corrositex®		pH ≤ 2 or ≥ 11.5	
	In vitro: OECD Test Guideline 430: Transcutaneous Electrical Resistance (TER)		In silico, OECD QSAR Toolbox	
	In vitro: OECD Test Guideline 431: Reconstructed Human Epidermis (RHE) methods, EpiDerm™ SCT, EpiSkin™, SkinEthic™ RHE, LabCyte EPI-MODEL24 SIT, and epiCS©;			

Attribute	OECD Test Methods	US EPA OPPTS Methods	Other Methods/Criteria	Alternative Approaches & Methods to Consider when Methods or Test Data are Unavailable
	In vitro: OECD Test Guideline 439 In vitro Skin Irritation: Reconstructed Human Epidermis (RHE): EpiDerm™ SIT, EpiSkin™, SkinEthic™ RHE, LabCyte EPI-MODEL24 SIT			
Eye Damage/ Irritation	In vivo: OECD Test Guideline 405 Acute Eye Irritation/Corrosion Rabbit Eye Test	Intentionally blank	pH ≤ 2 or ≥ 11.5	Intentionally blank
	In vitro: OECD Test Guideline 437 Bovine Corneal Opacity and Permeability (BCOP)		Human evidence may be used to classify this endpoint	
	In vitro: OECD Test Guideline 438 Isolated Chicken Eye (ICE)		Skin corrosion and weight of evidence from skin irritation studies may be considered and may lead to classification.	
	In vitro: OECD Test Guideline 460 Fluorescein Leakage (FL)			
	In vitro: OECD Test Guideline 491 Short Term Exposure (STE) Test		In silico, OECD QSAR Toolbox	
	In vitro: OECD Test Guideline 492 Reconstructed human Cornea-Like Epithelium Eye Irritation Test (RhCE EIT)			
Skin Penetration	OECD Test Guideline TG 428 (Skin absorption: in vitro method)	Intentionally blank	In Silico, IH Skin Perm	Intentionally blank
	OECD Test Guideline TG 427 (Skin absorption: in vivo method)		In Silico, EpiSuite (DermWin)	
	OECD Test Guideline TG 428 modified to include time course			

Attribute	OECD Test Methods	US EPA OPPTS Methods	Other Methods/Criteria	Alternative Approaches & Methods to Consider when Methods or Test Data are Unavailable
Systemic Toxicity	OECD Test Guideline 408: Repeated Dose 90-Day Oral Toxicity Study in Rodents	OPPTS Harmonized Guideline 870.3100: 90-Day oral toxicity in rodents	In silico, Expert-rule program: Toxtree (Revised Cramer Classification)	Intentionally blank
	OECD Test Guideline 409: Repeated Dose 90-Day Oral Toxicity Study in Non-Rodents	OPPTS Harmonized Guideline 870.3150: 90-Day oral toxicity in nonrodents	In silico, OECD QSAR Toolbox	
	OECD Test Guideline 411: Repeated Dose Dermal Toxicity: 90-day Study	OPPTS Harmonized Guideline 870.3250: 90-Day dermal toxicity		
	OECD Test Guideline 413: Repeated Dose Inhalation Toxicity: 90-day Study	OPPTS Harmonized Guideline 870.3465: 90-Day inhalation toxicity		
	OECD Test Guideline 407: Repeated Dose 28-day Oral Toxicity Study in Rodents	OPPTS Harmonized Guideline 870.3050: Repeated dose 28-day oral toxicity study in rodents		
	OECD Test Guideline 410: Repeated Dose Dermal Toxicity: 28-day Study	OPPTS Harmonized Guideline 870.3200: 28-Day dermal toxicity		
	OECD Test Guideline 412: Repeated Dose Inhalation Toxicity: 28-day Study			
	OECD Test Guideline 422: Combined Repeated Dose Toxicity Study with Repro/Dev Toxicity Screening test			

Attribute	OECD Test Methods	US EPA OPPTS Methods	Other Methods/Criteria	Alternative Approaches & Methods to Consider when Methods or Test Data are Unavailable
Neurotoxicity	OECD Test Guideline 424: Neurotoxicity in Rodents;	OPPTS Harmonized Guideline 870.6200: Neurotoxicity screening battery;	Intentionally blank	Intentionally blank
	OECD Test Guideline 426: Developmental Neurotoxicity Study can be used for screening	OPPTS Harmonized Guideline 870.6300 Developmental Neurotoxicity Study can be used to screen chemicals		
ENVIRONMENTAL TOXICITY ENDPOINTS				
Acute Aquatic Toxicity				
Fish	OECD Test Guideline 203: Fish, Acute Toxicity Test	OPPTS Harmonized Guideline 850.1075: Fish acute toxicity test, freshwater and marine	OPPTS Harmonized Guideline 850.1085: Fish acute toxicity mitigated by humic acid OPPTS Harmonized Guideline 850.1025: Oyster acute toxicity test OPPTS Harmonized Guideline 850.1045: Penaeid acute toxicity test OPPTS Harmonized Guideline 850.1055: Bivalve acute toxicity test OPPTS Harmonized Guideline 850.4400: Aquatic plant toxicity test using Lemna spp. Tiers I and IIc OECD Test Guideline 236: Fish Embryo Acute Toxicity test (FET) Various OSPAR Tests used in the offshore oil industry In silico, EpiSuite - ECOSAR In silico, OECD QSAR Toolbox	Intentionally blank
Aquatic Invertebrates	OECD Test Guideline 202, Daphnia sp., Acute Immobilisation Test	OPPTS Harmonized Guideline 850.1010: Aquatic invertebrate acute toxicity test, freshwater daphnids		
		OPPTS Harmonized Guideline 850.1035: Mysid acute toxicity test		
Algae	OECD Test Guideline 201, Alga, Growth Inhibition Test	OPPTS Harmonized Guideline 850.5400: Algal toxicity, Tiers I and II		

Attribute	OECD Test Methods	US EPA OPPTS Methods	Other Methods/Criteria	Alternative Approaches & Methods to Consider when Methods or Test Data are Unavailable
Chronic Aquatic Toxicity				
Fish	OECD Test Guideline 210: Fish, Early-life Stage Toxicity Test	Intentionally Blank	OECD Test Guideline 212: Fish short-term toxicity test on embryo and sac-fry stages OECD Test Guideline 215: Fish juvenile growth OECD Test Guideline 229: Fish Short Term Reproduction Assay In silico, EpiSuite - ECOSAR In silico, OECD QSAR Toolbox	Intentionally blank
Aquatic Invertebrates	OECD Test Guideline 211: Daphnia magna Reproduction Test			
Algae	OECD Test Guideline 201: Alga, Growth Inhibition Test			
Persistence/ Biodegradability	OECD Test Guideline 301A: Ready Biodegradability DOC Die-away	OPPTS Harmonized Guideline 835.3110: Ready biodegradability	OECD Test Guideline 304A: Inherent Biodegradability in Soil OECD Test Guideline 302A: Inherent Biodegradability: Modified SCAS Test In silico, EpiSuite - BIOWIN In silico, OECD QSAR Toolbox	Intentionally Blank
	OECD Test Guideline 301B: Ready Biodegradability CO2 Evolution (Modified Sturm Test)			
	OECD Test Guideline 301C: Ready Biodegradability MITI (I) (Ministry of International Trade and Industry, Japan			
	OECD Test Guideline 301D: Ready Biodegradability Closed Bottle			
	OECD Test Guideline 301E: Ready Biodegradability Modified OECD Screening			
	OECD Test Guideline 301F: Ready Biodegradability Manometric Respirometry			

Attribute	OECD Test Methods	US EPA OPPTS Methods	Other Methods/Criteria	Alternative Approaches & Methods to Consider when Methods or Test Data are Unavailable
	Simulation tests for half-life determination as outlined in Safer Choice Guidance: OECD Test Guideline 303A, OECD Test Guideline 309, OECD Test Guideline 314	Simulation tests for half-life determination as outlined in Safer Choice Guidance: OPPTS Harmonized Guideline 835.3280, OPPTS Harmonized Guideline 835.3170, OPPTS Harmonized Guideline 835.3180		
	OECD Test Guideline 302C: Inherent Biodegradability: Modified MITI Test (II)			
	OECD Test Guideline 302B: Inherent Biodegradability: Zahn-Wellens/ EVPA Test			
Bioaccumulation	OECD Test Guideline 305: Bioconcentration: Flow-through Fish Test	OPPTS Harmonized Guideline 850.1710: Oyster BCF OPPTS Harmonized Guideline 850.1730: Fish BCFf	In silico, EpiSuite - KOWWIN In silico, EpiSuite - BCFBAF In silico, OECD QSAR Toolbox	Intentionally blank
	OECD Test Guideline 107: Partition Coefficient (n-octanol/water): Shake Flask Method			
	OECD Test Guideline 117: Partition Coefficient (n-octanol/water), HPLC Method			
	OECD Test Guideline 123: Partition Coefficient (1-Octanol/Water): Slow-Stirring Method			

NOTES:

The methods listed in this table are to inform safety and environmental attributes for silicone chemistry alternatives for personal care and cosmetic products.

Although *in vivo* methods are listed, *in vitro* methods are also provided as alternatives to animal testing. For some endpoints, *in vitro* methods are preferred if not mandated under certain regulatory schemes, particularly for skin corrosion/irritation, eye damage/irritation, and skin sensitization.