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Safety Assessment of Polyene Group as Used in Cosmetics

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Abstract

The Expert Panel for Cosmetic Ingredient Safety (Panel) reviewed the safety of polyenes, which are reported to function in cosmetics primarily as film formers and viscosity increasing agents. The Panel reviewed relevant data related to these ingredients, not inggaps in the available safety data for some of the polyenes in this safety assessment. The data available for many of the ingredients are sufficient and can be extrapolated to support the safety of the entire group because of the similarities in the chemical structures, chemical properties, use concentrations, and reported functions across the group. The Panel concluded that polyenes were safe in cosmetics in the present practices of use and concentration described in this safety assessment.

Keywords

polyene group, safety, cosmetics

Introduction

The 26 ingredients listed below are simple polyolefins that are the polymerization products of vinyl-type monomers and are reported to primarily function as film formers and/or viscosity increasing agents—nonaqueous in cosmetic products. Although the molecular weights of the polyenes reviewed in this report vary over a wide range, structurally, these ingredients have many similarities, including (1) each is the product of the same vinyl-type polymerization methodologies; (2) each is manufactured from very similar starting materials (ie, olefin/alkene monomers); (3) each has similar, simple hydrocarbon structures without functional groups other than alkanes or alkenes; and (4) many are of sufficient molecular size to significantly decrease the chance for dermal penetration.

Butene/Propylene Copolymer	Isobutylene/Isoprene Copolymer
Butylene/Ethylene Copolymer	Isoprene/Pentadiene Copolymer
Butylene/Ethylene/Propylene Copolymer	Polybutene
Decene/Butene Copolymer	Poly(C4-12 Olefin)
Ethylene/Octene Copolymer	Poly(C6-14 Olefin)
Ethylene/Propylene Copolymer	Poly(C20-28 Olefin)
Hydrogenated Poly(C6-12 Olefin)	Poly(C30-45 Olefin)
Hydrogenated Poly(C6-14 Olefin)	Polydecene
Hydrogenated Poly(C6-20 Olefin)	Polyethylene
Hydrogenated Polybutene	Polyisobutene
Hydrogenated Polydecene	Polyisoprene
Hydrogenated Polydodecene	Polypentene
Hydrogenated Polyisobutene	Polypropylene

Polybutene (published in 1982), Polyethylene (published in 2007), Polyisobutene (published in 2008), and Hydrogenated Polyisobutene (published in 2008) have previously been reviewed by the Expert Panel for Cosmetic Ingredient Safety (Panel), which concluded that these ingredients are safe as cosmetic ingredients in the practices of use and concentration as described in each safety assessment.[1-4] Information from these safety assessments are summarized in appropriate sections of this report; the complete reports are available on the Cosmetic Ingredient Review (CIR) website (http://www.cir-safety.org/ingredients).

Some chemical and toxicological data on Hydrogenated Polydecene and Polybutene included in this safety assessment were obtained from robust summaries of data submitted to the European Chemical Agency (ECHA) by companies as part of the REACH chemical registration process. These data summaries are available on the ECHA website.[5,6] The ECHA data summaries include information on analogs (eg, diisobutylene, di-n-butene, tributene, triisobutylene, and tetrabutene for Polybutene; hydrogenated decene dimer and trimer for

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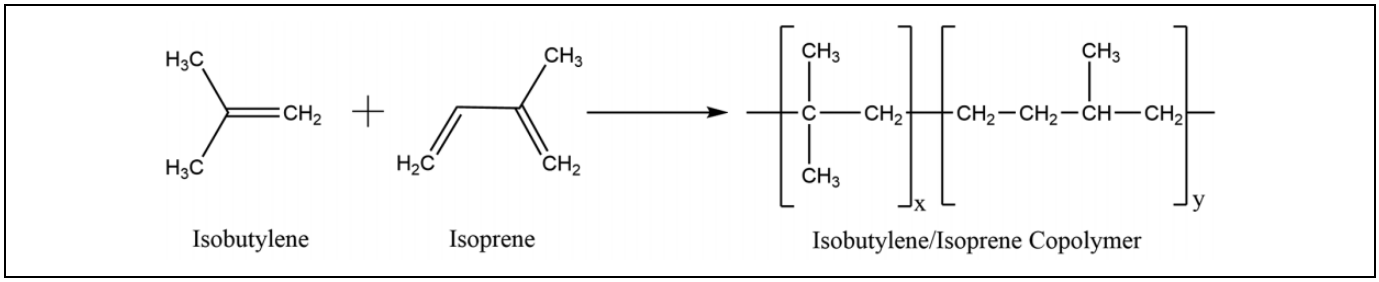


Figure 1. An example of polyene synthesis (Isobutylene/Isoprene Copolymer).

Hydrogenated Polydecene; and hydrogenated dodecene trimer for Hydrogenated Polydodecene) for read-across purposes. Where deemed appropriate, information from the summaries has been included in this report.

Chemistry

The definitions and CAS registry numbers, where available, of the polyene ingredients are presented in Table 1.

Polyenes are the polymerization products of vinyl-type monomers (ie, alkenes or olefins; eg, Figure 1). These polyolefins are either homopolymers (eg, Polybutene) or vinyl-type copolymers of 2 or more monomers (eg, butene/propene copolymers). The term "vinyl-type copolymers" means that all the monomers utilized to make these polymer ingredients have in common an ethylene unit whose pi electrons are directly involved in the polymerization process. Typically, a catalyst is utilized to initiate the polymerization.[7] There are a large number of relevant initiating catalysts, ranging from ultraviolet (UV) light to Ziegler-Natta-type catalysts, which can result in a range of varied characteristics, such as crystallinity (and resultant hardness). The synthesis of these ingredients is typically conducted in one or more organic solvents in the presence of one or more of these catalysts.

For example, formation of Polyisoprene occurs by reacting the isoprene monomer in the presence of catalyst in a hydrocarbon solution, usually hexane.[8] The process is stopped with the addition of a terminating reagent. The in situ stabilization of the polymer is often enhanced with the addition of an antioxidant. Subsequent steps in the process include stripping of the solvent, water washing of the polymer to remove catalyst and reagent residues, and finally pressing and formation of a granular product (for nonliquid polyenes).

Chemical Properties

Table 2 summarizes available data on chemical properties, including information from the original Panel safety assessments of Polybutene, Polyethylene, Polyisobutene, and Hydrogenated Polyisobutene. Further chemical data on these previously reviewed ingredients can be found in those reports.[1-3]

Many of these polyene ingredients are high-molecular-weight, large, inert polymers. The smaller, liquid ingredients in this group have a simple hydrocarbon structure, without functional groups other than alkanes or alkenes. These ingredients are completely insoluble in aqueous solutions or organic solvents but may be swellable in certain organic solvents.

Method of Manufacturing

Hydrogenated Polyisobutene. According to a supplier, Hydrogenated Polyisobutene is produced from the polymerization of isobutene, which is then hydrogenated, purified, and super refined before yielding the final product.[9]

Composition and Impurities

Ethylene/Octene Copolymer. A supplier reported that a trade name mixture comprised in part of Ethylene/Octene Copolymer contains 14% to 16% Ethylene/Octene Copolymer and 84% to 86% C14-22 alkane.[10] Residual monomer levels are 2 ppm octene and 0 ppm ethylene. Ethylene oxide, 1,4-dioxane, and heavy metals were reported to be below the detection limit of 0.1 ppm.[11]

A second trade name mixture was reported to contain 30% to 50% Ethylene/Octene Copolymer and ethylene/sodium acrylate copolymer, and 50% to 70% water.[10] The residual monomer levels were reported to be less than 165 ppm acrylic acid, less than 5 ppm ethylene, and less than 52 ppm octene. A heavy metals analysis reported arsenic was not detected (limited of detection, 27 ppb); however, lead and mercury levels were 22 ppb and 52 ppb, respectively (limits of detection for each were 5 ppb).[12]

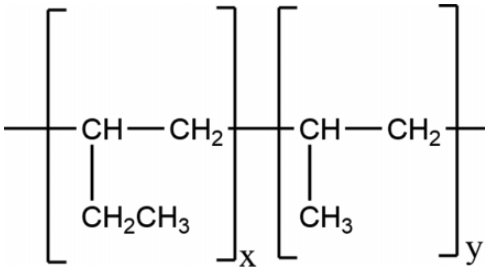
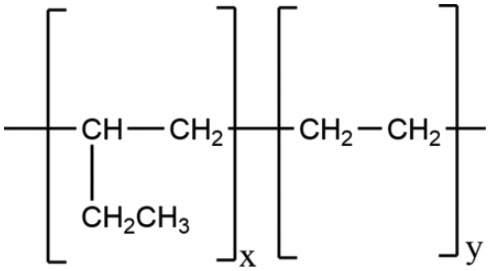
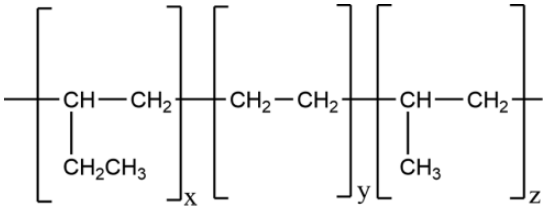
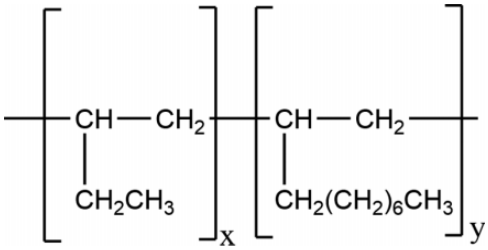
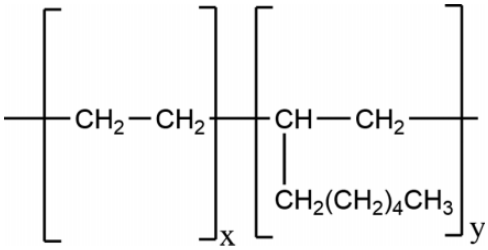
Ethylene/Propylene Copolymer. A redox titration of Ethylene/Propylene Copolymer measured 0.8 ppm of the starting material residue in the final product.[13]

Polybutene. Impurities of Polybutene include isoparaffins, vinylidene and terminal vinyl structures, chloride, and sulfur-containing compounds.[3]

Polyisobutene. A supplier reported that Polyisobutene does not contain detectable levels of residual solvents or monomers and has heavy metal specifications of lead < 10 ppm, arsenic < 2 ppm, and mercury < 1 ppm.[14,15]

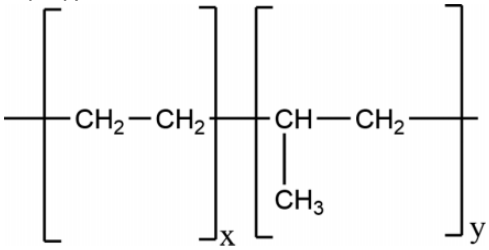
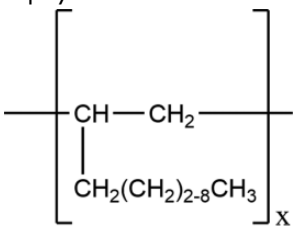
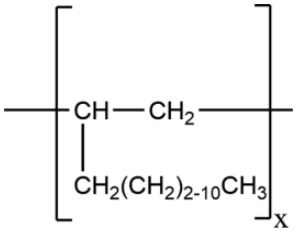
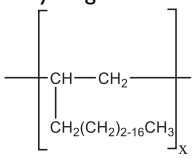
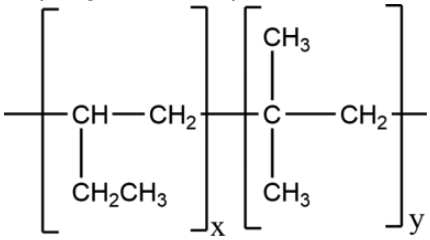
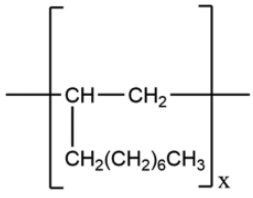
Hydrogenated Polyisobutene. A supplier reported that Hydrogenated Polyisobutene does not contain detectable levels of residual solvents or monomers and has heavy metal specifications

Table 1. Definitions, Idealized Structures, and Functions of the Ingredients in this Safety Assessment.[a,48]

Ingredient CAS No.	Definition and structure	Function(s)
Butene/Propylene Copolymer 29160-13-2	Butene/Propylene Copolymer is a copolymer of butene and propylene monomers. 	Film formers; slip modifiers; viscosity increasing agents—nonaqueous
Butylene/Ethylene Copolymer	Butylene/Ethylene Copolymer is a copolymer of butylene and ethylene monomers. 	Viscosity increasing agents—nonaqueous
Butylene/Ethylene/Propylene Copolymer	Butylene/Ethylene/Propylene Copolymer is a copolymer of butylene, ethylene and propylene monomers. 	Film formers
Decene/Butene Copolymer	Decene/Butene Copolymer is a polymer of butene and decene monomers. 	Viscosity increasing agents—nonaqueous
Ethylene/Octene Copolymer	Ethylene/Octene Copolymer is a copolymer of ethylene and 1-octene monomers. 	Film formers; viscosity increasing agents—nonaqueous

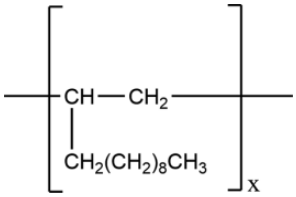
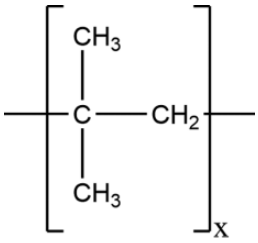
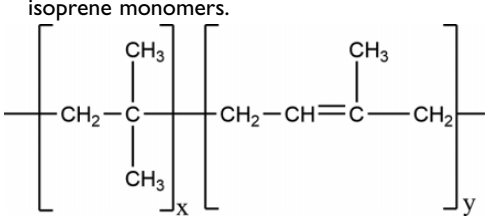
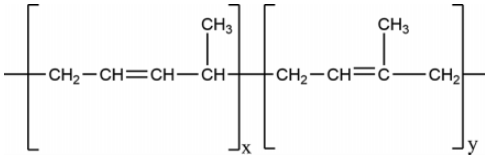
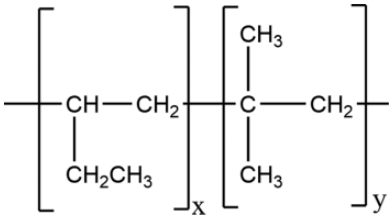
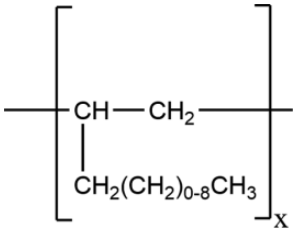
(continued)

Table 1. (continued)

Ingredient CAS No.	Definition and structure	Function(s)
Ethylene/Propylene Copolymer 9010-79-1	Ethylene/Propylene Copolymer is the copolymer of ethylene and propylene monomers. 	Film formers; viscosity increasing agents—nonaqueous
Hydrogenated Poly (C6-12 Olefin)	Hydrogenated Poly (C6-12 Olefin) is a series of low molecular weight polymers of olefin monomers, each containing 6 to 12 carbon atoms. 	Skin-conditioning agents—occlusive; viscosity increasing agents—nonaqueous
Hydrogenated Poly (C6-14 Olefin)	Hydrogenated Poly (C6-14 Olefin) are a series of low-molecular-weight polymers of olefin monomers, each containing 6 to 14 carbon atoms. 	Skin-conditioning agents—occlusive; viscosity increasing agents—nonaqueous
Hydrogenated Poly (C6-20 Olefin) 69430-35-9	Hydrogenated Poly (C6-20 Olefin) is a polymer synthesized from hydrogenated C6-20 olefins. 	Epilating agents
Hydrogenated Polybutene	Hydrogenated Polybutene is the end product of the controlled hydrogenation of Polybutene. 	Viscosity increasing agents—nonaqueous
Hydrogenated Polydecene 68037-01-4	Hydrogenated Polydecene is the end product of the controlled hydrogenation of Polydecene. 	Fragrance ingredients; hair conditioning agents; skin-conditioning agents—emollient; skin-conditioning agents—misc.; solvents

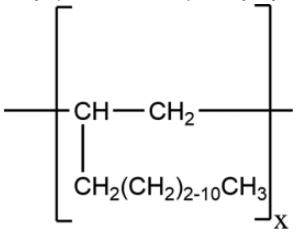
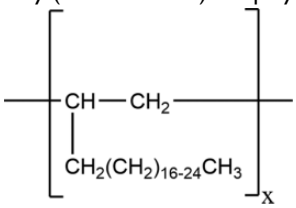
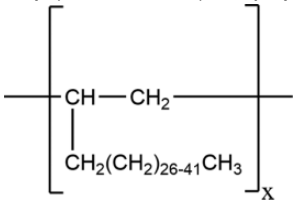
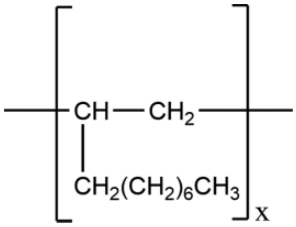
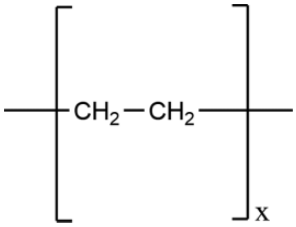
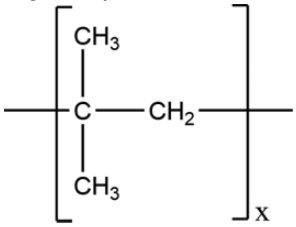
(continued)

Table 1. (continued)

Ingredient CAS No.	Definition and structure	Function(s)
Hydrogenated Polydodecene	Hydrogenated Polydodecene is the hydrogenated homopolymer of Dodecene. 	Binders; hair conditioning agents; skin-conditioning agents—emollient; solvents; viscosity increasing agents—nonaqueous
Hydrogenated Polyisobutene 68937-10-0	Hydrogenated Polyisobutene is the polymer that conforms generally to the formula: 	Skin-conditioning agents—emollient; viscosity increasing agents—nonaqueous
Isobutylene/Isoprene Copolymer 9010-85-9	Isobutylene/Isoprene Copolymer is a copolymer of isobutylene and isoprene monomers. 	Viscosity increasing agents—nonaqueous
Isoprene/Pentadiene Copolymer	Isoprene/Pentadiene Copolymer is a copolymer of isoprene and 1,3-pentadiene monomers. 	Viscosity increasing agents—nonaqueous
Polybutene 9003-28-5 9003-29-6	Polybutene is the polymer formed by the polymerization of a mixture of iso- and normal butenes. 	Binders; epilating agents; viscosity increasing agents—nonaqueous
Poly(C4-12 Olefin)	Poly (C4-12 Olefin) is a polymer synthesized from C4-12 olefins. 	Skin-conditioning agents—occlusive

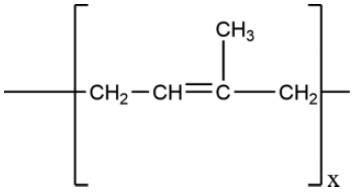
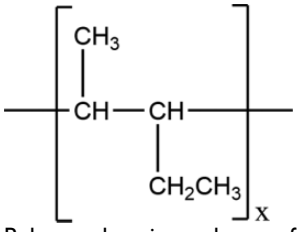
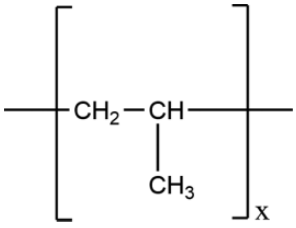
(continued)

Table 1. (continued)

Ingredient CAS No.	Definition and structure	Function(s)
Poly (C6-14 Olefin)	Poly (C6-14 Olefin) is a polymer synthesized from C6-14 olefins. 	Viscosity increasing agents—nonaqueous
Poly (C20-28 Olefin) 64743-02-8	Poly (C20-28 Olefin) is a polymer synthesized from C20-28 olefins. 	Binders; film formers; skin-conditioning agents—occlusive; surface modifiers; viscosity increasing agents—nonaqueous
Poly (C30-45 Olefin)	Poly (C30-45 Olefin) is a polymer synthesized from C30-45 olefins. 	Film formers
Polydecene 25189-70-2 37309-58-3	Polydecene is the polymer formed by the polymerization of decene. It conforms to the formula: 	Skin-conditioning agents—occlusive
Polyethylene 9002-88-4	Polyethylene is a polymer of ethylene monomers that conforms generally to the formula: 	Abrasives; adhesives; binders; bulking agents; emulsion stabilizers; film formers; oral care agents; viscosity increasing agents—nonaqueous
Polyisobutene 9003-27-4	Polyisobutene is the homopolymer of isobutylene that conforms generally to the formula: 	Binders; film formers; viscosity increasing agents—nonaqueous

(continued)

Table 1. (continued)

Ingredient CAS No.	Definition and structure	Function(s)
Polyisoprene 9003-31-0	Polyisoprene is the polymer of isoprene that conforms generally to the formula: 	Viscosity increasing agents—nonaqueous
Polypentene 9078-70-0	Polypentene is the polymer formed by the polymerization of pentene. It conforms to the formula: 	Film formers; viscosity increasing agents—nonaqueous
Polypropylene 9003-07-0	Polypropylene is a polymer of propylene monomers that conforms generally to the formula: 	Bulking agents; viscosity increasing agents—nonaqueous

[a]The idealized copolymer structures herein present a depiction of block copolymers only for the sake of simplicity and are not intended to suggest that block is the dominant form.

of lead < 10 ppm, arsenic < 2 ppm, and mercury < 1 ppm.[16-19] An anonymous source reported that Hydrogenated Polyisobutene may contain a maximum of 10 ppm n hexane as residual solvent.[9]

Hydrogenated Polydecene. A supplier reported that Hydrogenated Polydecene does not contain residual solvents, has a residual monomer specification (decene) of < 10 ppm, and has heavy metal specifications of lead < 10 ppm, arsenic < 2 ppm, and mercury < 1 ppm.[20-23]

Use

Cosmetic

The safety of the cosmetic ingredients included in this safety assessment is evaluated based on the expected use in cosmetics. The Panel utilizes data received from the US Food and Drug Administration (FDA) and the cosmetics industry in determining the expected cosmetic use. The data received from the FDA are those it collects from manufacturers on the use of individual ingredients in cosmetics by cosmetic product category in its Voluntary Cosmetic Registration Program (VCRP), and those from the cosmetic industry are submitted in response to a survey of the maximum reported use concentrations by category conducted by the Personal Care Products Council (Council).

According to the 2015 VCRP data, Polyethylene is reported to be used in 2,773 formulations; the single category with the most reported uses was lipstick with 885 (Tables 3 and 4).[24] Hydrogenated Polyisobutene is reported to be used in 1,963 formulations; the single category with the most reported uses was lipstick with 865. Most of the other in-use ingredients are primarily used in leave-on products and lipsticks. The results of the concentration of use survey conducted in 2013 and 2014 by the Council indicate Hydrogenated Polyisobutene has the highest reported maximum concentration of use; it is used at up to 95% in lipsticks.[25,26]

Both historical and current use data for Polybutene, Polyethylene, Polyisobutene, and Hydrogenated Polyisobutene are provided in Table 4. Concentrations of use for Polybutene and Hydrogenated Polyisobutene have remained about the same, with the highest maximum use concentration of Hydrogenated Polyisobutene at 95% in lip products. The highest maximum use concentration for Polyethylene has increased from 24% (eye shadow) to 67.6% (skin cleansing agents), while the highest maximum use concentration for Polyisobutene has decreased from 76% to 40% (both concentrations in lip products). Uses for all 4 ingredients have

Table 2. Physical and Chemical Properties of Polyenes.

Property	Value	Reference
	Ethylene/Octene Copolymer	
Molecular weight (Da)	24,038 (number average), 52,743 (weight average) with 0.06% below 500 and 0.29% below 1,000	10
	Polybutene	
Form	Light colored, nondrying, sticky viscous liquid	49-51
Solubility	Insoluble in water, soluble in hydrocarbon and chlorinated hydrocarbon solvents	49-51
Melting point (°C)	124-130	49-51
Density (g/mL)	0.92	49-51
	Polyethylene	
Molecular weight (Da)	198-500,000	1,52
Odor	Odorless	53
Melting point (°C)	85-110	1
Flash point (°C)	221	1
Density (g/mL)	0.910-0.925	1
λ_{max} (nm)	161.5	54
	Polyisobutene	
Molecular weight (Da)	900 minimum, 654-2,168	2,14,15,37,38
Form	White to yellowish or pale rubbery solid	2
Odor	Slight rubber/petroleum odor	2
Flash point (°C)	165	2
Solubility	Insoluble in water	2
Density(at 20 °C; g/mL)	0.92	2
	Hydrogenated Polyisobutene	
Molecular weight (Da)	Average 430, range 187-468	2,9,16-19,39-42
Form	Clear liquid	55
Odor	Odorless	55
Log K_{ow}	13.27	2
Solubility	Negligible in water	2
Boiling point (°C)	35	56
Freezing point (°C)	Below −30	55
Density (at 20 °C; g/mL)	0.819-0.830	55
	Hydrogenated Polydecene	
Molecular weight (Da)	367-596	20-23,43
Form (at 20 °C and 1,013 hPa)	Clear liquid	5
Odor	Odorless	5
Log K_{ow}	> 6.5	5
Solubility in water (at 20 °C; mg/L)	< 0.1	5
Vapor pressure (at 20 °C)	< 0.545	5
Freezing point (at 1,013 hPa; °C)	−57	5
Density (at 15.6 °C; g/mL)	0.82-0.83	5

increased by several fold since their original reviews. The ingredients not in use according to the VCRP data and industry survey are listed in Table 5.

In some cases, reports of uses were received from the VCRP, but concentration of use data was not provided. For example, Hydrogenated Polybutene is reported to be used in 51 formulations, but no use concentration data were reported. In other cases, no uses were reported in the VCRP, but concentration of use data were received from industry. Hydrogenated Poly (C6-20 Olefin) had no reported uses in the VCRP, but a use concentration in a lipstick was provided in the industry survey. Therefore, it should be presumed there is at least one use in every category for which a concentration is reported.

Some of these ingredients were reported to be used in pump and aerosol hair sprays, underarm deodorant sprays, face and neck sprays, body and handsprays, and aerosol suntan products and could be incidentally inhaled. For example, Hydrogenated

Table 3. Frequency (2015) and Concentration of Use (2013) According to Duration and Type of Exposure for Polyene Ingredients.[24-26]

	# of uses	Max conc. of use (%)	# of uses	Max conc. of use (%)	# of uses	Max conc. of use (%)	# of uses	Max conc. of use (%)
	Butylene/Ethylene Copolymer		Butylene/Ethylene/Propylene Copolymer		Decene/Butene Copolymer		Ethylene/Propylene Copolymer	
Totals[†]	1	1.5	14	4.5	3	NR	107	0.0063-12.5
Duration of use								
Leave on	1	NR	14	4.5	3	NR	107	0.0063-12.5
Rinse off	NR	1.5	NR	NR	NR	NR	NR	2
Diluted for (bath) use	NR	NR	NR	NR	NR	NR	NR	NR
Exposure type								
Eye area	NR	NR	2	NR	1	NR	11	0.0063-4
Incidental ingestion	1	NR	8	NR	2	NR	72	0.0097-12.5
Incidental inhalation—spray	NR	NR	Spray: NR Possible: 1[a]	NR	NR	NR	Spray: 4 Possible: 6[a]; 1[b]	Spray: 0.11 Possible: 0.21[a]
Incidental inhalation—powder	NR	NR	NR	NR	NR	NR	Powder: 1 Possible: 1[b]	NR
Dermal contact	NR	1.5	5	4.5	NR	NR	32	0.0063-4
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair—non-coloring	NR	NR	NR	NR	NR	NR	3	2
Hair—coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous membrane	1	1.5	8	NR	2	NR	72	0.0097-12.5
Baby products	NR	NR	NR	NR	NR	NR	NR	NR
	Hydrogenated Poly (C6-14 Olefin) [c]		Hydrogenated Poly (C6-20 Olefin)		Hydrogenated Polybutene		Hydrogenated Polydecene	
Totals[†]	82	0.25-58	NR	10	51	NR	713	0.005-59
Duration of use								
Leave on	79	58	NR	10	47	NR	681	0.035-59
Rinse off	3	0.25-1	NR	NR	4	NR	32	0.005-49
Diluted for (bath) use	NR	NR	NR	NR	NR	NR	NR	35
Exposure type								
Eye area	9	NR	NR	NR	14	NR	77	2-38
Incidental ingestion	16	58	NR	10	26	NR	188	5.2-59
Incidental inhalation—spray	Spray: NR Possible: 10[a]; 14[b]	NR	NR	NR	NR	NR	Spray: 17 Possible: 224[a]; 115[b]	Spray: 1.8-42 Possible: 0.88-5[a]
Incidental inhalation—powder	Powder: 2 Possible: 14[b]	NR	NR	NR	NR	NR	Powder: 4 Possible: 115[b]	Powder: 0.9-10.5
Dermal contact	66	NR	NR	NR	24	NR	482	0.035-49
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	Not spray: 2-13.8
Hair—non-coloring	NR	NR	NR	NR	NR	NR	38	0.005-36
Hair—coloring	NR	0.25-1	NR	NR	NR	NR	2	1-11
Nail	NR	NR	NR	NR	NR	NR	1	NR
Mucous membrane	16	58	NR	10	28	NR	191	5.2-59
Baby products	NR	NR	NR	NR	NR	NR	NR	NR

(continued)

Table 3. (continued)

	# of uses	Max conc. of use (%)	# of uses	Max conc. of use (%)	# of uses	Max conc. of use (%)	# of uses	Max conc. of use (%)
	Poly (C30-45 Olefin)		Polydecene		Polyisoprene		Polypropylene	
Totals[†]	2	0.6-26.1	156	0.098-47.9	28	0.098-47	24	0.05-68.6
Duration of use								
Leave on	2	0.6-26.1	129	0.098-47.9	26	0.098-47	20	0.05-68.6
Rinse off	NR	NR	27	25	2	1.8	4	0.2-66
Diluted for (bath) use	NR	NR	NR	NR	NR	NR	NR	NR
Exposure type								
Eye area	1	NR	8	0.098-6	2	0.49-47	6	0.4-68.6
Incidental ingestion	NR	NR	75	10.2-47.9	3	2-12.2	NR	4
Incidental inhalation—spray	NR	Spray: 26.1	Spray: 1 Possible: 12[a]; 8[b]	NR	Spray: NR Possible: 9[a]; 6[b]	NR	Spray: NR Possible: 2[a]; 6[b]	NR
Incidental inhalation—powder	NR	NR	Powder: 7 Possible: 8[b]	NR	Powder: 3 Possible: 6[b]	NR	Powder: NR Possible: 6[b]	Powder: 2.8
Dermal contact	2	0.6-26.1	63	0.098-25	25	0.098-47	18	0.05-66
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair—non-coloring	NR	NR	2	NR	NR	NR	NR	NR
Hair-coloring	NR	NR	16	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	1	NR
Mucous membrane	NR	NR	75	10.2-47.9	3	1.8-12.2	1	4-66
Baby products	NR	NR	NR	NR	NR	NR	NR	NR

NR = not reported; VCRP = Voluntary Cosmetic Registration Program.

† 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 may be sprays, but it is not specified whether the reported uses are sprays.

[b]Not specified whether a powder or a spray, so this information is captured for both categories of incidental inhalation.

[c]Hydrogenated C6-14 Olefin Polymers is a synonym for Hydrogenated Poly(C6-14 Olefin). The VCRP database has entries for both names and the data have been added together.

Table 4. Current and Historical Frequency and Concentration of Use According to Duration and Exposure.[1-3,24,26]

	# of uses		Max conc. of use (%)		# of uses		Max conc. of use (%)	
	Polybutene				Polyethylene			
	2015	1976	2013	1976	2015	2002	2013	2004
Totals†	1,823	85	0.1-82.4	>1->50*	2,773	717	0.0097-67.6	0.09-24
Duration of use								
Leave on	1,808	83	0.1-82.4	>1->50	2,271	615	0.0097-52.6	0.09-24
Rinse off	15	2	8-20	>5-10	501	92	0.05-67.6	0.3-11
Diluted for (bath) use	NR	NR	NR	NR	1	10	10	4-18
Exposure type								
Eye area	239	10	0.5-13.1	>1-5	734	382	0.06-21	3-24
Incidental ingestion	1,322	70	6-82.4	>1->50	885	67	0.0097-18.9	3-16
Incidental inhalation—spray	Spray: 2 Possible: 12[a]; 8[b]	Spray: NR Possible: 2[a]	Spray: 0.1 Possible: 20[a]	Spray: NR Possible: >1-25[a]	Spray: 17 Possible: 120[a]; 70[b]	Spray: 1 Possible: 23[a]; 17[b]	Spray: 0.5-52.6 Possible: 0.47-12[a]	Spray: 3-5 Possible: 0.5-10[a]; 1-16[b]
Incidental inhalation—powder	Powder: 11 Possible: 8[b]	NR	Powder: 0.92-4	NR	Powder: 82 Possible: 70[b]	Powder: 32 Possible: 17[b]; 1[c]	Powder: 4-30	Powder: 3-10 Possible: 1-16[b]
Dermal contact	425	13	0.1-73	>1-25	1,765	603	0.03-67.6	0.2-24
Deodorant (underarm)	NR	NR	NR	NR	Possible spray: 8	NR	Spray: 1.6 Not spray: 1-12.1	Possible spray: 7
Hair—non-coloring	4	2	NR	>5-10	19	5	0.26-6	2
Hair—coloring	NR	NR	NR	NR	2	3	5-6	NR
Nail	NR	NR	8	NR	32	NR	0.42-15	0.09-3
Mucous membrane	1,327	70	6-82.4	>1->50	1,185	93	0.0097-18.9	0.3-18
Baby products	NR	NR	NR	NR	NR	1	NR	3
	Polyisobutene				Hydrogenated Polyisobutene			
	2015	2005	2013	2005	2015	2005	2013	2005
Totals†	310	30	0.24-40	0.3-76	1,963	654	0.00055-95	0.001-96
Duration of use								
Leave on	295	29	0.24-40	0.3-76	1,916	639	0.001-95	0.001-96
Rinse off	15	1	1.1-3.5	4	47	15	0.00055-51	2-85
Diluted for (bath) use	NR	NR	NR	NR	NR	NR	NR	3-85
Exposure type								
Eye area	108	11	0.45-36.3	1-30	227	78	0.09-67.7	0.1-40
Incidental ingestion	54	12	6-40	4-76	865	318	0.29-95	0.001-96
Incidental inhalation—spray	Spray: 6 Possible: 42[a]; 30[b]	Spray: 2 Possible: 1[a]	Spray: 5.5-7 Possible: 0.5[a]	Spray: NR Possible: 0.5[a]	Spray: 10 Possible: 196[a]; 219[b]	Spray: 5 Possible: 39[a]; 18[b]	Spray: 0.048-31 Possible: 0.53-58.9[a]	Spray: 10 Possible: 3-15[a]; 0.5-42[b]
Incidental inhalation—powder	Powder: 4 Possible: 30[b]	NR	NR	NR	Powder: 42 Possible: 219[b]	Powder: 24 Possible: 18[b]	Powder: 1-4	Powder: 0.1-5 Possible: 0.5-42[b]; 4[c]
Dermal contact	186	7	0.24-36.3	0.3-46	1,058	325	0.001-93	0.1-85
Deodorant (underarm)	NR	NR	NR	NR	Possible spray: 4	NR	NR	Possible spray: 2
Hair—non-coloring	5	3	NR	NR	15	NR	0.00055-58.9	15-17
Hair—coloring	NR	NR	NR	NR	3	1	0.048-20	NR
Nail	NR	NR	NR	NR	7	5	23-68.5	0.2-3
Mucous membrane	54	12	6-40	4-76	871	323	0.29-95	0.001-96
Baby products	NR	NR	NR	NR	NR	NR	NR	4

CIR = Cosmetic Ingredient Review; NR = not reported.

† 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.

* Earlier CIR safety assessments reported concentrations as ranges, not exact values.

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

[b]Not specified whether a powder or a spray, so this information is captured for both categories of incidental inhalation.

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

Table 5. Polyene Ingredients With No Reported Uses.[24-26]

Butene/Propylene Copolymer
Ethylene/Octene Copolymer
Hydrogenated Polybutene
Hydrogenated Polydodecene
Isobutylene/Isoprene Copolymer
Isoprene/Pentadiene Copolymer
Poly (C4-12 Olefin)
Poly(C6-14 Olefin)
Poly(C20-28 Olefin)
Polypentene

Polyisobutene was reported to be used in face and neck sprays at a maximum concentration of 8.5%, and Polyethylene was reported to be used in aerosol deodorants at a maximum concentration of 1.6%. In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters >10 μm, with propellant sprays yielding a greater fraction of droplets/particles below 10 μm compared with pump sprays.[27-30] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and bronchial regions and would not be respirable (ie, they would not enter the lungs) to any appreciable amount.[28,29] There is some evidence indicating that deodorant spray products can release substantially larger fractions of particulates having aerodynamic equivalent diameters in the range considered to be respirable.[29] However, the information is not sufficient to determine whether significantly greater lung exposures result from the use of deodorant sprays, compared to other cosmetic sprays. The polyene ingredients in this safety assessment currently are not restricted from use in any way under the rules governing cosmetic products in the European Union (EU).[31]

Non-Cosmetic

Many of the polyene ingredients have been approved by the US FDA for use as indirect food additives and in medical devices. Additionally, Isobutylene/Isoprene Copolymer, Polyethylene, and Polyisobutene are approved direct food additives for chewing gum bases.

Polyethylene and Polypropylene are used as negative control materials for International Organization for Standardization (ISO 10993-6) international standard biological evaluation of medical devices.[32] Ultra-high-molecular-weight Polyethylene is the most used biomaterial for the articulating surface of total joint replacements.[33] Polyisobutene is used in transdermal drug delivery patches and patch adhesives.[34,35] Polyisoprene (*trans*-1,4) is widely used as a component of root canal filling material.[36] Table 6 lists regulated uses in foods and medical devices.

Toxicokinetics

Although many of these polyene ingredients are high-molecular-weight, large, inert polymers, the smaller, liquid ingredients in this group each comprise simple hydrocarbon structure without functional groups other than alkanes or alkenes. Thus, dermal penetration is limited for the large and small polymers in this group. These ingredients are completely insoluble in aqueous solutions or organic solvents but may be swellable in certain organic solvents.

Absorption

Hydrogenated Polydecene. In one study, the absorption potential of undiluted Hydrogenated Polydecene was assessed in male Fischer rats.[5] Groups of 3 rats/time point received a single or daily (for 15 days) oral gavage dose of 30, 210, or 1,500 mg [3 H]-Hydrogenated Polydecene. Tissues and body fluids were sampled at 0.08, 0.25, 0.5, 1, 2, 4, 8, 24, 48, 72, 120, and/or 168 h post-dosing. With all 3 dose levels, very little of the administered dose was absorbed. What was absorbed was found in the liver, fat, lymph nodes, kidney, and spleen. The majority of the test compound was excreted in the feces (> 92%). Urinary excretion was low (< 1%), and very little of the dose was recovered in the bile (0.01%).

Biocompatibility

Polyethylene. Cellular and tissue responses to Polyethylene, determined as part of implant biocompatibility testing, include fibrous connective tissue build-up around the implant material that varies as a function of the physical form of the implant material.[1] Specific assays for osteoblast proliferation and collagen synthesis demonstrated a reduction as a function of exposure to Polyethylene particles that is inversely related to particle size. However, Polyethylene particles had a stimulatory effect on monocyte-derived macrophages, prolonging the survival of these cells in culture.

Toxicological Studies

Single Dose (Acute) Toxicity

Animal acute dose toxicity studies are presented in Table 7.[5,6,37-43] In acute oral toxicity studies in rats, the LD_{50}sof diisobutylene and triisobutylene were > 2,000 mg/kg/body weight (bw) each. The oral LD_{50} s of di-n-butene, tributene, and tetrabutene (containing 30% pentabutene) in rats were > 10,000 mg/kg each. The oral LD_{50} values for Ethylene/Octene Copolymer, undiluted Hydrogenated Polydecene and undiluted Hydrogenated Polydodecene, were > 5,000 mg/kg in rat studies. The LD_{50} of undiluted Polyisobutene was > 15,400 mg/kg in an oral rat study.

Acute dermal studies of diisobutylene and Hydrogenated Polydodecene found the LD_{50} values > 2,000 mg/kg in rats. In rabbit studies, the dermal LD_{50} values for Ethylene/Octene Copolymer, hydrogenated decene dimer, Hydrogenated Polyisobutene, and Polyisobutene were > 5,000 mg/kg, > 3,000 mg/kg, >2,000 mg/kg, and > 25,000 mg/kg, respectively.

In acute inhalation studies, the LC_{50} of diisobutylene vapor in albino rats was > 4,185 ppm (19,171 mg/m^3) after a 4-hour, single, whole-body exposure. The LC_{50} for an aerosol of

Table 6. FDA-Approved Uses of Polyenes.

Ingredients	Regulation	CFR reference
	Food use	
Isobutylene/Isoprene Copolymer; Polyethylene; Polyisobutene	Food additives permitted for direct addition to food for human consumption—chewing gum base	21 CFR172.615
Hydrogenated Polyisobutene; Isobutylene/Isoprene Copolymer; Polybutene; Polyethylene; Polyisobutene; Polyisoprene; Polypropylene; Hydrogenated Polybutene;	Adhesives approved for use as indirect food additives	21 CFR175.105
Polybutene; Polyisobutene; Polyisoprene;	Pressure-sensitive adhesives approved for use as indirect food additives	21 CFR175.125
Hydrogenated Polyisobutene; Polybutene; Polyethylene; Polyisobutene; Polypropylene; Hydrogenated Polybutene	Resinous and polymeric coatings—adhesives and components of coatings approved for use as indirect food additives	21 CFR175.300
Hydrogenated Polybutene	Components of paper and paperboard in contact with aqueous and fatty foods approved for use as indirect food additives	21 CFR176.170
Isobutylene/Isoprene Copolymer; Polybutene; Polyethylene; Polyisobutene; Polyisoprene; Hydrogenated Polybutene	Components of paper and paperboard in contact with dry food approved for use as indirect food additives	21 CFR176.180
Polyethylene	Defoaming agents used in coatings approved for use as indirect food additives	21 CFR176.200
Polyethylene	Defoaming agents used in the manufacture of paper and paperboard approved for use as indirect food additives	21 CFR176.210
Polyethylene; Polyisobutene; Polypropylene	Cellophane approved for use as indirect food additives	21 CFR177.1200
Ethylene/Propylene Copolymer; Isobutylene/Isoprene Copolymer; Polyisobutene	Approved for use in closures with sealing gaskets for food containers—indirect food additives	21 CFR177.1210
Isobutylene/Isoprene Copolymer; Polyisobutene	Isobutylene polymers approved for use as indirect food additives	21 CFR177.1420
Butylene/Ethylene/Propylene Copolymer; Ethylene/Octene Copolymer; Ethylene/Propylene Copolymer; Polyethylene; Polypropylene	Olefin polymers approved for use as indirect food additives	21 CFR177.1520
Butylene/Ethylene Copolymer;	Poly-1-butene resins and butene/ethylene copolymers approved for use as indirect food additives	21 CFR177.1570
Ethylene/Propylene Copolymer; Isobutylene/Isoprene Copolymer; Polybutene; Polyethylene; Polyisoprene	Rubber articles intended for repeated use approved for use as indirect food additives	21 CFR177.2600
Polybutene; Polyethylene; Polyisobutene; Hydrogenated Polybutene	Lubricants with incidental food contact approved as indirect food additives (addition to food not to exceed 10 ppm for Polybutene, Hydrogenated Polybutene, and Polyethylene; for use only as a thickening agent in mineral oil lubricants in Polyisobutene)	21 CFR178.3570
Polyisobutene; Hydrogenated Polybutene	Plasticizers in polymeric substances approved as indirect food additives	21 CFR178.3740
Polyethylene	Reinforced wax approved for use as indirect food additives	21 CFR178.3850
Hydrogenated Polybutene	Release agents approved for use as indirect food additives	21 CFR 178.3860
Polyisobutene; Hydrogenated Polybutene	Surface lubricants used in the manufacture of metallic articles approved for uses as indirect food additives	21 CFR178.3910
Polypropylene	Packaging materials for use during the irradiation of prepackaged foods	21 CFR179.45
Polyethylene	Polyethylene—approved as a food additive permitted in feed and drinking water of animals	21 CFR573.780

(continued)

Table 6. (continued)

Ingredients	Regulation	CFR reference
	Drug/medical use	
Polypropylene	Intercardiac patch or pledget—cardiovascular device	21 CFR 870.3470
Polyethylene	Ear nose and throat devices—prostheses of the ear and mandible	21 CFR874.3430; .3450; .3495; .3620; .3695; .3880; .3930
Polypropylene	Nonabsorbable Polypropylene surgical suture—general and plastic surgery device	21 CFR878.5010
Polypropylene	Approved use as a finger joint polymer constrained prosthesis—orthopedic device	21 CFR888.3230
Polyethylene	Approved use as bone cap; ankle joint prosthesis, elbow joint prosthesis; finger joint prosthesis; hip joint prosthesis; knee joint prosthesis; shoulder joint prosthesis; wrist join prosthesis—orthopedic devices	21 CFR888.3000; .3100; .3110; .3120; .3150; .3160; .3200; .3220; .3310; .3340; .3350; .3353; .3358; .3390; .3490; .3500; .3510; .3520; .3530; .3535; .3540; .3550; .3560; .3565; .3640; .3650; .3660; .3670; .3680; .3800; .3810

FDA = Food and Drug Administration.

Hydrogenated Polydecene was > 5.2 mg/L with a 4-hour exposure in rats. The LC_{50} for the dimer of hydrogenated decene was 1.17 mg/L in rats. In another acute inhalation study of the dimer of hydrogenated decene, the LC_{50} could not be determined in rats tested at 5 mg/L because 9/10 animals died within 3 days of administration of the test material. The LC_{50} for Hydrogenated Polydodecene was > 5.06 mg/L. The LC_{50} for 100% Hydrogenated Polyisobutene was > 5 mg/L. The oral, inhalation and dermal acute dose toxicity data that were presented in the original reviews of Polybutene, Polyethylene, and Hydrogenated Polyisobutene are summarized below and not in the tables.

Oral

Polybutene. When tested for acute oral toxicity in albino rats, concentrations of Polybutene ranging from 15% to 75% were relatively harmless (average molecular weight not specified).[3]

Polyethylene. The LD_{50} for Polyethylene (average molecular weight of 450) in rats (201-223 g) was found to be > 2,000 mg/kg, and in Polyethylene with an average molecular weight of 655 Da, the LD_{50} was determined as >5.0 g/kg.[1]

Hydrogenated Polyisobutene. No deaths in mice were observed in an acute oral toxicity test at a maximum dose of 89.608 g/kg of a Hydrogenated Polyisobutene mixture.[2] No deaths were observed in several oral toxicity rat studies of 5 g/kg Hydrogenated Polyisobutene; however, lethargy and wetness in the anogenital area after dosing was observed. The authors of these studies also concluded that the LD_{50} is greater than 5.0 g/kg bw. The average molecular weight was reported to be 900 Da in one of the studies.

Inhalation

Polybutene. Polybutene produced no abnormalities in rats during a 4-hour inhalation exposure up to concentrations of 18.5 mg/L.[3]

Dermal

Polybutene. In acute dermal toxicity tests, Polybutene in formulations produced no abnormalities or irritation in rabbits. The LD_{50} of Polybutene in formulation was greater than 10.25 g/kg (average molecular weight not specified).[3]

Repeated Dose Toxicity Studies

Repeated dose toxicity studies in animals are presented in Table 8.[5,37-43] No treatment-related gross microscopic changes were observed following exposure to 100% Polyisobutene in a 90-day dietary study of rats and 2-year dietary studies in rats or dogs. No adverse effects were observed in oral repeated dose studies of Hydrogenated Polydecene, with the no observed adverse effect levels (NOAELs) determined to be 1,000 mg/kg/d in one 90-day rat study and over 4,000 mg/kg/d in another. In a 4-week oral repeated dose rat study, the NOAEL for Hydrogenated Polydecene was 6,245 mg/kg/d in males and 6,771 mg/kg/d in females. Gross necropsy, histopathology, and microscopic findings did not reveal any significant treatment-related findings. The NOAEL for the oral administration of the trimer of hydrogenated dodecene in 2 respective oral repeated dose toxicity studies in rats was 1,000 mg/kg/d. Treatment-related effects on mortality, clinical signs, bw, food consumption, hematology, clinical chemistry, organ weights, or gross and histologic pathology were not observed in either study. In a 4-week dermal study in rats, 100% Hydrogenated Polyisobutene produced minimal to mild dermal irritation in the majority of treated animals. Histopathologic examinations of the high-dose group found effects limited to the application site and included minimal to mild epidermal hyperplasia and hyperkeratosis with reactive hyperplasia of the underlying inguinal lymph nodes.

The oral and dermal repeated dose toxicity data that were presented in the original reviews of Polybutene and Polyethylene are summarized below and not in the tables.

Table 7. Acute Toxicity Studies in Animals.

Ingredient and concentration/ dose	Method	Results/conclusions	References
		Oral	
Ethylene/Octene Copolymer (14%-16%) in a trade name mixture	Acute oral toxicity study in rats (no further details provided)	$LD_{50} > 5{,}000$ mg/kg	11
Ethylene/Octene Copolymer and sodium acrylate copolymer (30%-50%) in a trade name mixture	Acute oral toxicity study in rats (no further details provided)	$LD_{50} > 2{,}000$ mg/kg	12
Polybutene analog diisobutylene	Acute oral toxicity study in rats (no further details provided	$LD_{50} > 2{,}000$ mg/kg, no mortalities observed	6
Polybutene analog triisobutylene	Acute oral toxicity study in rats (no further details provided)	$LD_{50} > 2{,}000$ mg/kg, no mortalities observed	6
Polybutene analog di-n-butene	Acute oral toxicity study in rats (no further details provided)	$LD_{50} > 10{,}000$ mg/kg, 1 animal had partial thickening of the forestomach and another had partial hyperemia of the small intestine membrane, no mortalities observed	6
Polybutene analog tributene	Acute oral toxicity study in rats (no further details provided)	$LD_{50} > 10{,}000$ mg/kg, no mortalities observed	6
Polybutene analog tetrabutene (containing 30% pentabutene)	Acute oral toxicity study in rats (no further details provided)	$LD_{50} > 10{,}000$ mg/kg, no mortalities observed	6
Polyisobutene (100%), MW range 654-2168	Acute oral toxicity study in rats (no further details provided)	$LD_{50} > 15{,}400$ mg/kg	37,38
Hydrogenated Polyisobutene (100%), MW range 187-468	Acute oral toxicity study in rats (no further details provided)	$LD_{50} > 5{,}000$mg/kg	39-42
Hydrogenated Polydecene (undiluted), average MW not specified	Acute oral toxicity study in Sprague-Dawley rats (5 rats/sex)	$LD_{50} > 5{,}000$ mg/kg	5
Hydrogenated Polydecene(100%), MW range 367-596	Acute oral toxicity study in rats (no further details provided)	$LD_{50} > 5{,}000$ mg/kg	43
Hydrogenated Polydodecene (undiluted), average MW not specified	Acute oral toxicity study in Sprague-Dawley rats (5 rats/sex)	$LD_{50} > 5{,}000$ mg/kg	5
		Dermal	
Ethylene/Octene Copolymer (14%-16%) in a trade name mixture	Acute dermal toxicity study in rabbits (no further details provided)	Estimated $LD_{50} > 5{,}000$ mg/kg	11
Ethylene/Octene Copolymer and sodium acrylate copolymer (30%-50%) in a trade name mixture	Acute dermal toxicity study in rabbits (no further details provided)	Estimated $LD_{50} > 2{,}000$ mg/kg	12
Polybutene analog diisobutylene	Acute dermal toxicity study in rats; exposure under occlusive patches for 24 hours (no further details provided)	$LD_{50} > 2{,}000$ mg/kg; no mortalities or overt signs of toxicity were observed	6
Polyisobutene (100%); MW range 654-2168	Acute dermal toxicity study in rabbits (no further details provided)	$LD_{50} > 25{,}000$ mg/kg	37,38
Hydrogenated Polyisobutene (100%); MW range 187-468	Acute dermal toxicity study in rabbits (no further details provided)	$LD_{50} > 2{,}000$ mg/kg	39-42
Hydrogenated Polydecene analog hydrogenated decene dimer (undiluted); dose tested = 3,000 mg/kg	Acute dermal toxicity study in New Zealand White rabbits (2 rabbits/ sex); material applied to clipped	Estimated $LD_{50} > 3{,}000$ mg/kg; skin reactions observed at 24 hours post-patch removal included pale red erythema and slight to mild edema; by day 14, only slight edema and desquamation were observed; 1 female	5

(continued)

Table 7. (continued)

Ingredient and concentration/ dose	Method	Results/conclusions	References
	skin on the back for 24 hours; occluded and rinsed	rabbit that died on day 9 of the observation period was observed to be emaciated prior to death; no other clinical, behavioral, or systemic signs of toxicity were observed; no treatment-related signs of toxicity were observed at necropsy	
Hydrogenated Polydodecene (undiluted); concentration tested = 2,000 mg/kg; average MW not specified	Acute dermal toxicity study in Sprague-Dawley rats (5 rats/sex); material applied to an area of 37 cm^2 clipped skin for 24 hours; occluded and rinsed	$LD_{50} > 2{,}000$ mg/kg; no clinical signs of toxicity or skin irritation were observed; bw appeared unaffected by treatment and there were no treatment-related signs of toxicity observed at necropsy	5
		Inhalation	
Polybutene analog diisobutylene	4-hour, single, whole-body inhalation toxicity study in albino rats (no further details provided)	$LC_{50} \geq 4{,}185$ ppm (19,171 mg/m3), no mortalities or overt signs of toxicity were observed	6
Hydrogenated Polyisobutene (100%), MW range 187-468	4-hour inhalation study in rats (no further details provided)	$LC_{50} > 5$ mg/L	39-42
Hydrogenated Polydecene, average MW not specified	4-hour, nose-only inhalation toxicity study in Sprague-Dawley-derived rats (6 rats/sex)	$LC_{50} > 5.2$ mg/L, no mortalities were observed, no significant clinical signs were observed during and after the exposure period, and no treatment-related signs of toxicity were observed at necropsy	5
Hydrogenated Polydecene analog hydrogenated decene dimer, concentrations tested = 0.77, 0.94, 1.1, 1.4, or 5.1 mg/L	4-hour inhalation (aerosol/vapor) toxicity study in groups Sprague-Dawley rats (5 rats/sex)	Combined $LC_{50} = 1.17$ mg/L; all animals treated with 5.1 mg/L died within 2 days, 2-5 females each from all the remaining treatment groups died, no males in the 0.77 or 0.94 dose groups died but 2 males each in the remaining dose groups died; clinical signs included dyspnea and nasal discharge; bw gain was reduced in the first week, but within normal parameters the second week; treatment-related effects of the lung were observed during gross necropsy of only the animals that died during the study; microscopic lesions in the lung were observed in all of the high-dose animals	5
Hydrogenated Polydecene analog hydrogenated decene dimer, concentration tested = 5 mg/L	Acute whole-body 1-hour inhalation toxicity study in Sprague-Dawley rats (5 rats/sex)	LC_{50} not determined; 9/10 treated animals died within 3 days; clinical signs included reduced activity, increased respiration rate, respiratory sounds, labored breathing, irregular breathing, muzzle and abdominal staining, partially closed eyes, hunched back, and lying on the side; in the one female that survived treatment, all respiratory signs were normal by day 5, but muzzle staining persisted until day 9 and marked loss in bw was observed through day 4; at necropsy, the surviving female had absolute and relative lung and trachea weights greater than the controls and the heart appeared to be affected (no further details); in the animals that died following treatment, treatment-related increases in respiratory findings were observed (no further details)	5
Hydrogenated Polydodecene, average MW not specified	4-hour, nose-only inhalation toxicity study in Sprague-Dawley rats (5 rats/sex)	$LC_{50} > 5.06$ mg/L; clinical signs observed after removal from the exposure chamber included wet fur, hunched posture, piloerection, increased respiration rate, ptosis, and isolated incidents of decreased respiration rate and red/brown stain on the head; 1 hour after exposure, the only observable clinical signs included hunched posture, piloerection, and increased respiration rate; by day 2 postexposure, all animals had recovered and appeared to be normal; no treatment-related changes observed in bw; no treatment-related signs of toxicity observed at necropsy.	5

Table 8. Repeated Dose Toxicity Studies in Animals.

Ingredient and concentration/dose	Method	Results/conclusions	References
		Oral	
Polyisobutene (100%); concentrations tested = 0; 800; 4,000; or 20,000 ppm; MW range 654-2,168	2-year dietary toxicity study in Charles River rats (no further details provided)	After 12 months, no treatment-related gross or microscopic changes were observed; following 24 months, no treatment-related effects on bws, feed consumption, mortality, clinical observations, hematology, or urinalysis were observed; in the high dose group, 3 of 6 males that died between weeks 17 and 24 exhibited hematuria while another male in this dose group exhibited similar reactions but recovered within 2 weeks; necropsy of the 3 rats found that 2 of the rats had clotted blood in the urinary tract, bladder, stomach, and intestines while the third rat had no significant gross pathologic changes; no increases in frequency of neoplastic lesions were observed in any dose group	37,38
Polyisobutene (100%); doses tested = 0, 40, 200, or 1,000 mg/kg; MW range 654-2168	2-year oral toxicity study in Beagle dogs (no further details provided)	No treatment-related effects on bw, feed consumption, mortality, clinical signs, hematology, blood chemistry, urinalysis, liver function, organ weights, or gross pathologic and histopathologic changes (no further details provided)	37,38
Hydrogenated Polyisobutene (0% or 5%); MW range 187-468	90-day dietary toxicity study in rats; half of the animal groups were killed at 90 days, and the other half were killed 30 days later following a recovery period (no further details provided)	No effects were observed on bw, bw gain, urinalysis, hematology, or clinical chemistry parameters; when compared to controls, liver weights were increased in both males and females and kidney weights were increased in males; no organ weight differences between treated and control animals were observed following the recovery period; no treatment-related histopathologic changes were observed (no further details provided)	39-42
Hydrogenated Polydecene; concentrations tested = 0; 8,000; 20,000; or 50,000 ppm (equivalent overall mean daily intakes were 1,039; 2,538; or 6,245 mg/kg/d for males and 995; 2,481; or 6,771 mg/kg/d for females); average MW not specified	4-week dietary toxicity study in F-344 rats (5 sex/dose)	No observed adverse effect level (NOAEL) = 6,245 mg/kg/d in males and 6,771 mg/kg/d in females; no clinical signs of toxicity or mortality were observed in any rats during the study; overall bw gain and feed consumption of females in the 50,000 ppm dose group was higher than the controls; a dose-dependent decrease in mandibular lymph node weights (absolute and relative to bw) was observed in males and females but these results were statistically significant only for 50,000 pm females and were not considered adverse effects since there were no other findings; gross necropsy, histopathology, and microscopic findings did not reveal any significant treatment-related findings	5
Hydrogenated Polydecene (100%); doses up to 1,000 mg/kg/d; MW range 367-596	90-day oral toxicity study in rats (no further details provided)	No observed effect level (NOEL) = 1,000 mg/kg/d	43
Hydrogenated Polydecene in Polyethylene glycol via gavage at dose levels of 0, 100, 500, or 1,000 mg/kg/bw/d for 91 days (average molecular weight not specified	90-day oral toxicity study, groups of 20 male and 20 female Sprague-Dawley rats received test material via gavage.	NOAEL = 1,000 mg/kg/d; toxicity of the test material was examined in F_1 generation rats following reproduction study; F_1 generation rats of each dose group, including the vehicle control, had minor gastrointestinal effects; transient changes in bw, bw gain, feed consumption, hematology, and organ weights were observed but not considered to be treatment-related; a significant increase in prothrombin time was observed in males of the 1,000 mg/kg/d dose group but no corresponding decreases in platelets or macroscopic or microscopic changes were observed so this result was not considered biologically significant; no treatment-related changes in clinical chemistry, mortality, or ophthalmology were observed (no further details provided)	5
Hydrogenated Polydecene; concentrations tested = 0, 1,000; 7,000; or 50,000 ppm	90-day oral toxicity study of F-344 rats (10 rats/sex/dose); an additional 5 rats/sex were	NOAEL = 50,000 ppm (4,159.4 mg/kg/d in males and 4,619.9 mg/kg/d in females); clinical signs of toxicity observed in the 50,000 ppm group included oily and ungroomed coats, soft feces, and	5

(continued)

Table 8. (continued)

Ingredient and concentration/dose	Method	Results/conclusions	References
(equivalent to 77.5, 553.7, and 4,159.4 mg/kg/d, respectively, in males and 85.5, 611.5, and 4,619.9 mg/kg/d, respectively, in females); average MW was not specified	administered control feed or 50,000 ppm in their diet for 13 weeks and left untreated for the following 4 weeks to examine recovery	brown staining; hair loss occurred at a greater incidence in treated animals when compared to controls; oily coats continued through the first week of the recovery period, particularly in females receiving 50,000 ppm; during recovery weeks 2-4, rats appeared ungroomed and exhibited hair loss; soft feces occasionally observed in the 7,000 ppm females; slight increase in feed consumption in the high-dose group compared to controls (8% in males and 10% in females) that continued through the recovery period but there was no effect observed on either bw or feed efficiency; slight (<5%) but significant increases in erythrocyte counts, hemoglobin, and packed cell volume in males of the 7,000 and 50,000 ppm groups with dose-related increase in hemoglobin was not observed at the end of the recovery period; slight (6%) but significant increase in platelet counts in high-dose males and females was not observed at the end of the recovery period; absolute and relative liver weights in treated males were slightly lower but the liver weights were comparable to controls at the end of the recovery period; no treatment-related effects noted in the bone marrow, clinical chemistry, urinalysis, gross pathology, or histopathology	
Hydrogenated dodecene trimer (analog of Hydrogenated Polydodecene); doses tested = 0 or 1,000 mg/kg/bw/d	28-day repeated dose oral toxicity study in Sprague-Dawley CD rats (5 rats/sex/dose: an additional 2 satellite groups (0 and 1,000 mg/kg/d) were also maintained without treatment for 14 days following the end of the dosing period	NOAEL was determined to be 1,000 mg/kg/d; treatment-related effects in mortality, clinical signs, bw, feed consumption, hematology, clinical chemistry, organ weights, or gross and histologic pathology were not observed	5
Hydrogenated dodecene trimer (analog of Hydrogenated Polydodecene) in arachis oil; doses tested = 0, 50, 250, or 1,000 mg/kg/d	10-week oral gavage repeated dose toxicity study in 3 groups of 10 male and 10 female Sprague-Dawley Crl:CD (SD) IGS BR strain rats (10 rats/sex/group).	NOAEL = 1,000 mg/kg/d; during the dosing period, one rat in the control group and one rat in the 250 mg/kg/d dose group died but deaths were not treatment-related; no signs of clinical toxicity or effects on behavioral and functional performance, sensory reactivity, bw, or feed and water consumption were observed following treatment with the test material; no significant treatment-related effects were observed in the hematological and clinical chemistry assessments or during the gross pathology examination	5
		Dermal	
Hydrogenated Polyisobutene (100%); doses tested = 0, 0.5, 1.0, or 1.5 mL/kg for 5 days/wk; MW range 187-468	4-week dermal toxicity study in Sprague-Dawley rats (no further details provided)	No mortalities were observed during the study and no statistically significant differences in bws, bw gain, hematology, or clinical chemistry parameters were observed between treated and control animals; relative kidney weights were increased in high-dose males and relative heart weights were decreased in low-dose males but these changes were not considered toxicologically significant because the kidney weight changes were not accompanied with any histopathologic effects and the heart weight changes were not decreased in a dose-related manner; minimal to mild dermal irritation consisting of redness, paleness, scaling, rippling and pinpoint scabbing of the skin was observed in the majority of treated animals; histopathologic examinations were performed on the high-dose and control groups only; effects observed in the treated animals were limited to the application site and included minimal to mild epidermal hyperplasia and hyperkeratosis of the application site with reactive hyperplasia of the underlying inguinal lymph nodes	39-42

Oral

Polybutene. A 2-year chronic oral toxicity study of Polybutene (75% concentrate) in Charles River albino rats given up to 20,000 ppm Polybutene blended into their regular diets revealed no gross or microscopic pathological changes that could be correlated with Polybutene ingestion.[3] No significant differences were found after 24 months of feeding in the bws or weight of food consumption, hematological results, urology, or tumor formation between the animals fed Polybutene and those that were not. In the 20,000 ppm group, 3 of 6 males that died between weeks 17 and 24 exhibited hematuria. In a 2-year chronic oral toxicity study of Polybutene (75% concentrate) in Beagle dogs, daily oral administration of Polybutene at doses up to 1,000 mg/kg/d caused no abnormalities in bw, food consumption, survival, behavioral patterns, hematology, blood chemistry, urinalysis, liver function, gross and histopathologic examinations, or organ weights and ratios. Average molecular weights of Polybutene were not specified in these studies.

Polyethylene. Toxicity testing in rats showed no adverse effects to Polyethylene at doses of 7.95 g/kg or at 1.25%, 2.50%, or 5.00% in feed for 90 days.[1] The average molecular weight of Polyethylene was not specified in this study.

Dermal

Polybutene. Polybutene did not affect hepatic or skin enzymatic activities in rats following once daily treatments for 6 days (average molecular weight not specified).[3]

Reproductive and Developmental Toxicology

Polybutene

No teratogenic effects were found when Polybutene was fed to rats at 1% or 10% in the diet for 6 months.[3] A 3-generation reproductive study in Charles River albino rats that ingested up to 20,000 ppm Polybutene demonstrated that, except for the test (F_2) male parental animals that were fed 20,000 ppm Polybutene, none of the animals in successive generations differed from controls with regard to weight gains. The F_2 male parental animals showed slight weight gain depression, although their growth patterns were still within the normal range. In all 3 generations, there were no significant differences between test and control animals regarding litter size, the number of stillborn, and the number of viable pups during lactation. The survival, bws, and reactions of test animals were comparable to those of controls. Average molecular weights were not specified in these studies.

Hydrogenated Polydecene

The reproductive effects of Hydrogenated Polydecene were studied in rats that received the test material via gavage (average molecular weight not specified).[5] Groups of 30 male and 30 female Sprague-Dawley rats received 0, 100, 500, or 1,000 mg/kg/bw/d Hydrogenated Polydecene in Polyethylene glycol daily for 4 weeks prior to mating and through mating. At the end of mating, males were sacrificed. Females were treated through gestation and until lactation day 21. No treatment-related effects were observed on clinical signs, bw, or gross pathology in the parental generation or in the pups through lactation day 21. There were no treatment related effects on reproduction or pup viability. The NOAELs for parental systemic effects, parental reproductive effects, and offspring effects in this one generation rat study are each 1,000 mg/kg/bw/d.

Polyisobutene

In a 3-generation reproductive toxicity study, an unreported number of Charles River rats received 0, 800, or 20,000 ppm 100% Polyisobutene in their feed (molecular weight range 654-2,168 Da).[37,38] No further details about dosing were provided. Weight gain was slightly reduced in the second generation high-dose male rats, but the changes were within normal control ranges. No other effects on bws, clinical signs, organ weights, or histopathology were observed. No treatment-related reproductive effects were noted in any of the parameters measured (no furthered details provided). No differences were observed in offspring survival, litter size, number of stillborn pups, and number of viable pups in any generation of the treated groups when compared to controls. No remarkable postmortem findings were reported.

Hydrogenated Polydodecene

The reproductive effects of the trimer of Hydrogenated Polydodecene were studied in 1 generation of rats that received the test material via gavage.[5] Groups of 24 male and 24 female Sprague-Dawley rats received 0, 50, 250, or 1,000 mg/kg/d of the test material in arachis oil daily for 20 weeks (during maturation, mating, gestation, and lactation). No treatment-related effects on offspring growth or development were observed. Litter sizes were comparable to controls in all dose groups. No adverse effects were observed during gross necropsy or histopathological examination. The NOAEL for reproductive and development toxicity in this rat study is 1,000 mg/kg/d.

Genotoxicity

In Vitro

Ethylene/Octene Copolymer. A trade name mixture containing 30% to 50% Ethylene/Octene Copolymer and sodium acrylate copolymer was not mutagenic in an Ames test or in an in vitro chromosomal aberration test (no further details provided).[12]

Polyethylene. Genotoxicity testing of Polyethylene was negative in 2 bacterial studies.[1] Average molecular weights were not specified in these studies.

Polyisobutene. In a study to determine the ability of various insulating fluids to induce transformation in the Syrian hamster

embryo cell transformation assay and to enhance 3-methylcholanthrene-induced transformation of C3H/10T1/2 cells, a low-viscosity Polyisobutene-based oil did not induce transformation activity and was slightly cytotoxic.[2] In the 2-stage transformation assay of C3H/10T1/2 cells, the Polyisobutene oil had promoter activity. Average molecular weights were not specified in these studies.

Hydrogenated Polydecene. Hydrogenated Polydecene was not mutagenic in an Ames test at concentrations up to 500 μg/plate (molecular weight range 367-596 Da; no further details provided).[43]

Hydrogenated Polydecene (average molecular weight not specified) was not mutagenic in a reverse gene mutation assay in *Salmonella typhimurium* strains TA1535, TA1537, TA98, and TA100 and *Escherichia coli* strain WP2uvrA.[5] The test material was incorporated in emulsions with sorbitan stearate and polysorbate 60 at concentrations of 156.25; 312.5; 625; 1,250; 2,500; or 5,000 μg/plate, with and without metabolic activation using the preincubation method. The positive controls yielded expected results.

In reverse mutation assays, *S typhimurium* strains TA98, TA100, TA1535, and TA1537 were treated with Hydrogenated Polydecene (average molecular weight not specified) at concentrations up to 10 mg/plate.[5] The positive controls yielded expected results. Hydrogenated Polydecene was not mutagenic with or without S9 metabolic activation at all tested concentrations.

Hydrogenated Polydodecene. The genotoxic potential of the trimer of Hydrogenated Polydodecene was assayed in 2chromosome aberration experiments using human lymphocyte cultures.[5] In the first experiment, the concentrations tested were 0; 39; 78.1; 156.25; 312.5; 625; 1,250; 2,500; and 5,000 μg/mL. In the second experiment, the concentrations tested were 625, 1,250, 2,500, and 5,000μg/ml for 20 h or 1,250, 2,500, and 5,000 μg/mL for a 44-hour harvest time. All experiments were conducted in duplicate, with and without S9 metabolic activation. Cytotoxicity was not observed in a range finding test conducted prior to the main assay at concentrations $\leq$ 5,000 μg/mL. The test material did not induce chromosomal aberrations or polyploidy cells, with or without metabolic activation. Positive controls, ethyl methane sulfonate in the absence of S9, and cyclophosphamide in the presence of S9, yielded expected results. The authors concluded that the trimer of Hydrogenated Polydodecene was not clastogenic to human lymphocytes in vitro when tested at concentrations $\leq$ 5,000 μg/mL.

In a mammalian cell gene mutation assay (HGPRT locus), Chinese hamster ovary (CHO) cells cultured in vitro were exposed to the trimer of Hydrogenated Polydodecene in ethanol at concentrations of 0; 313; 625; 1,250; 2,500; or 5,000 μg/mL with and without metabolic activation for 4 hours.[5] In the range-finding test, relative cloning frequencies (RCEs) ranged from 97% to 73% for concentrations ranging from 0.5 to 5,000 μg/mL without metabolic activation. Relative cloning frequencies were 122% to 80% for the same concentration range with metabolic activation. Relative cloning frequencies in the first mutation assay were 92% to 77% and 111% to 89% for concentrations ranging 313 to 5,000 μg/mL with and without metabolic activation, respectively. The activated portion of the first mutation assay was repeated and RCE was 100% to 71% for the same dose range. In the confirmatory assay, the RCEs among the test material-treated cultures ranged from 50% to 23% and 89% to 52% for the concentrations of 313 to 5,000 μg/mL with and without metabolic activation, respectively. A significant response was observed at 625 μg/mL when compared to the solvent control data in the repeat definitive mutation assay with activation; however, the increase was not significant when it was compared to the historical, cumulative solvent control data. The same was true at 2,500 μg/mL, with activation, in the confirmatory mutation assay. The increase in the number of mutants was not significant when compared to historical, cumulative solvent control data. The response seen in the definitive mutation assay at 625 μg/mL was not reproduced in the confirmatory assay. Controls were within the historical negative control values. The trimer of Hydrogenated Polydodecene was not mutagenic in this mammalian cell gene mutation assay.

Carcinogenicity

Polyethylene

Numerous investigations on the tumor production of Polyethylene implantation have produced mixed results.[1] Polyethylene causes tumors in rats implanted with squares of the test substance; however, testing involving implanting coverslips and powdered Polyethylene suggests that tumors are caused by the physical reaction to imbedded plastic films and not the Polyethylene itself. International Agency for Research on Cancer lists Polyethylene as "not classifiable as to carcinogenicity in humans" based on no adequate human data and inadequate animal data. Average molecular weights were not specified.

Polyisobutene

In a carcinogenicity study conducted to determine the skin tumorigenicity effects of certain oils used for impregnation of paper-insulated power cables and their synthetic alternatives, including Polyisobutene oil, no evidence of a direct tumorigenic or carcinogenic effect was reported and Polyisobutene oil (average molecular weight 250 Da) appeared to reduce the number of 7,12-dimethylbenz[a]anthracene-induced tumors in mice.[2]

Polyisobutene (100%) was not carcinogenic in rats (dosed up to 20,000 ppm) or dogs (dosed up to 1,000 mg/kg) in oral studies described in Table 9 (molecular weight range 654-2,168 Da).[37,38]

Polypropylene

International Agency for Research on Cancer determined that Polypropylene is not classifiable as to its carcinogenicity to

humans (group 3) based on no adequate human data and inadequate animal data.[44]

Irritation and Sensitization

Irritation

Nonhuman and human dermal irritation studies are presented in Table 9, and nonhuman ocular irritation studies are presented in Table 10.[5,12,37-43,45,46] Ethylene/octene copolymer and sodium acrylate copolymer (30%-50% in a trade name mixture was minimally/slightly irritating to rabbit skin. Polyisobutene and Hydrogenated Polyisobutene at 100% were not irritating to rabbit skin in respective irritation studies. Hydrogenated Polydecene and the trimer of hydrogenated decene were not primary irritants or corrosives in several rabbit studies. No significant irritation was observed in human subjects in a cumulative irritation test of Ethylene/Octene Copolymer and sodium acrylate copolymer (30%-50%) in a trade name mixture. No adverse effects were reported in human subjects following irritation studies of a formulation containing 8% Hydrogenated Polyisobutene and Hydrogenated Polyisobutene at 100%. No adverse effects were reported following dermal exposure to formulations containing Hydrogenated Polydecene with equal amounts of cetyl ethylhexanoate and pentaerythrityl tetraethylhexanoate tested at total concentrations up to 35% in a study in human subjects.

Ethylene/octene copolymer and sodium acrylate copolymer (30%-50% in a trade name mixture) was minimally/slightly irritating to rabbit eyes. Polyisobutene and Hydrogenated Polyisobutene at 100% were not irritating to rabbit eyes in respective irritation studies. Two primary eye irritation studies in rabbits found undiluted Hydrogenated Polydecene not to be an ocular irritant, while another study found the material to be moderately irritating.

The dermal, ocular, and mucous membrane irritation data that were presented in the original reviews of Polybutene, Polyethylene, Polyisobutene, and Hydrogenated Polyisobutene are summarized below and not in the tables.

Dermal

Polybutene. In primary skin irritation studies, Polybutene in formulations including lipsticks produced no abnormalities or irritation in rabbits at concentrations up to 15%; however, mild irritation was observed at concentrations greater than 15%.[3] Average molecular weights were not specified. Human primary irritation tests of a lipstick formulation containing 20% Polybutene produced no irritation. The average molecular weight was not specified.

Polyethylene. Dermal irritation studies on rabbits in which 0.5 g of Polyethylene (average molecular weight of 450 Da) was administered in 0.5 mL of water caused no irritation or corrosive effects.[1] When the same procedure was used to test Polyethylene with an average molecular weight of 655 Da, a primary irritation index score of 0.2 was found and Polyethylene was classified as a mild irritant.

Hydrogenated Polyisobutene. A skin irritation study in 6 rabbits using four patches each containing 0.5 g/patch of a Hydrogenated Polyisobutene mixture caused no reactions in any of the animals on intact or abraded skin.[2] The primary irritation index was 0.0. There was a primary irritation index score of 1.8 for rabbits treated with undiluted Hydrogenated Polyisobutene on the intact or abraded skin. Rabbits dosed dermally with 0.5 mL Hydrogenated Polyisobutene) on intact and abraded skin exhibited a primary irritation index of 0.38; not a dermal irritant. In a similar study, Hydrogenated Polyisobutene produced a primary irritation index of 0.96; also not a dermal irritant. Average molecular weights were not specified in these studies.

In humans, no primary skin irritation was produced in a 72-hour primary skin irritation patch test study with 100% Hydrogenated Polyisobutene in 25 male and female participants.[2] There was no irritancy observed in humans during a 24-hour single-insult patch test with a lip gloss containing 66.11% Hydrogenated Polyisobutene. Average molecular weights were not specified in these studies.

Ocular

Polybutene. Rabbits suffered only minimal eye irritation when Polybutene at concentrations up to 75% was instilled into the eyes with and withoutwashouts.[3] Average molecular weights were not specified.

Polyethylene. Polyethylene (molecular weight of 450 Da) was tested as a solid material (66 mg) in the eyes of rabbits.[1] The test substance caused a maximum group mean score of 11.0 and was classified as a mild irritant. All treated eyes appeared normal 48 hours after application. The same procedure, with 55 mg of Polyethylene of average molecular weight of 655, was carried out on white rabbits. The mean maximum group score produced by Polyethylene was 11.7, and it was classified as a mild irritant. All treated eyes appeared normal 72 hours after treatment. When white rabbits were tested with 13% Polyethylene beads, the maximum ocular score was 8/110 with resolution after 48 hours, and no corneal abrasions were observed.

Polyisobutene. Irritant and corrosive effects were examined following a single instillation of Polyisobutene into rabbit eyes.[2] No corneal or iridial damage was recorded in the study. One eye had irritation to the conjunctivae by 72 hours, which was present as slight hyperemia. The average molecular weight was not specified.

Hydrogenated Polyisobutene. When 0.1-mL Hydrogenated Polyisobutene was instilled into the conjunctival sac of rabbit eyes, the test material caused slight conjunctival irritation in 33% of eyes which cleared up by day 2.[2] The authors determined that Hydrogenated Polyisobutene is not an eye irritant. Another study of Hydrogenated Polyisobutene under similar test conditions produced the same results. No signs of ocular irritation were observed in a Draize study of 3 rabbits exposed to a facial lotion containing 3% Hydrogenated Polyisobutene. In a 7-day eye irritation study on rabbits, no eye irritation was

Table 9. Dermal Irritation Studies.

Test article	Concentration/Dose	Test population	Procedure	Results	Reference
			Nonhuman		
Ethylene/Octene Copolymer and sodium acrylate copolymer (30%-50%) in a trade name mixture	Concentration/dose not reported	Rabbit skin	Details not provided	Minimally/slightly irritating	12
Polyisobutene; MW range 654-2,168	100%	Rabbit skin	Details not provided	Nonirritating	37,38
Hydrogenated Polyisobutene; MW range 187-468	100%	Rabbit skin	Details not provided	Nonirritating	39-42
Hydrogenated Polydecene; MW range 367-596	0.5 mL of 100%	Rabbits	Modified Draize primary skin irritation test (no further details provided)	Nonirritating, primary irritation index 3.1	43
Hydrogenated Polydecene; average MW not specified	0.5 mL, concentration not reported	6 New Zealand White rabbits	- Primary skin irritation study on clipped or abraded skin - Test sites occluded - Remaining test material was washed off at 24 hours - Animals were observed for skin reactions at 24 and 72 hours	- At 24 hours, slight erythema was observed in 4 of the abraded sites and 5 of the intact sites, slight edema was observed on 3 of the abraded sites, edema was observed at an abraded site at the end of treatment, all effects had reversed 2 days postexposure - After 72 hours, the mean erythema score was 0.42 for both the intact and abraded skin, the mean edema score after 72 hours was 0.17 for intact skin and 0.08 for abraded skin - Based on these results, the study authors calculated a primary dermal irritation index of 0.5 - Not a primary irritant or corrosive	5
Hydrogenated Polydecene, average MW not specified	0.5 mL, concentration not reported	6 female New Zealand White rabbits	- Primary skin irritation study on clipped or abraded skin - Test sites occluded - Remaining test material was washed off at 24 hours - Animals were observed for skin reactions at 24 and 72 hours	- Over 72 hours, the mean erythema score for intact skin was 0.75, mean erythema score for abraded skin was 0.67 - The mean edema score for intact and abraded skin over 72 hours was 0.25 and 0.08, respectively - All rabbits had very slight to well-defined erythema on both intact and abraded sites and slight edema on 3 intact and 1 abraded site at the end of treatment - No difference in severity between intact and abraded sites - 2 days after treatment, only 1 abraded site still had evidence of slight erythema - The primary dermal irritation index was calculated to be 0.9 - Not a primary irritant or corrosive	5

(continued)

Table 9. (continued)

Test article	Concentration/Dose	Test population	Procedure	Results	Reference
Hydrogenated decene trimer	0.5 mL of undiluted test material	Groups of 3 New Zealand White rabbits	- Draize study - Test area was 2.5 cm^2 and semioccluded for up to 4 hours - Animals observed for 7 days.	- No treatment-related changes in bw observed - Very slight erythema and edema observed in 1 rabbit through 72 hours - At 72 hours, the skin lost its elasticity and flexibility - At 7 days, slight desquamation observed - No effects observed in the other 2 rabbits - Mild irritant according to Draize system but nonirritating according to EU classification system	5
			Human		
Ethylene/Octene Copolymer and sodium acrylate copolymer (30%-50%) in a trade name mixture	Details not provided	Details not provided	Cumulative irritation test (no further details provided)	No significant irritation	12
Polyisobutene; MW range 654-2,168	100%	Details not provided	Human skin patch test (no further details provided)	Nonirritating	37,38
Hydrogenated Polyisobutene in formulation, average MW not specified	8%	10 female subjects	Single application to the skin (no further details provided)	No adverse effects were reported	46
Hydrogenated Polyisobutene; MW range 187-468	100%	Details not provided	Human skin patch test (no further details provided)	Nonirritating	39-42
Hydrogenated Polydecene with equal amounts of cetyl ethylhexanoate and pentaerythrityl tetraethyl hexanoate; average MW not specified.	Total concentrations up to 35% in combined product	98 subjects	A study of formulations with differing ratios of polyols and oils on the skin	No adverse effects	45

EU = European Union.

Table 10. Ocular Irritation Studies.

Test article	Concentration/Dose	Test population	Procedure	Results	Reference
			Ocular—Nonhuman		
Ethylene/Octene Copolymer and sodium acrylate copolymer (30%-50%) in a trade name mixture	Details not provided	Rabbits	Details not provided	Minimally/slightly irritating	12
Polyisobutene; MW range 654-2,168	100%	Rabbits	Details not provided	Nonirritating	37,38
Hydrogenated Polyisobutene; MW range 187-468	100%	Rabbits	Details not provided	Nonirritating	39-42
Hydrogenated Polydecene: MW range 367-596	0.1 mL of 100% test material	Rabbits	Modified Draize primary eye irritation test (no further details provided)	Nonirritating (irritation score 0 to 6 out of 110 in individual rabbits)	43
Hydrogenated Polydecene; average MW not specified	0.1 mL of undiluted test material	New Zealand White rabbits, 3/sex	- Test material instilled into the conjunctival sac of the right eye of each animal - Eyes not rinsed. - Animals then observed for 72 hours.	- No corneal lesions or iris changes - Conjunctival changes included mild erythema in 5 of the 6 rabbits that were still present in 3 of the rabbits at 72 h and swelling occurred in 3 of the rabbits - None of the rabbits had any discharge - Individual total scores over the 3 time points for all changes observed ranged from 0 to 4 of a possible score of 110 - Nonirritating	5
Hydrogenated Polydecene; average MW not specified	0.1 mL, concentration not reported	9 male New Zealand White rabbits	- Test material instilled into the conjunctival sac of one eye while the other eye served as control - Eyes were examined for ocular irritancy at 1, 24, 48, and 72 hours posttreatment - Both eyes of 3 of 9 treated rabbits were rinsed with distilled water and the rinsed eyes were examined for ocular irritancy at 1, 24, 48, and 72 hours	- None of the rabbits exhibited corneal lesions or iris changes - In unrinsed eyes, moderate to severe conjunctival redness with oily residue was noted at 1 hours, but by 24 hours, there was only slight redness and the eye was clear by 48 hours - In rinsed eyes, there was no to slight conjunctival redness 1 hours after treatment with oily residue around the eye; the eyes were clear by 24 hours - Moderately irritating	5

observed in washed or unwashed eyes following treatment with 0.1-mL Hydrogenated Polyisobutene. An unknown concentration of Hydrogenated Polyisobutene instilled into the right eyes of 6 rabbits produced a score of 1 on the Draize scale. No other effects were observed. Average molecular weights were not specified in these studies.

In human, no adverse reactions or ocular irritation were reported in 59 subjects in a 29-day in-use study of 3different formulations of cosmetic foundations/concealer products that contained Hydrogenated Polyisobutene.[2] The concentration of Hydrogenated Polyisobutene was not specified in 2 of the 3 formulations, while the third contained 4% Hydrogenated Polyisobutene. Average molecular weights were not specified.

Mucous Membrane

Polybutene. Undiluted Polybutene produced no irritation or signs of systemic toxicity when applied to the vaginas of rabbits.[3] Average molecular weight was not specified.

Sensitization

Nonhuman and human sensitization studies are presented in Table 11.[5,11,12,43,47] Tradename mixtures containing Ethylene/Octene Copolymer were not sensitizing in a guinea pig maximization test (at 14%-16%) or in a local lymph node assay (LLNA; at 30%-50%). Hydrogenated Polydecene was not a dermal sensitizer in guinea pig maximization tests at concentrations up to 100%. The dimer of hydrogenated decene was not a dermal sensitizer in guinea pig maximization studies at 5%. The trimer of hydrogenated decene in propylene glycol was a slight sensitizer according to an LLNA. The stimulation indices were 1.56, 1.89, and 3.54 for the test concentrations of 25%, 50%, and 100%, respectively. Ethylene/octene copolymer was not a sensitizer in a human repeat insult patch test (HRIPT). A lip gloss containing 12.33% Polyisoprene was not a sensitizer according to the results of an HRIPT.

The sensitization data that were presented in the original reviews of Polybutene, Polyethylene, and Hydrogenated Polyisobutene are summarized below and not in the tables.

Polybutene. Repeated insult patch tests of 3.1% to 50% Polybutene in formulations produced no sensitization.[3] Average molecular weights were not specified.

Polyethylene. Polyethylene (average molecular weight of 450 Da) did not cause dermal sensitization in guinea pigs tested with 50% Polyethylene (wt/wt) in arachis oil BP.[1] In a repeat insult patch test of 201 volunteers, a product containing 13% Polyethylene beads was tested in a series of 9 consecutive administrations. There was no irritation observed with any of the induction patches. Challenge patches produced only a slight response in 1 subject, and the investigators concluded that Polyethylene has a low irritation and sensitization potential.

Hydrogenated Polyisobutene. Hydrogenated Polyisobutene was intradermally injected in an area of the skin on the back and flanks of guinea pigs.[2] Erythema and edema were observed after most inoculations, but no sensitization reactions were observed. Hydrogenated Polyisobutene injections (5%) in guinea pigs using a maximization procedure resulted in no observed reactions and an irritation index of 0.0 in both challenge phases I and II. Average molecular weights were not specified in these studies.

Repeat-insult patch tests performed to evaluate the primary irritancy/sensitization potential of formulations containing 1.44% or 4% Hydrogenated Polyisobutene in 54 male and female subjects found no reactions greater than slight erythema.[2] In a modified repeat-insult patch test under double-blind conditions, no irritation or sensitization was found in human skin patched with a makeup remover containing 51% Hydrogenated Polyisobutene. Hydrogenated Polyisobutene at up to 100% was not sensitizing in a Draize repeat insult patch in 200 subjects. Average molecular weights were not specified.

Phototoxicity

Polybutene. Photo patch tests of formulations with concentrations ranging from 15% to 50% Polybutene produced no reactions.[3] Average molecular weights were not specified.

Hydrogenated Polyisobutene. The phototoxic potential of cosmetic foundations/concealer products containing 4% Hydrogenated Polyisobutene or 1.44% Hydrogenated Polyisobutene, and a blank patch under long-wavelength UV light source (320-400 nm) was studied in 26 fair-skinned volunteers.[2] No significant reactions were reported. Formulations containing 1.44% or 4% Hydrogenated Polyisobutene were evaluated to determine their potential to induce a photoallergic reaction in the skin of 30 subjects. No response was reported at induction, rest, or challenge. Average molecular weights were not specified.

Comedogenicity

Polyisobutene. The comedogenic potential of Polyisobutene was studied using adult New Zealand White rabbits.[2] The test material was applied to the right ear of each animal daily on 5 consecutive days per week for 3 weeks. There were no signs of hyperkeratosis or comedone formation during weeks 1 and 2. By the third week, 2 treated ears exhibited signs of hyperkeratosis. The ear of the third rabbit, however, remained clear. Histological examination showed no signs of follicular hyperkeratosis on the treated, untreated, or control ears of any rabbits. The average molecular weight of Polyisobutene was not specified.

Clinical Studies

Polyethylene

There have only been a few cases of reactions to the implantation of Polyethylene in humans.[1] In the 3 published accounts, Polyethylene strips used for breast augmentation caused

Table 11. Sensitization Studies.

Test article	Concentration/dose	Test population	Procedure	Results	Reference
			Nonhuman		
Ethylene/Octene Copolymer (14%-16%) in a trade name mixture	Details not provided	Guinea pigs	Gguinea pig maximization and Buehler assays (no further details provided)	Not sensitizing	11
Ethylene/Octene Copolymer and sodium acrylate copolymer (30%-50%) in a trade name mixture	Details not provided	Mice	Local lymph node assay (LLNA; no further details provided)	Not sensitizing	12
Hydrogenated Polydecene; MW range 367-596	Intradermal induction dose was 5%; topical induction and challenge doses were 10%	Guinea pigs	Magnusson and Kligman skin sensitization test (no further details provided)	Not sensitizing	43
Hydrogenated Polydecene: average MW not specified	Concentrations up to 10% v/v	Hartley guinea pigs, 10 male and 10 females	- Guinea pig maximization test - Test material administered intradermally at 5.0% vol/vol in mineral oil - One week after the intradermal induction, treatment groups were induced by topical application of the 10% vol/vol test material in mineral oil for 48 hours - 14 days following topical induction, all animals received a 10% vol/vol test material in mineral oil challenge application at naive sites	- One female in the test group exhibited abnormal gait, flaccid body tone and tremors on day 9 of the study and was found dead on day 10 of the study, but the death was not considered treatment-related - No signs of skin irritation, edema, or erythema were observed in any of the remaining male or female treatment or vehicle control group animals throughout the study period - No other signs of clinical toxicity were noticed following administration of the test material. - Animals that received the positive control experienced expected results - bws were comparable to vehicle controls through the study period - Not sensitizing	5
Hydrogenated Polydecene in corn oil; average MW not specified.	Concentrations up to 100%	20 Dunkin-Hartley guinea pigs	- Maximization study - 6 intradermal injections of the test material (2 injections at 50% aqueous Freund's Complete Adjuvant, 2 injections of 100% test material, and 2 injections of 100% test material in 25% aqueous Freund's Complete Adjuvant) - Control group animals were treated with 6 intradermal injections (2 injections of 50% aqueous Freund's Complete Adjuvant, 2 injections vehicle, and 2	- During challenge, 2 test group animals exhibited positive responses (details not provided) to the test material - No positive responses were observed in the control animals - A rechallenge was conducted using 50% and 100% Hydrogenated Polydecene and a positive response was observed in one animal exposed to 100% Hydrogenated Polydecene - Not sensitizing	5

(continued)

Table 11. (continued)

Test article	Concentration/dose	Test population	Procedure	Results	Reference
			injections of the vehicle in 25% aqueous Freund's Complete Adjuvant) - On test day 6, no irritation was observed so the test sites were treated with 0.5 mL of 10% sodium lauryl sulfate - On test day 7, each test group animal was treated with a topical application of the test material for 48 hours - Control group received vehicle only - On test day 20, animals were challenged with 100% test material via topical application		
Hydrogenated Polydecene; average MW not specified	Details not provided	10 male Hartley guinea pigs	- Animals were patched with Webril pads containing 0.5-mL test material on the midline of the back - A positive control group was patched with DNCB - A challenge dose of 0.5 mL of the test material and the positive control was administered 2 weeks after the final sensitization dose.	- 8 of the 10 animals in the treated group had slight erythema and edema - All animals in the positive control group also exhibited slight erythema and edema - Not sensitizing	5
Hydrogenated decene dimer (an analog of Hydrogenated Polydecene)	Induction and challenge concentration s = 5% wt/vol in spectrum oil	10 male and 10 female Hartley guinea pigs	- Delayed contact hypersensitivity study - Animals induced 3 times weekly with occlusive 6-hour exposures for 3 weeks - Following a 2-week rest period, the test animals and a naive control group were challenged - Animals were scored for skin reactions at 24 and 48 hours following the challenge phase	- The primary challenge resulted in a grade 1 response, which was of less incidence and severity than the naïve control group. - Not sensitizing	5
Hydrogenated decene, dimer	Intradermally induced with 5% test material in mineral oil; topically challenged with 10% test material	10 male and 10 female Hartley guinea pigs	- Magnusson-Kligman maximization test protocol - A negative control group was induced with vehicle alone and a positive control group received DNCB.	- No signs of skin irritation, edema, or erythema were observed in any of treated animals or vehicle control group animals throughout the study period - No other signs of clinical toxicity were observed - Individual and group mean bws were comparable to vehicle controls through the study period - Not sensitizing.	5

(continued)

Table 11. (continued)

Test article	Concentration/dose	Test population	Procedure	Results	Reference
Hydrogenated decene trimer in propylene glycol	25%, 50%, and 100%	Mice	LLNA (No further details provided)	- Stimulation indices were 1.56, 1.89, and 3.54 for the test concentrations of 25%, 50%, and 100%, respectively - EC3values were not provided - Slight sensitizer	5
			Human		
Ethylene/Octene Copolymer in a trade name mixture	Details not provided	Details not provided	HRIPT; no further details provided	No irritation or sensitization observed	12
Polyisoprene	12.33% in a lip gloss	103 subjects	- HRIPT - 0.2 g test material applied to upper back with a 1 in ^{2} pad and semioccluded for 24 hours - Total of 9 induction patches - After 2-week rest, challenge patch applied to naive site for 24 hours and sites were scored 24 and 72 hours postapplication	No irritation or sensitization observed	47

LLNA = local lymph node assay.

increased histological activity around the implant. There have also been occupational case reports on ocular irritation and systemic sclerosis in workers exposed to Polyethylene. Such workers are also exposed to other irritants. Clinical testing of intrauterine devices made of Polyethylene failed to conclusively identify statistically significant adverse effects, although squamous metaplasia was observed in treated women.

Summary

The polyene ingredients in this report are simple polyolefins that are the polymerization products of vinyl-type monomers. The polyenes reviewed in this report cover a wide range of molecular weights but have very similar structures and reaction starting materials (monomers). Polyenes function primarily as film formers and/or viscosity increasing agents—nonaqueous in cosmetic products.

According to the 2015 US FDA VCRP data, Polyethylene is reported to be used in 2,773 formulations; the single category with the most reported uses was lipstick with 885.Hydrogenated Polyisobutene is reported to be used in 1,963 formulations; the single category with the most reported uses was lipstick with 865. Most of the other in-use ingredients are primarily used in leave-on products and lipsticks. The results of the concentration of use survey conducted in 2013 and 2014 by the Council indicate Hydrogenated Polyisobutene has the highest reported maximum concentration of use; it is used at up to 95% in lipsticks.

For the ingredients that were previously reviewed by the Panel, concentrations of use for Polybutene and Hydrogenated Polyisobutene have remained about the same, with the highest maximum use concentration of 95%for Hydrogenated Polyisobutene in lip products. The highest maximum use concentration for Polyethylene has increased from 24% (eye shadow) to 67.6% (skin cleansing agents), while the highest maximum use concentration for Polyisobutene has decreased from 76% to 40% (both concentrations in lip products). Uses for all 4 ingredients have increased by several folds since their original reviews.

Many of the polyene ingredients have been approved by the FDA for use as food additives and in medical devices. An oral study that assessed the absorption potential of undiluted Hydrogenated Polydecene in rats found that most of the test compound was excreted in the feces without being absorbed ($> 92\%$). Urinary excretion was low ($< 1\%$), and very little of the dose was recovered in the bile (0.01%).

In acute oral toxicity studies in rats, the LD_{50}s of diisobutylene, and triisobutylene were $>$ 2,000 mg/kg/bw each. The oral LD_{50}s of di-n-butene, tributene, and tetrabutene (containing 30% pentabutene) in rats were $>$ 10,000 mg/kg each. The oral LD_{50} values for Ethylene/Octene Copolymer, undiluted Hydrogenated Polydecene and undiluted Hydrogenated Polydodecene were $>$ 5,000 mg/kg in rat studies. The LD_{50} of undiluted Polyisobutene was $>$ 15,400 mg/kg in an oral rat study.

Acute dermal studies of diisobutylene and Hydrogenated Polydodecene found the LD_{50} values $>$ 2,000 mg/kg in rats. In rabbit studies, the dermal LD_{50} values for Ethylene/Octene Copolymer, hydrogenated decene dimer, Hydrogenated Polyisobutene, and Polyisobutene were $>$ 5,000 mg/kg, $>$ 3,000 mg/kg, $>$2,000 mg/kg, and $>$25,000 mg/kg, respectively.

In acute inhalation studies, the LC_{50} of diisobutylene vapor in albino rats was $>$ 4,185 ppm (19,171 mg/m^3) after a 4-hour, single, whole-body exposure. The LC_{50} for an aerosol of Hydrogenated Polydecene was $>$ 5.2 mg/L in rats. The LC_{50} for the dimer of hydrogenated decene was 1.17 mg/L in rats. In another acute inhalation study of the dimer of hydrogenated decene, the LC_{50} could not be determined in rats tested at 5 mg/L because 9/10 animals died within 3 days of administration of the test material. The LC_{50} for Hydrogenated Polydodecene was $>$ 5.06 mg/L. The LC_{50} for 100% Hydrogenated Polyisobutene was $>$ 5 mg/L.

No treatment-related gross microscopic changes were observed following exposure to 100% Polyisobutene in a 90-day dietary study of rats and 2-year dietary studies in rats or dogs. No adverse effects were observed in oral repeated dose studies of Hydrogenated Polydecene, with the NOAELs determined to be 1,000 mg/kg/d in one 90-day rat study and over 4,000 mg/kg/d in another. In a 4-week oral repeated dose rat study, the NOAEL for Hydrogenated Polydecene was 6,245 mg/kg/d in males and 6,771 mg/kg/d in females. Gross necropsy, histopathology, and microscopic findings did not reveal any significant treatment-related findings. The NOAEL for the oral administration of the trimer of hydrogenated dodecene in 2 respective oral repeated dose toxicity studies in rats was 1,000 mg/kg/d. Treatment-related effects on mortality, clinical signs, bw, food consumption, hematology, clinical chemistry, organ weights, or gross and histologic pathology were not observed in either study. In a 4-week dermal study in rats, 100% Hydrogenated Polyisobutene produced minimal to mild dermal irritation in most treated animals. Histopathologic examinations of the high-dose group found effects limited to the application site and included minimal to mild epidermal hyperplasia and hyperkeratosis with reactive hyperplasia of the underlying inguinal lymph nodes.

In rat reproductive studies of Hydrogenated Polydecene and the trimer of Hydrogenated Polydodecene, the NOAELs for parental systemic and reproductive effects and for offspring were 1,000 mg/kg bw/d for the respective studies. No treatment-related effects were observed on clinical signs, bw, or gross pathology in the parental generation or in the pups. There were no treatment related effects on reproduction or pup viability. In a 3-generation reproductive dietary toxicity study, an unreported number of Charles River rats received 0, 800, or 20,000 ppm 100% Polyisobutene produced no treatment-related reproductive effects in any generation of the treated groups when compared to controls.

A trade name mixture containing 30% to 50% Ethylene/Octene Copolymer and sodium acrylate copolymer was not mutagenic in an Ames test or in an in vitro chromosomal aberration test Hydrogenated Polydecene at concentrations up to 10 mg/plate was not mutagenic in Ames assays, with or without

metabolic activation. The trimer of Hydrogenated Polydodecene was not clastogenic to human lymphocytes nor was it mutagenic in CHO cells (HGPRT locus assay) in vitro when tested at concentrations up to 5,000 μg/mL.

International Agency for Research on Cancer determined that Polypropylene is not classifiable as to its carcinogenicity to humans (group 3). Polyisobutene (100%) was not carcinogenic in rats (dosed up to 20,000 ppm) or dogs (dosed up to 1,000 mg/kg) in oral studies.

Ethylene/octene copolymer and sodium acrylate copolymer (30%-50% in a trade name mixture) was minimally/slightly irritating to rabbit skin. Polyisobutene and Hydrogenated Polyisobutene at 100% were not irritating to rabbit skin in respective irritation studies. Hydrogenated Polydecene and the trimer of hydrogenated decene were not primary irritants or corrosives in several rabbit studies. No significant irritation was observed in human subjects in a cumulative irritation test of Ethylene/Octene Copolymer and sodium acrylate copolymer (30%-50%) in a trade name mixture. No adverse effects were reported in human subjects following irritation studies of a formulation containing 8% Hydrogenated Polyisobutene and Hydrogenated Polyisobutene at 100%. No adverse effects were reported following dermal exposure to formulations containing Hydrogenated Polydecene with equal amounts of cetyl ethylhexanoate and pentaerythrityl tetraethyl hexanoate tested at total concentrations up to 35% in a study in human subjects.

Ethylene/octene copolymer and sodium acrylate copolymer (30%-50% in a trade name mixture was minimally/slightly irritating to rabbit eyes. Polyisobutene and Hydrogenated Polyisobutene at 100% were not irritating to rabbit eyes in respective irritation studies. Two primary eye irritation studies in rabbits found undiluted Hydrogenated Polydecene not to be an ocular irritant, while another study found the material to be moderately irritating.

Ethylene/octene copolymer was not sensitizing in a guinea pig maximization test or in an LLNA. Hydrogenated Polydecene was not a dermal sensitizer in guinea pig maximization tests at concentrations up to 100%. The dimer of hydrogenated decene was not a dermal sensitizer in one guinea pig maximization study and was given a grade 1 response in another. The trimer of hydrogenated decene in propylene glycol was a slight sensitizer according to an LLNA. The stimulation indices were 1.56, 1.89, and 3.54 for the test concentrations of 25%, 50%, and 100%, respectively. Ethylene/octene copolymer was not a sensitizer in a HRIPT. Polyisoprene was not a sensitizer according to the results of a HRIPT at 12.33% in a lip gloss.

Discussion

The Panel considered the available data on polyenes, including those from the previous safety assessments on Polybutene, Polyethylene, Polyisobutene, and Hydrogenated Polyisobutene, and noted low systemic toxicity at high doses in single-dose and repeated-dose animal studies, no teratogenic effects in animal studies, and no genotoxicity in in vitro and in vivo studies. The Panel noted that use concentrations were as high as 95% in lipsticks, but a human dermal sensitization study of 100% Hydrogenated Polyisobutene in the previous safety assessment of this ingredient was negative, and no irritation or sensitization was observed in multiple tests of some of the other polyene ingredients. The Panel recognized that polyenes are approved for use in foods (directly and indirectly) and drug and medical devices.

The Panel also noted that although molecular weights are in the range that could be dermally absorbed, the lack of heteroatom functional groups dramatically limits solubility and would prevent significant absorption. The lack of functional groups also limits interactions with other biomolecules and accounts for the apparent biological inertness of these ingredients.

The Panel noted gaps in the available safety data for some of the polyenes in this safety assessment. The data available for many of the ingredients are sufficient and can be extrapolated to support the safety of the entire group because of the similarities in the chemical structures, physicochemical properties, use concentrations, and reported functions across the group.

The Panel discussed the issue of incidental inhalation exposure in pump and aerosol hair sprays, underarm deodorant sprays, face and neck sprays, body and hand sprays, and aerosol suntan products. The limited data available from inhalation studies, including acute exposure data, suggest little potential for respiratory effects at relevant doses. The Panel considered pertinent data indicating that incidental inhalation exposures to polyenes in such cosmetic products would not cause adverse health effects, including data characterizing the potential for polyenes to cause systemic toxicity, ocular or dermal irritation or sensitization, and other effects. The Panel noted that 95% to 99% of droplets/particles produced in cosmetic aerosols would not be respirable to any appreciable amount. The potential for inhalation toxicity is not limited to respirable droplets/particles deposited in the lungs. In principle, inhaled droplets/particles deposited in the nasopharyngeal and thoracic regions of the respiratory tract may cause toxic effects depending on their chemical and other properties. However, coupled with the small actual exposure in the breathing zone and the concentrations at which the ingredients are 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 http://www.cir-safety.org/cir-findings.

Conclusion

The Panel concluded that the following polyene ingredients are safe in cosmetics in the present practices of use and concentration described in this safety assessment:

Butene/Propylene Copolymer*	Isobutylene/Isoprene Copolymer*
Butylene/Ethylene Copolymer	Isoprene/Pentadiene Copolymer*
Butylene/Ethylene/Propylene Copolymer	Polybutene

(continued)

(*Continued*)

Decene/Butene Copolymer	Poly(C4-12 Olefin)*
Ethylene/Octene Copolymer*	Poly(C6-14 Olefin)*
Ethylene/Propylene Copolymer	Poly(C20-28 Olefin)*
Hydrogenated Poly(C6-12 Olefin)	Poly(C30-45 Olefin)
Hydrogenated Poly(C6-14 Olefin)	Polydecene
Hydrogenated Poly(C6-20 Olefin)	Polyethylene
Hydrogenated Polybutene*	Polyisobutene
Hydrogenated Polydecene	Polyisoprene
Hydrogenated Polydodecene*	Polypentene*
Hydrogenated Polyisobutene	Polypropylene

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

Author Contributions

Burnett, C. contributed to conception and design, contributed to acquisition, analysis, and interpretation, drafted manuscript, and critically revised manuscript; Bergfeld, W., Belsito, D., Hill, R., Klaassen, C., Liebler, D., Marks, J., Shank, R., Slaga, T., Snyder, P., and Gill, L. contributed to conception and design, contributed to analysis and interpretation, and critically revised manuscript; Heldreth, B. contributed to design, contributed to analysis and interpretation, and critically revised manuscript. All authors gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

Authors' Note

Unpublished sources cited in this report are available from the Executive Director, Cosmetic Ingredient Review, 1620 L Street, NW, Suite 1200, Washington, DC 20036, USA.

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