

Safety Assessment of Methyl Glucose Polyethers and Esters as Used in Cosmetics

International Journal of Toxicology
2016, Vol. 35(Supplement 2) 12S-40S
© The Author(s) 2016
Reprints and permission:
sagepub.com/journalsPermissions.nav
DOI: 10.1177/1091581816670322
journals.sagepub.com/home/ijt



Wilbur Johnson Jr¹, Bart Heldreth², Wilma F. Bergfeld³,
Donald V. Belsito³, Ronald A. Hill³, Curtis D. Klaassen³,
Daniel C. Liebler³, James G. Marks Jr³, Ronald C. Shank³,
Thomas J. Slaga³, Paul W. Snyder³, and F. Alan Andersen⁴

Abstract

The Cosmetic Ingredient Review Expert Panel (Panel) reviewed the safety of methyl glucose polyethers and esters which function in cosmetics as skin/hair-conditioning agents, surfactants, or viscosity increasing agents. The esters included in this assessment are mono-, di-, or tricarboxyester substituted methyl glucosides, and the polyethers are mixtures of various chain lengths. The Panel reviewed available animal and clinical data, including the molecular weights, log K_{ow} s, and other properties in making its determination of safety on these ingredients. Where there were data gaps, similarities between molecular structures, physicochemical and biological characteristics, and functions and concentrations in cosmetics allowed for extrapolation of the available toxicological data to assess the safety of the entire group. The Panel concluded that there likely would be no significant systemic exposure from cosmetic use of these ingredients, and that these ingredients are safe in cosmetic formulations in the present practices of use and concentration.

Keywords

cosmetics, methyl glucose polyethers, safety

Introduction

This report assesses the safety of methyl glucose polyethers and esters which are defined in the *International Cosmetic Ingredient Dictionary and Handbook* as cosmetic ingredients.¹ Data on methyl glucoside (methyl α -D-glucopyranoside), backbone monomer of methyl glucose polyether and ester structures, are included to fill gaps in the data needed for the evaluation of these ingredients. The methyl glucose polyethers function as skin and hair-conditioning agents, whereas, the methyl glucose esters function only as skin-conditioning agents in cosmetic products.¹ Ingredients classified as both methyl glucose polyethers and esters based on their chemical structures function as skin-conditioning agents, surfactants, and viscosity-increasing agents in cosmetic products.

Chemistry

Definition and Structure

The definitions and functions of the methyl glucose polyethers and esters reviewed in this safety assessment are included in Table 1. Because each of these ingredients represents a multitude of substitution arrangements, numbers of substitutions, or chain lengths, one structure would not fully represent these ingredients, therefore, an “idealized” structure that gives the

best practical representation of the actual structure and available molecular weight data are included in Table 2.

The ingredients in this group each have a methyl glucoside core. Glucose is a common, naturally occurring monosaccharide. Glucosides are those glucose molecules modified at the anomeric alcohol functional group. Accordingly, methyl glucosides are those ingredients composed of glucose molecules with a methyl ether group at the anomeric carbon (Figure 1). These ingredients vary by the identity and quantity of modifications at the other glucose alcohol functional groups, modified via traditional esterification or polyetherification techniques.

The ester ingredients are mono-, di-, or tricarboxyester substituted methyl glucosides. Those ingredients, wherein a

¹ Cosmetic Ingredient Review Senior Scientific Analyst/Writer, Cosmetic Ingredient Review, Washington, DC, USA

² Cosmetic Ingredient Review Chemist, Cosmetic Ingredient Review, Washington, DC, USA

³ Cosmetic Ingredient Review Expert Panel Member, Cosmetic Ingredient Review, Washington, DC, USA

⁴ Former Director, Cosmetic Ingredient Review, Washington, DC, USA

Corresponding Author:

Lillian J. Gill, Cosmetic Ingredient Review, 1620L Street, NW, Suite, 1200, Washington, DC 20036, USA.
Email: cirinfo@cir-safety.org

Table 1. Definitions and Functions of the Ingredients in This Safety Assessment.^{a,1}

Ingredient CAS number	Definition	Function
Esters		
Methyl glucose caprylate/caprinate [473802-96-9]	Methyl glucose caprylate/caprinate is the ester of methyl glucoside and a mixture of caprylic and capric acids.	Skin-conditioning agents—emollient
Methyl glucose dioleate 122703-32-6 [82933-91-3]	Methyl glucose dioleate is the diester of a methyl glucoside and oleic acid.	Skin-conditioning agents—emollient
Methyl glucose isostearate	Methyl glucose isostearate is the ester of methyl glucoside and isostearic acid.	Skin-conditioning agents—emollient
Methyl glucose laurate	Methyl glucose laurate is the ester of methyl glucoside and lauric acid.	Skin-conditioning agents—emollient
Methyl glucose sesquicaprylate/sesquicaprate [473802-96-9]	Methyl glucose sesquicaprylate/sesquicaprate is a mixture of mono- and diesters of a methyl glucoside and caprylic and capric acids.	Skin-conditioning agents—emollient
Methyl glucose sesquicoate	Methyl glucose sesquicoate is a mixture of mono- and diesters of a methyl glucoside and coconut acid.	Skin-conditioning agents—emollient
Methyl glucose sesquiosostearate [138985-20-3]	Methyl glucose sesquiosostearate is a mixture of mono- and diesters of a methyl glucoside and isostearic acid.	Skin-conditioning agents—emollient
Methyl glucose sesquilaurate	Methyl glucose sesquilaurate is a mixture of mono- and diesters of methyl glucoside and lauric acid.	Skin-conditioning agents—emollient
Methyl glucose sesquioleate	Methyl glucose sesquioleate is a mixture of mono- and diesters of a methyl glucoside and oleic acid.	Skin-conditioning agents—emollient
Methyl glucose sesquistearate [68936-95-8]	Methyl glucose sesquistearate is a mixture of mono- and diesters of a methyl glucoside and stearic acid.	Skin-conditioning agents—emollient
Polyethers		
PPG-10 methyl glucose ether	PPG-10 methyl glucose ether is the polypropylene glycol ether of methyl glucose wherein the number of propylene glycol repeat units has an average value of 10.	Hair-conditioning agents; skin-conditioning agents—miscellaneous
PPG-20 methyl glucose ether	PPG-20 methyl glucose ether is the polypropylene glycol ether of methyl glucose wherein the number of propylene glycol repeat units has an average value of 20.	Hair-conditioning agents; skin-conditioning agents—miscellaneous
PPG-25 methyl glucose ether	PPG-25 methyl glucose ether is the polypropylene glycol ether of methyl glucose wherein the number of propylene glycol repeat units has an average value of 25.	Hair-conditioning agents; skin-conditioning agents—miscellaneous
PPG-20 methyl glucose ether acetate	PPG-20 methyl glucose ether acetate is the ester of PPG-20 methyl glucose ether and acetic acid.	Skin-conditioning agents—miscellaneous
PPG-20 methyl glucose ether distearate	PPG-20 methyl glucose ether distearate is the diester of PPG-20 methyl glucose ether and stearic acid.	Skin-conditioning agents—emollient
Methyl gluceth-10 [68239-42-9 generic to any length PEG]	Methyl gluceth-10 is the polyethylene glycol ether of methyl glucose wherein the number of ethylene glycol repeat units has an average value of 10.	Skin-conditioning agents—humectant
Methyl gluceth-20 [68239-42-9 generic to any length PEG]	Methyl gluceth-20 is the polyethylene glycol ether of methyl glucose wherein the number of ethylene glycol repeat units has an average value of 20.	Skin-conditioning agents—Humectant
Esters and polyethers		
PEG-120 methyl glucose dioleate [86893-19-8]	PEG-120 methyl glucose dioleate is the polyethylene glycol ether of the diester of methyl glucose and oleic acid with an average of 120 moles of ethylene oxide.	Surfactants—cleansing agents
PEG-20 methyl glucose distearate	PEG-20 methyl glucose distearate is the polyethylene glycol ether of the diester of methyl glucose and stearic acid with an average of 20 moles of ethylene oxide.	Skin-conditioning agents—emollient; surfactants—emulsifying agents
PEG-80 methyl glucose laurate	PEG-80 methyl glucose laurate is the polyethylene glycol ether of the ester of methyl glucose and lauric acid with an average of 80 moles of ethylene oxide.	Skin-conditioning agents—emollient; surfactants—cleansing agents; surfactants—solubilizing agents
PEG-20 methyl glucose sesquicaprylate/sesquicaprate	PEG-20 methyl glucose sesquicaprylate/sesquicaprate is the polyethylene glycol ether of the mono and diesters of methyl glucose and caprylic and capric acids with an average of 20 moles of ethylene oxide.	Skin-conditioning agents—emollient; surfactants—emulsifying agents

(continued)

Table 1. (continued)

Ingredient CAS number	Definition	Function
PEG-20 methyl glucose sesquilaurate	PEG-20 methyl glucose sesquilaurate is the polyethylene glycol ether of the mono and diesters of methyl glucose and lauric acid with an average of 20 moles of ethylene oxide.	Skin-conditioning agents—emollient; surfactants—emulsifying agents
PEG-20 methyl glucose sesquistearate	PEG-20 methyl glucose sesquistearate is the polyethylene glycol ether of the mono and diesters of methyl glucose and stearic acid with an average of 20 moles of ethylene oxide.	Skin-conditioning agents—emollient; surfactants—emulsifying agents
PEG-120 methyl glucose triisostearate	PEG-120 methyl glucose triisostearate is the polyethylene glycol ether of the triester of methyl glucose and isostearic acid with an average of 120 moles of ethylene oxide.	Viscosity-increasing agents—aqueous
PEG-120 methyl glucose trioleate	PEG-120 methyl glucose trioleate is the polyethylene glycol ether of the triester of methyl glucose and oleic acid with an average of 120 moles of ethylene oxide.	Skin-conditioning agents—emollient; surfactants—cleansing agents; viscosity-increasing agents—aqueous

Abbreviations: CAS, Chemical Abstracts Service; CIR, Cosmetic Ingredient Review; PEG, polyethylene glycol; PPG polypropylene glycol.

^aThe italicized text represents additions made by CIR staff.

specific degree of esterification is not provided in the definition, are expected to be monoesters.

The polyether ingredients in this report consist of polyethylene glycol (PEG) or polypropylene glycol (PPG) ethers. The number of polyether repeat units specified for each ingredient has 2 possible and distinct meanings, which are recited in the definitions. Under one meaning, the number represents a mixture of polyether chain lengths with that number marking the average, and presumably having a narrow distribution, at one alcohol site (eg, PPG-10 methyl glucose ether). Under the other meaning, the number represents a mixture of polyether chain lengths that are possibly distributed across one or more glucose alcohol sites, with that number marking the sum of all the polyether chain lengths in that molecule (eg, PEG-120 methyl glucose dioleate).

Physical and Chemical Properties

Polypropylene glycol-20 methyl glucose ether acetate is soluble in oils and organic solvents, but is essentially insoluble in water.² A log K_{ow} of 13.98 has been reported for D-glucopyranoside, methyl, 2,6-di-9-octadecenoate, (Z,Z)-(Chemical Abstracts Service Number 82933-91-3), another name for methyl glucose dioleate.³ A log $K_{ow} \approx 7.09$ has been reported for methyl glucose sesquistearate.⁴

Specifications for methyl glucoside-coconut oil ester (methyl glucose sesquicoate) as a direct food additive are as follows⁵: acid number (10-20), hydroxyl number (200-300), pH (4.8-5.0, for 5% aqueous), and saponification number (178-190).

Physical and chemical properties associated with methyl glucose polyether and ester trade name materials are included in Tables 3, 4, and 5.⁶ Studies on most of these trade name materials are included in the toxicology section of this article.

Additionally, the chemical and physical properties of isostearic acid (esters with methyl α -D-glucoside [registered with the European Chemicals Industry, ECHA], defined as 80% methyl glucoside isostearate esters [mainly di-], 16% isostearic acid, and 4% methyl glucoside)⁷ are included in Table 6. Data on this mixture are also included in the toxicology section.

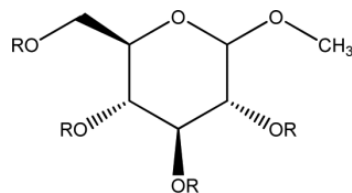
Method of Manufacture

Methyl glucoside (methyl α -D-glucopyranoside) forms the backbone of the methyl glucose polyethers and esters reviewed in this safety assessment. It is cyclic or “internal” full acetal that is formed from 1 mole of methanol and 1 mole of glucose. It has been characterized as an unusually stable glucoside that exists in discrete α or β forms.¹⁶ The pathways for methyl glucoside ester and polyether methyl glucoside synthesis starting from methyl glucoside are diagrammed in Figure 1.

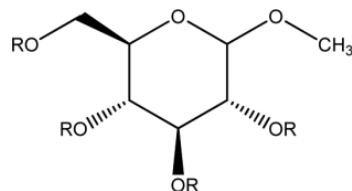
Manufacture of methyl glucoside esters, such as methyl glucose caprylate/caprinate, methyl glucose dioleate, methyl glucose isostearate, methyl glucose laurate, methyl glucose sesquicaprylate/sesquicaprate, methyl glucose sesquicoate, methyl glucose sesquiisostearate, methyl glucose sesquilaurate, methyl glucose sesquioleate, and methyl glucose sesquistearate, is typically achieved via transesterification of an appropriate fatty acid methyl ester (eg, methyl laurate to get methyl glucose laurate) with methyl glucoside (releasing methanol as a by-product).⁸⁻¹³ However, esterifications via a variety of other classical techniques, such as reacting the free fatty acids with methyl glucoside and a catalyst, are also known methods of manufacture for these ingredients.^{14,15} Under most conditions, the primary alcohol group at C6 of the methyl glucoside core is the most reactive to esterification and is the first site to be substituted.

Table 2. Idealized Structures, Molecular Weights, and LogP_{ow}'s of Ingredients in This Safety Assessment.

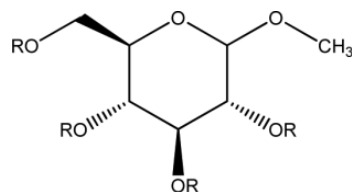
Methyl glucose caprylate/caprate



Wherein 3 R groups are hydrogen and 1 R group is a fatty acyl moiety 8-10 carbons long

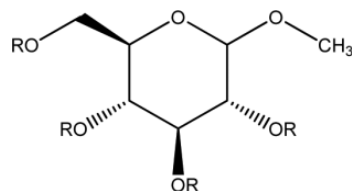
Methyl glucose dioleate (MW = 722 DA)⁶⁴Wherein 2 R groups are hydrogen and 2 R groups are Ω -9 unsaturated fatty acyl moieties 18 carbons long

Methyl glucose isostearate

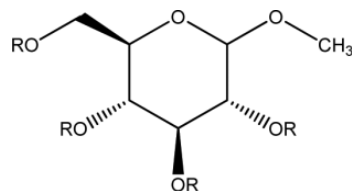


Wherein 3 R groups are hydrogen and 1 R group is a branched, fatty acyl moiety 18 carbons long

Methyl glucose laurate

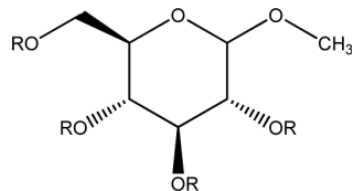


Wherein 3 R groups are hydrogen and 1 R group is a fatty acyl moiety 12 carbons long

Methyl glucose sesquicaprylate/
sesquicaprate

Wherein 2 or 3 R groups are hydrogen and the other R group(s) is (are) fatty acyl moiety (moieties) 8-10 carbons long

Methyl glucose sesquicoate

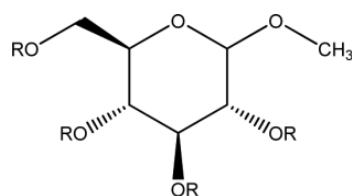


Wherein 2 or 3 R groups are hydrogen and the other R group(s) is (are) fatty acyl moiety (moieties) resultant from the reaction of methyl glucoside and coconut acid

(continued)

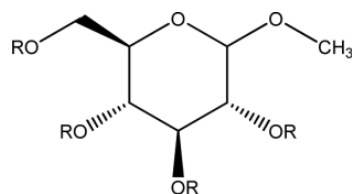
Table 2. (continued)

Methyl glucose sesquiosostearate



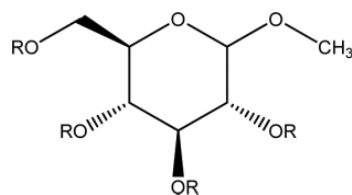
Wherein 2 or 3 R groups are hydrogen and the other R group(s) is (are) branched, fatty acyl moiety (moieties) 18 carbons long

Methyl glucose sesquilaurate



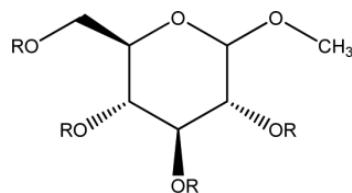
Wherein 2 or 3 R groups are hydrogen and the other R group(s) is (are) fatty acyl moiety (moieties) 12 carbons long

Methyl glucose sesquioleate



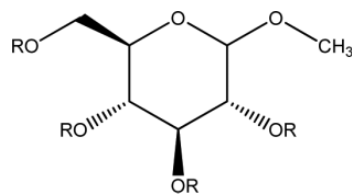
Wherein 2 or 3 R groups are hydrogen and the other R group(s) is (are) Ω -9 unsaturated fatty acyl moiety (moieties) 18 carbons long

Methyl glucose sesquistearate
(MW = 460 DA; log K_{OW} \approx 7.09)⁴



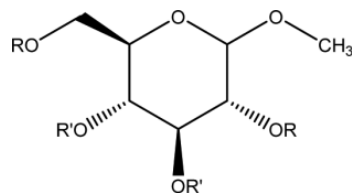
Wherein 2 or 3 R groups are hydrogen and the other R group(s) is (are) fatty acyl moiety (moieties) 18 carbons long

PEG-120 methyl glucose dioleate
(structure from Chemical Abstracts Service Registry file⁶⁵; MW = 6,037 DA)⁶⁶



Wherein R groups are Ω -9 unsaturated fatty acyl moieties 18 carbons long and R' groups are polyethylene glycol chains, with an average combined length of 120 glycol repeat units

PEG-20 methyl glucose distearate

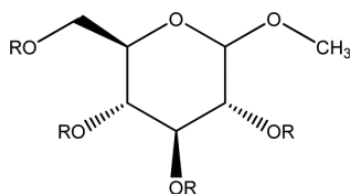


Wherein 2 R groups are fatty acyl moieties 18 carbons long and 2 R groups are polyethylene glycol chains, with a combined average length of 20 glycol repeat units

(continued)

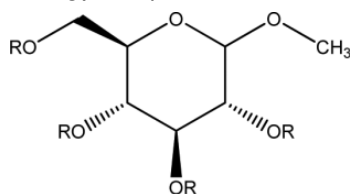
Table 2. (continued)

PEG-80 methyl glucose laurate



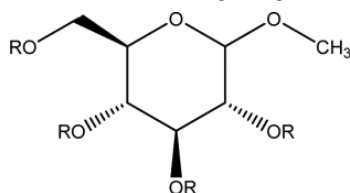
Wherein 1 R group is a fatty acyl moiety 12 carbons long and 3 R groups are polyethylene glycol chains, with a combined average length of 80 glycol repeat units

PEG-20 methyl glucose sesquicaprylate/sesquicaprate

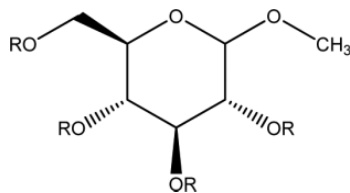


Wherein 1 or 2 R group(s) is (are) fatty acyl moiety (moieties) 8-10 carbons long and the other R groups are polyethylene glycol chains, with a combined average length of 20 glycol repeat units

PEG-20 methyl glucose sesquilaurate

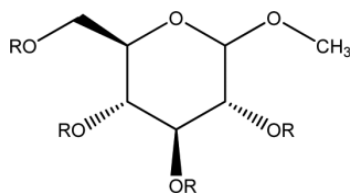


Wherein 1 or 2 R group(s) is (are) fatty acyl moiety (moieties) 12 carbons long and the other R groups are polyethylene glycol chains, with a combined average length of 20 glycol repeat units

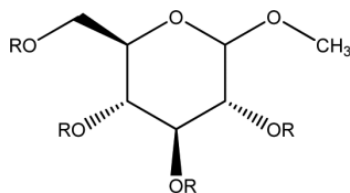
PEG-20 methyl glucose sesquistearate (MW = 1,265 DA)⁶⁷

Wherein 1 or 2 R group(s) is (are) fatty acyl moiety (moieties) 18 carbons long and the other R groups are polyethylene glycol chains, with a combined average length of 20 glycol repeat units

PEG-120 methyl glucose triisostearate

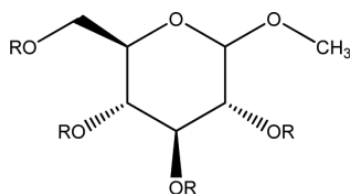


Wherein 3 R group are fatty acyl moieties 18 carbons long and the other R group is a polyethylene glycol chain, with an average length of 120 glycol repeat units

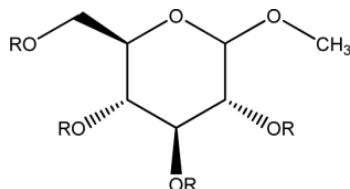
PEG-120 Methyl glucose trioleate (MW = 6,322 DA)⁶⁸

Wherein 3 R groups are Ω -9 unsaturated fatty acyl moieties 18 carbons long and the other R group is a polyethylene glycol chain, with an average length of 120 glycol repeat units

(continued)

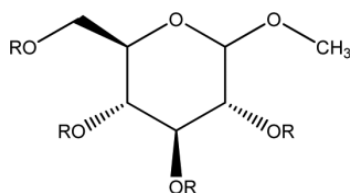
Table 2. (continued)PPG-10 methyl glucose ether
(MW = 797 DA)⁶⁹

Wherein R is hydrogen or a polypropylene glycol chain, with an average length of 10 glycol repeat units

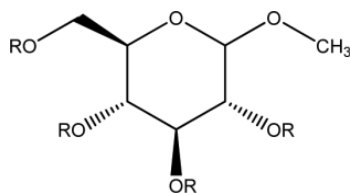
PPG-20 methyl glucose ether
(MW = 1,300 DA)⁷⁰

Wherein R is hydrogen or a polypropylene glycol chain, with an average length of 20 glycol repeat units

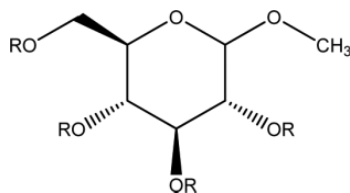
PPG-25 methyl glucose ether



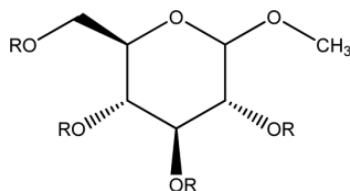
Wherein R is hydrogen or a polypropylene glycol chain, with an average length of 25 glycol repeat units

PPG-20 methyl glucose ether
acetate

Wherein R is hydrogen, acetate, or a polypropylene glycol chain, with an average length of 20 glycol repeat units

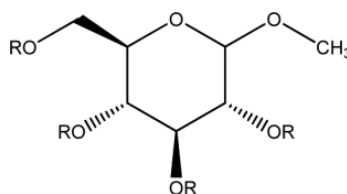
PPG-20 methyl glucose ether
distearate

Wherein 2 R groups fatty acyl moieties are 18 carbons long and the other R groups are hydrogen, or a polypropylene glycol chain, with an average length of 20 glycol repeat units

Methyl gluceth-10 (MW = 634
DA)⁷¹

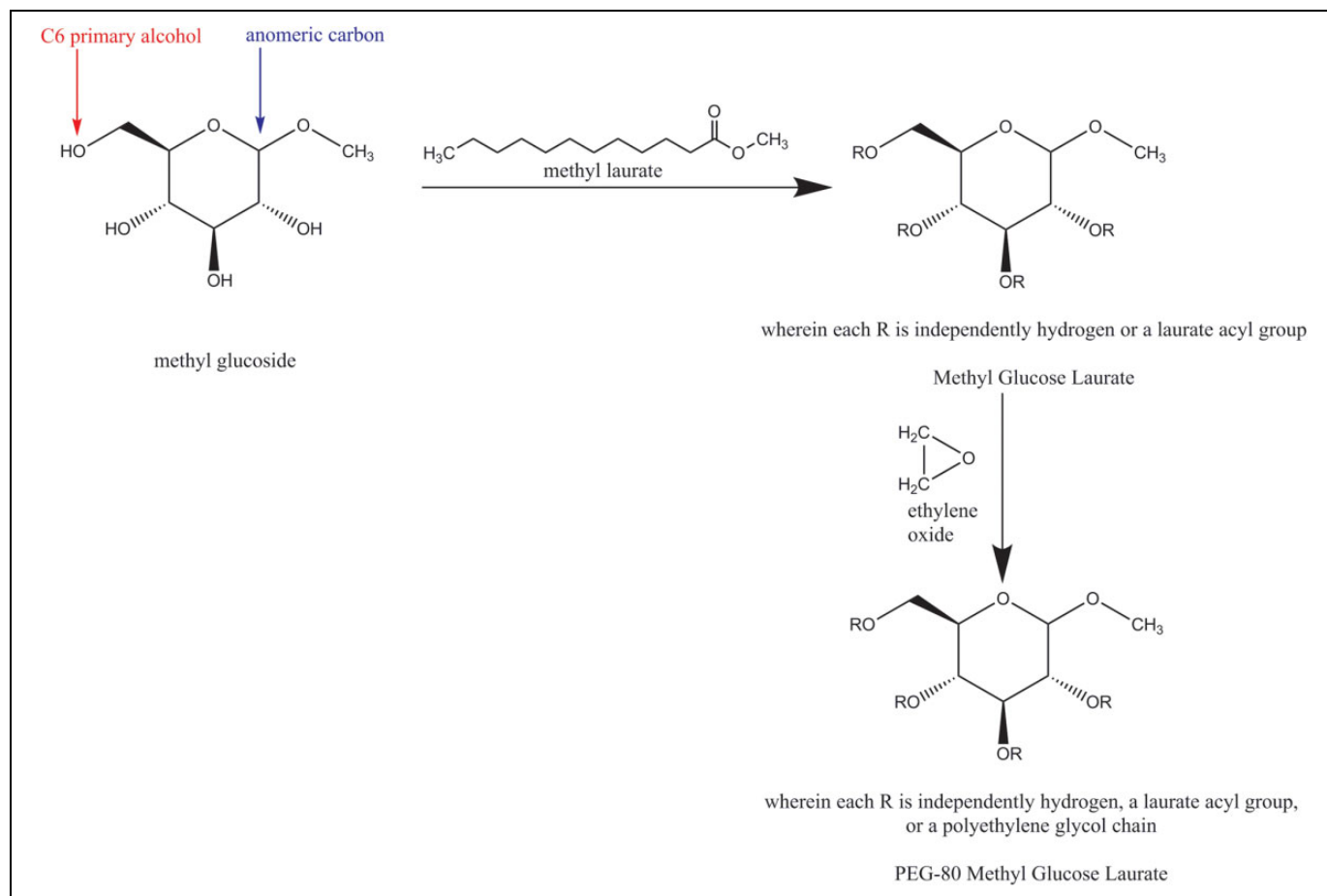
Wherein R is hydrogen or a polyethylene glycol chain, with an average length of 10 glycol repeat units

(continued)

Table 2. (continued)Methyl gluceth-20
(MW = 1,074 DA)⁷¹

Wherein R is hydrogen or a polyethylene glycol chain, with an average length of 20 glycol repeat units

Abbreviations: MW, molecular weight; PEG, polyethylene glycol; PPG polypropylene glycol.

**Figure 1.** Methyl glucose laurate synthesis and PEG-80 methyl glucose laurate synthesis.

The polyether methyl glucosides, such as PPG-10 methyl glucose ether, PPG-20 methyl glucose ether, PPG-25 methyl glucose ether, methyl gluceth-10, and methyl gluceth-20, are typically manufactured by reaction of methyl glucoside with the required amount of the appropriate epoxide (eg, propylene oxide is used to produce PPG-10 methyl glucose; ethylene oxide is utilized to produce methyl gluceth-10).¹⁰ For those ingredients with both ester and polyether groups, such as PEG-120 methyl glucose dioleate, PEG-20 methyl glucose distearate, PEG-80 methyl glucose laurate, PEG-20 methyl glucose sesquicaprylate/sesquicaprate, PEG-20 methyl glucose sesquilaurate, PEG-20 methyl glucose sesquistearate, PEG-120 methyl glucose triisostearate, PEG-120 methyl glucose

trioleate, PPG-20 methyl glucose ether acetate, and PPG-20 methyl glucose ether distearate, these same methods are utilized, sequentially. An example would be PEG-80 methyl glucose laurate, which is produced in 2 steps: (1) esterification of methyl glucoside with methyl laurate, followed by (2) polyetherification with ethylene oxide.

Impurities

The following impurities data on methyl glucose polyethers and esters are included in Tables 4 and 5: ash ($\leq 0.5\%$ wt.), arsenic (< 2 ppm), and heavy metals (< 20 ppm).

Table 3. Physical Properties of Methyl Glucose Polyether and Ester Trade Name Materials.⁶

Ingredient	Trade name	Form
Methyl glucose dioleate	Glucate DO Emulsifier (TN1)	Amber viscous liquid
Methyl glucose sesquistearate	Glucate SS Emulsifier (TN2)	Off white flakes
PPG-10 methyl glucose ether	Glucam P-10 Humectant (TN3)	Pale yellow viscous liquid
PPG-20 methyl glucose ether	Glucam P-20 Humectant (TN4)	Pale yellow medium viscosity liquid
PPG-20 methyl glucose ether distearate	Glucam P-20 Distearate Emollient (TN5)	Pale amber liquid
Methyl gluceth-10	Glucam E-10 Humectant (TN6)	Pale yellow medium viscosity liquid
Methyl gluceth-20	Glucam E-20 Humectant (TN7)	Pale yellow thin liquid
PEG-120 methyl glucose dioleate	Glucamate DOE-120 Thickener (TN8)	Pale yellow waxy solid flake
PEG-120 methyl glucose dioleate	Glucamate DOE-120 Syrup Thickener (TN9)	Pale yellow high viscosity liquid
PEG-20 methyl glucose sesquistearate	Glucamate SSE-20 Emulsifier (TN10)	Pale yellow soft liquid
PEG-20 methyl glucose trioleate (and) propylene glycol (and) water	Glucamate LT Thickener (TN11)	Pale yellow liquid
PEG-120 methyl glucose trioleate (and) propanediol	Glucamate VLT Thickener (TN12)	Pale yellow liquid

Abbreviations: PEG, polyethylene glycol; PPG polypropylene glycol.

Table 4. Properties From Technical Data Sheets on Methyl Glucose Polyether and Ester Trade Name Material.^{a,5}

Properties	TN1 ^a	TN2	TN3	TN4	TN5	TN6	TN7	TN8	TN9	TN10	TN11	TN12
Odor	Charac.	Mild	Mild	Mild	Charac.	Mild	Mild	Mild	Mild	Mild	Mild	Mild
Acid number, mg/g	7	10	0.8	0.8	2.1	1.2	0.8	1 max	0.8	1.2		
Hydroxyl value, mg/g	155	285	295	170	60	350-370	215	14-26		102		
Active content, %	100	100	100	100	100	100	100	100	70	100	40	70
Moisture, % wt.	<0.5	0.8	<1.0	<1.0	<1.0	<1.0	<1.0			<0.5		
Saponification value, mg/g	155	133	0.8	1.3	65	1.1 max	0.8	14-26	15	45		
Iodine value	68	0.5	<1.0	<1.0		<1.0	<1.0	5-15	8	0.8		
Color, Gardner	7	6	1	1 max	4			4 max	3	3		
Melt range, class I, °C		48-55										
Cloud point, °C										75		
pH, aqueous solution/as supplied						6		4.5-7.5	6	6	6.5	6.5
Ash, % wt.		<0.5	<0.5	<0.5	<0.5	<0.5	<0.5			<0.25		

Abbreviations: Charac., characteristic; TN, trade name.

^aFull trade names for TN# abbreviations are listed in Table 3.

Use

Cosmetic

The methyl glucose polyethers reportedly function as skin and hair-conditioning agents, whereas, the methyl glucose esters reportedly function only as skin-conditioning agents in cosmetic products.¹ Ingredients classified as both methyl glucose polyethers and esters based on their chemical structures function as skin-conditioning agents, surfactants, and viscosity-increasing agents in cosmetic products. According to the information supplied to the Food and Drug Administration (FDA) by industry as part of the Voluntary Cosmetic Registration Program (VCRP) in 2013 (summarized in Table 7), methyl glucose dioleate, methyl glucose sesquioleate, methyl glucose sesquistearate, PPG-10 methyl glucose ether, PPG-20 methyl glucose ether, PPG-20 methyl glucose ether distearate, methyl gluceth-10, methyl gluceth-20, PEG-120 methyl glucose dioleate, PEG-20 methyl glucose distearate, PEG-20 methyl glucose sesquistearate, and PEG-120 methyl glucose trioleate are being used in cosmetic products.¹⁷ A survey of ingredient use concentrations that was conducted by the Personal Care Products

Council (Council) in 2013 (Table 7) indicates that the polyethers and esters are being used at concentrations up to 15% and 4%, respectively.^{18,19} The maximum use concentration was 15% for methyl gluceth-10 and methyl gluceth-20 used in rinse-off skin-cleansing products. For leave-on products, the 15% maximum use concentration was for methyl gluceth-10 used in face and neck creams, lotions, and powders (not sprays). The Council survey results also provided a use concentration for the newly reported VCRP use(s) of methyl glucose sesquistearate (1% maximum use concentration), but not PEG-20 methyl glucose sesquistearate, in lipsticks. Additionally, a maximum use concentration of 0.05% for PEG-20 methyl glucose distearate in lipsticks was reported in this survey. Uses of methyl glucose sesquistearate and PEG-20 methyl glucose sesquistearate, but not PEG-20 methyl glucose distearate, in lipsticks were also reported in FDA's VCRP.

Cosmetic products containing methyl glucose polyethers and esters may be applied to the skin and hair, or, incidentally, may come in contact with the eyes and mucous membranes. Products containing these ingredients may be applied as frequently as several times per day and may come in contact with

Table 5. Specifications for Methyl Glucose Polyether and Ester Trade Name Materials.⁵

Specifications	TN1 ^a	TN2	TN3	TN4	TN5	TN6	TN7	TN8	TN9	TN10	TN11	TN12
Acid value, mg/g	0-8	0-11	0-1	0-1	0-2.5	0-1.5	0-1	0-1	0-1	0-1.5		
Color, Gardner	0-8	0-7	0-1	0-1	0-5	0-4	0-4	0-4	0-4	0-4	7 max	6 max
Active content, % wt	100	100	100	100	100	100	100	100	70	100	34-43	68-72
Viscosity, mPa-s											5,000 max	2,500-20,000
Melt range, class I, °C		48-55										
Turbidity, NTU neat at 25°C												0-20
Cloud point, °C												
Hydroxyl value, mg/g	140-165		285-305	160-180	50-70	350-370	205-225	14-26		71-79		
Iodine value	60-75		0-1	0-1	0-1	0-1	0-1	5-15	3-11	0-1		
Moisture, % weight	0-0.5	0.1	0-1	0-1	0-1	0-1.5	0-1.5	14-26	9-20	0-0.5		
Saponification value, mg/g	145-160	125-140	0-1	0-1.5	58-72	5.5-8.0	0-1.5	4.5-7.5	4.5-7.5	4.5-7.5	4.5-8.0	5.5-8.0
pH, aqueous solution												
Ash, % wt		0-0.5	0-0.5	0-0.5	0-0.5	0-0.5	0-0.5			0-0.25		
Arsenic	<2 ppm	<2 ppm	<2 ppm	<2 ppm	<2 ppm	<2 ppm	<2 ppm	<2 ppm	<2 ppm	<2 ppm	<2 ppm	<2 ppm
Heavy metals	max	max	max	max	max	max	max	max	max	max	max	max
Microbiological count, TBC	<20 ppm	<20 ppm	<20 ppm	<20 ppm	<20 ppm	<20 ppm	<20 ppm	<20 ppm	<20 ppm	<20 ppm	<20 ppm	<20 ppm
	max	max	max	max	max	max	max	max	max	max	max	max
	<10/g	<10/g	<10/g	<10/g	<10/g	<10/g	<10/g	<10/g	<10/g	<10/g	<10/g	<10/g

Abbreviations: NTU, nephelometric turbidity unit; TBC, total bacterial count.

^aFull trade names for TN# abbreviations are listed in Table 3.

Table 6. Properties of Isostearic Acid, Esters With Methyl α -D-Glucoside.⁷

Form	Viscous, slightly yellow organic liquid at 20°C and 1,013 hPa ⁷²
Stability	Stable for at least 1 day when dissolved in methanol
Density	1 g/cm ³ at 20°C ⁷²
Solubility	Water solubility <0.5 mg/L at 19.7°C
pH (determined when measuring H ₂ O solubility)	7.4 at 0.5 mg/L and 8.3 at 10 mg/L
Vapor pressure	<0.0147 Pa
Melting point	Not observed in -90°C to 360°C range ⁷²
Boiling point	>360°C
Flash point	Not observed up to 286°C at 101.3-102.1 kPa
Auto ignition temperature	415°C at 1,008.2-1,032.5 hPa
logP _{ow}	>6.5 at 25°C and pH 7
pKa (dissociation constant)	13.1 for methyl glucoside and 12.9-16.5 for the monoester

the skin or hair for variable periods following application. Daily or occasional use may extend over many years.

Polyethylene glycol-20 methyl glucose sesquistearate (aerosol hair sprays), methyl gluceth-10 (body and hand sprays), and methyl gluceth-20 (pump hair sprays, hair grooming pump sprays, hair preparation spray gel, moisturizing sprays, and indoor tanning aerosol preparations) are used in products that are sprayed (highest maximum use concentration = 2%). Additionally, methyl glucose dioleate, methyl glucose sesquistearate, PPG-10 methyl glucose ether, PPG-20 methyl glucose ether, methyl gluceth-10, methyl gluceth-20, PEG-120 methyl glucose dioleate, PEG-20 methyl glucose sesquistearate, and PEG-120 methyl glucose trioleate may be used in face/body powders (highest maximum use concentration = 15%, for methyl gluceth-10; lower values for remaining ingredients). Because these ingredients are used in aerosol/pump hair sprays or powders, they could possibly be inhaled. In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters >10 μ m, with propellant sprays yielding a greater fraction of droplets/particles below 10 μ m, compared with pump sprays.²⁰⁻²³ 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.^{20,21}

Noncosmetic

Methyl glucoside-coconut oil ester (methyl glucose sesquicoate) is listed among the food additives permitted for direct addition to food for human consumption.⁵ This methyl glucose ester is used as an aid in crystallization of sucrose and dextrose at a level not to exceed the minimum quantity required to produce its intended effect. It is also used as a surfactant in molasses, at a level not to exceed 320 ppm. As an indirect food

additive, methyl glucose sesquicoate may be safely used as a processing aid (filter aid) in the manufacture of starch, including industrial starch-modified, intended for use as a component of articles that contact food.²⁴

Toxicokinetics

Data on the absorption (including percutaneous absorption), distribution, metabolism, and excretion of methyl glucose polyethers and esters were not found in the published literature, and unpublished data were not provided.

Methyl Glucoside

The pulmonary absorption of lipid-insoluble α -methyl-D-[U-¹⁴C]glucoside (specific activity = 275 mCi/mmol) was studied using 5 to 6 male Sprague Dawley rats.²⁵ The labeled compound + unlabeled compound (total concentration = 0.01-20 mM) was dissolved in phosphate solution (pH = 7.4), and 100 μ L of solution was injected just above the point of tracheal bifurcation. After 3 hours, the lungs and trachea were removed and assayed for unabsorbed radioactivity. When the 1-hour pulmonary absorption of α -methyl-D-glucoside was measured over a 2000-fold range of the initial concentration (0.01-20 mM), the amount of compound absorbed was directly proportional to the concentration. The percentage absorption remained constant at 66% to 69% of the dose. α -Methyl-D-glucoside appeared to have been absorbed solely by diffusion through membrane pores, considering that there was no evidence of saturation in the absorption process and the rate of absorption was comparable to that of mannitol and other hydrophobic compounds of comparable molecular size.

Methyl-D-glucoside has been described as a nonmetabolizable glucose derivative²⁶ and a nonreducing derivative of glucose that does not undergo alkaline hydrolysis.²⁷

Toxicology

Acute Toxicity

Oral

Methyl glucose dioleate. The acute oral toxicity of methyl glucose dioleate was evaluated using 10 Wistar-derived albino rats (5 males, 5 females).²⁸ The animals were dosed orally (by gavage; dose = 5 g/kg body weight), observed for 14 days, and then killed. Complete gross necropsy was performed on each animal. The test material was not toxic when administered orally (LD₅₀ > 5 g/kg).

Methyl glucose sesquistearate. Methyl glucose sesquistearate was evaluated in an acute oral toxicity study involving albino rats (5 males, 5 females).²⁹ The animals were observed for 14 days after dosing. There was no evidence of gross pathology at necropsy of surviving animals. An LD₅₀ of > 5 g/kg was reported.

In another study, the acute oral toxicity of methyl glucose sesquistearate in rats was evaluated according to the

Table 7. Current Frequency and Concentration of Use According to Duration and Type of Exposure.^{a,17-19}

	Number of uses	Conc. (%)	Number of uses	Conc. (%)	Number of uses	Conc. (%)
	MG dioleate		MG sesquioleate		MG sesquiosostearate	
Exposure type						
Eye area	NR	NR	NR	NR	NR	NR
Incidental ingestion	NR	NR	NR	NR	NR	NR
Incidental inhalation—Sprays	4	NR	NR	NR	NR	NR
Incidental inhalation—powders	NR	0.6	NR	NR	NR	NR
Dermal contact	10	0.2-0.6	1	NR	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair—noncoloring	1	4	NR	NR	NR	0.1
Hair—coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous membrane	NR	NR	NR	NR	NR	NR
Baby products	NR	NR	NR	NR	NR	NR
Duration of use						
Leave-on	11	0.2- 0.6	1	NR	NR	NR
Rinse-off	NR	4	NR	NR	NR	0.1
Diluted for (bath) use	NR	NR	NR	NR	NR	NR
Totals/conc. range	11	0.2-4	1	NR	NR	0.1
	MG sesquistearate		PPG-10 MG ether		PPG-20 MG ether	
Exposure type						
Eye area	29	0.3-2	1	NR	NR	0.5
Incidental ingestion ^b	13	1	NR	NR	NR	NR
Incidental inhalation—sprays	7	0.5-0.8	2	NR	8	0.1-1
Incidental inhalation—powders	NR	NR	NR	0.8	1	0.4
Dermal contact	169	0.3-5.19	9	0.8	42	0.1-3
Deodorant (underarm)	NR	NR	NR	NR	5	0.1
Hair—noncoloring	2	0.5-2	11	2	14	NR
Hair—coloring	NR	0.5	1	0.5	NR	NR
Nail	NR	0.8	1	NR	1	NR
Mucous membrane	17	0.4-1	4	NR	2	NR
Baby products	NR	NR	NR	NR	NR	NR
Duration of use						
Leave-on	161	0.3-5.19	11	0.8-2	36	0.1-3
Rinse-off	25	0.4-4	11	0.5	21	0.1-0.5
Diluted for (bath) use	NR	NR	NR	NR	NR	NR
Totals/conc. range	186	0.3-5.19	22	0.5-2	57	0.1-3
	PPG-20 MG ether distearate		Methyl gluceth-10		Methyl gluceth-20	
Exposure type						
Eye area	NR	NR	2	1-5	15	2-6
Incidental ingestion ^b	NR	0.05	NR	NR	NR	NR
Incidental inhalation—sprays	NR	NR	1	1	12	0.5-2
Incidental inhalation—powders	NR	NR	NR	0.02-15	1	1-10
Dermal contact	2	4	63	0.02-15	386	0.04-15
Deodorant (underarm)	NR	NR	NR	NR	3	NR
Hair—noncoloring	NR	NR	10	0.0003-11	39	0.2-5
Hair—coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	5	3	2-5
Mucous membrane	NR	NR	6	0.02	207	0.04-6
Baby products	NR	NR	NR	NR	NR	NR
Duration of use						
Leave-on	2	4	60	0.02-15	154	0.2-10
Rinse-off	NR	NR	13	0.0003-15	252	0.04-15
Diluted for (bath) use	NR	NR	NR	NR	22	0.08-1
Totals/conc. range	2	0.05-4	73	0.0003-15	428	0.04-15

(continued)

Table 7. (continued)

	Number of uses	Conc. (%)	Number of uses	Conc. (%)	Number of uses	Conc. (%)
	PEG-120 MG dioleate		PEG-20 MG distearate		PEG-20 MG sesquistearate	
Exposure type						
Eye area	3	6	NR	NR	19	0.1-1
Incidental ingestion ^b	NR	NR	NR	0.05	1	NR
Incidental inhalation—sprays	2	NR	NR	NR	1	0.9-1
Incidental inhalation—powders	NR	0.4-4	NR	NR	NR	1-10
Dermal contact	370	0.2-6	2	NR	121	0.1-10
Deodorant (underarm)	1	NR	NR	NR	NR	NR
Hair—noncoloring	74	0.1-2	1	NR	2	0.9-3
Hair—coloring	NR	NR	NR	NR	1	0.5
Nail	NR	NR	NR	NR	1	1-3
Mucous membrane	292	0.2-4	NR	0.05	20	2-4
Baby products	4	1	NR	NR	NR	NR
Duration of use						
Leave-on	11	0.4-4	3	0.05	88	0.1-10
Rinse-off	415	0.1-6	NR	NR	40	0.5-6
Diluted for (bath) use	20	0.8-3	NR	NR	NR	2
Totals/conc. range	446	0.1-6	3	0.05	128	0.1-10
PEG-120 MG trioleate						
Exposure type						
Eye area	NR	NR				
Incidental ingestion	NR	NR				
Incidental inhalation—sprays	NR	0.1				
Incidental inhalation—powders	NR	0.1-0.5				
Dermal contact	3	0.1-0.5				
Deodorant (underarm)	NR	NR				
Hair—noncoloring	4	NR				
Hair—coloring	NR	NR				
Nail	NR	NR				
Mucous membrane	1	0.1-0.5				
Baby products	NR	NR				
Duration of use						
Leave-on	NR	0.1-0.5				
Rinse-off	7	0.1-0.5				
Diluted for (bath) use	NR	NR				
Totals/conc. range	7	0.1-0.5				

Abbreviations: MG, methyl glucose; NR, not reported; PEG, polyethylene glycol; PPG polypropylene glycol; Totals, rinse-off + leave-on product uses.

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

^bUsed in lipsticks.

Organization for Economic Cooperation and Development (OECD) 401 test protocol. Additional study details were not provided. An LD₅₀ of >2,000 mg/kg was reported.

Polypropylene glycol-10 methyl glucose ether. An LD₅₀ of > 13.8 mL/kg is reported in an acute oral toxicity study of PPG-10 methyl glucose ether in rats (number and strain not stated).³⁰ Details relating to the test protocol were not stated.

Polypropylene glycol-20 methyl glucose ether. The acute oral toxicity of PPG-20 methyl glucose ether was evaluated using rats (number and strain not stated).³¹ Details relating to the test protocol were not stated. An LD₅₀ of >3 mL/kg was reported.

Polypropylene glycol-20 methyl glucose ether distearate. An LD₅₀ of >5 g/kg was reported for PPG-20 methyl glucose ether

distearate in a study involving rats (number and strain not stated).³² Details relating to the test protocol were not stated.

Polyethylene glycol-120 methyl glucose dioleate. An LD₅₀ of >5 g/kg was also reported for PEG-120 methyl glucose dioleate in a study involving rats (number and strain not stated).³³ Details relating to the test protocol were not stated.

Polyethylene glycol-20 methyl glucose sesquistearate. The acute oral toxicity of PEG-20 methyl glucose sesquistearate was evaluated using 10 Wistar-derived albino rats (5 males, 5 females).³⁴ The animals were dosed orally (by gavage; dose = 5 g/kg body weight), observed for 14 days, and then killed. Complete gross necropsy was performed on each animal. Gross changes were not observed in any of the animals, and the LD₅₀ was >5 g/kg.

Polyethylene glycol-120 methyl glucose trioleate. The acute oral toxicity of PEG-120 methyl glucose trioleate (and) propylene glycol (and) was evaluated using rats (number and strain not stated). None of the animals died, and the LD₅₀ and no observable effect level (NOEL; for systemic toxicity) were > 12g/kg.³⁵ Because the test material contains 37% to 43% PEG-120 methyl glucose trioleate, the LD₅₀ for PEG-120 methyl glucose trioleate in this study was actually >4.44 to 5.16 g/kg.³⁶

Isostearic acid, esters with methyl α -D-glucoside. In an acute oral toxicity study performed according to the OECD TG 423 protocol, a single oral dose (gavage) of isostearic acid, esters with methyl α -D-glucoside (in 1% carboxymethyl cellulose and water) was administered to groups of 6 fasted, young adult Wistar rats (3 males, 3 females per group).⁷ Initially, the test material was administered at a dose of 300 mg/kg body weight. Additional groups received doses of 300 and 2,000 mg/kg body weight. The animals were observed daily and macroscopic examination was performed after terminal sacrifice on day 15. Body weight gain was classified as normal, and none of the animals died. Hunched posture and/or piloerection were observed in all animals on day 1, and, in the first group of animals, on day 2. There was no evidence of abnormalities at macroscopic, postmortem examination. The test material was classified as practically nontoxic (LD₅₀ > 2,000 mg/kg body weight).

Dermal

Polyethylene glycol-120 methyl glucose trioleate. The acute dermal toxicity of PEG-120 methyl glucose trioleate (and) propylene glycol (and) water was evaluated using rats (number and strain not stated). A single dose of the test substance (12 g/kg) was applied under occlusion. None of the animals died, and the LD₅₀ and NOEL (for systemic toxicity) were >12 g/kg.³⁵ Because the test material contains 37% to 43% PEG-120 methyl glucose trioleate, the actual LD₅₀ for PEG-120 methyl glucose trioleate in this study was >4.44 to 5.16 g/kg.³⁶

Repeated Dose Toxicity

Isostearic acid, esters with methyl α -D-glucoside. A combined repeated dose toxicity study with a reproduction/developmental toxicity screening test was carried out according to the OECD 422 test protocol.⁷ Isostearic acid, esters with methyl α -D-glucoside (in 1% aqueous carboxymethyl cellulose) was administered orally (gavage) to the following dose groups (10 male and 10 female Han rats/dose group) daily: 50, 150, and 1,000 mg/kg body weight per day. The fourth group served as the negative control. The males were dosed for 2 weeks prior to mating, during mating, and up to termination (30 days total). Females were dosed for 2 weeks prior to mating, during mating, during post coitum, and for at least 4 days of lactation (42-44 days total). Ten litters per dose group were delivered. Findings for the 1,000 mg/kg dose group were as follows: statistically significant reduction in hemoglobin, cholesterol, and protein levels (males), and elevated white blood cell counts

(determined for only 2 females) plus alkaline phosphatase levels (males), and increased liver weights (absolute and relative) in males and females.

There were no treatment-related changes in mortality, clinical appearance, functional observations, body weight, food consumption, and macroscopic and microscopic examination found in adult rats. At a dosage of 1,000 mg/kg/d, the parental NOEL was 150 mg/kg/d. The parental no observed adverse effect level (NOAEL) was defined as \geq 1,000 mg/kg/d, based on the findings observed at 1,000 mg/kg/d. It was noted that the findings at this dose level were not considered adverse and were without any corroborative findings, such as histopathological changes. Results relating to reproductive and developmental toxicity are included in that section of the report.⁷

Ocular Irritation

Methyl glucose dioleate. The ocular irritation potential of methyl glucose dioleate (as 20% gravimetric mineral oil suspension) was evaluated in the Draize test using 6 New Zealand albino rabbits.²⁸ The test material (0.1 mL; dose not stated) was instilled into 1 eye, and the contralateral eye served as the untreated control. The eyes were not rinsed after instillation. Reactions were scored for up to 72 hours postinstillation. It was concluded that the test material was not an ocular irritant under the conditions of this study.

Methyl glucose sesquistearate. The ocular irritation potential of undiluted methyl glucose sesquistearate was evaluated in the Draize test using 6 New Zealand albino rabbits.²⁹ The preceding test procedure was used. It was concluded that the test material was nonirritating to the eyes of rabbits.

Polypropylene glycol-10 methyl glucose ether. The ocular irritation potential of 100% PPG-10 methyl glucose ether was evaluated in rabbits (number and strain not stated) using the Draize test.³⁰ The test substance was classified as a mild transient irritant.

Polypropylene glycol-20 methyl glucose ether. The ocular irritation potential of 100% PPG-20 methyl glucose ether was evaluated in rabbits (number and strain not stated) using the Draize test.³¹ The test substance was classified as a mild transient irritant.

Polypropylene glycol-20 methyl glucose ether distearate. In another Draize test, PPG-20 methyl glucose ether distearate was classified as practically nonirritating in rabbits (number and strain not stated) when tested at a concentration of 100%.³²

Polyethylene glycol-120 methyl glucose dioleate. The ocular irritation potential of PEG-120 methyl glucose dioleate was evaluated in the Draize test using 5 male or female New Zealand albino rabbits.³⁷ The test substance (100 μ L) was instilled into 1 eye of each animal, followed by massaging for 30 seconds. Untreated eyes served as controls. Reactions were scored at 24, 48, 72 hours, and 7 days postinstillation, and maximum average Draize scores (MASs; range = 0-110) were determined.

PEG-120 methyl glucose dioleate was classified as a slight irritant (MAS = 8.8). An in vitro assay was conducted to determine if there was a correlation with the in vivo Draize test conducted on rabbits. Using sheep red blood cells, this in vitro assay assessed hemolysis and protein denaturation. The extent of hemolysis was determined spectrophotometrically. Assay results for PEG-120 methyl glucose dioleate were as follows: effective concentration that caused 50% hemolysis (H50) = 1,125.56 µg/mL; denaturation index (DI) = 12.82%; H50/DI = 87.80. The Pearson and Spearman correlation coefficients between the log H50/DI and the MAS were 0.752 and 0.705, respectively. Thus, PEG-120 methyl glucose dioleate was also classified as a slight irritant in the in vitro assay.

The ocular irritation potential of 100% PEG-120 methyl glucose dioleate was evaluated in the Draize test using rabbits (number and strain not stated).³³ The test substance did not induce ocular irritation. In comparative irritation tests, an unspecified concentration of the test substance significantly reduced the ocular irritation induced by SLS and AOS in rabbits (number and strain not stated). The 2 abbreviated chemical names were not defined.

Polyethylene glycol-20 methyl glucose sesquisteate. The ocular irritation potential of undiluted PEG-20 methyl glucose sesquisteate was evaluated in the Draize test using 9 New Zealand albino rabbits.³⁴ The test material (0.1 mL) was instilled into the right eye, and the left eye served as the untreated control. The eyes of 3 and 6 rabbits were rinsed and unrinsed, respectively, after instillation. Reactions were scored for up to 72 hours postinstillation. It was concluded that the test material was a minimal transient ocular irritant.

In another Draize test, the ocular irritation potential of PEG-20 methyl glucose sesquisteate (as 25% gravimetric aqueous suspension) was evaluated using 6 New Zealand white rabbits (6 months old).³⁸ The procedure was similar to the one in the preceding study, except that none of the eyes were rinsed after instillation. The test material was classified as a minimal ocular irritant.

Polyethylene glycol-120 methyl glucose trioleate. In an ocular irritation test, 0.1 mL of PEG-120 methyl glucose trioleate (and) propylene glycol (and) water (contains 34% to 43% active PEG-120 methyl glucose trioleate) were instilled into the eyes of rabbits (number and strain not stated) according to the Draize protocol.³⁵ None of the animals died. A total maximum average Draize score of 2 (range = 0-110) was reported at 1 hour postinstillation, and a score of 0 was reported at 48 hours postinstillation.

Skin Irritation and Sensitization

Animal and human skin irritation/sensitization studies are summarized in this section and in Table 8. Most of the results are classified as negative.

Methyl glucose dioleate

Animal. The skin irritation potential of methyl glucose dioleate (20% w/w mineral oil suspension) was evaluated in a

Draize skin irritation test using 6 New Zealand albino rabbits.²⁸ The test material (0.5 mL) was applied, under a 2.5 cm² occlusive patch to clipped areas of intact or abraded skin. The 2 test sites were on opposite sides of the vertebral column. The trunk was then covered with an impermeable occlusive wrapping for 24 hours. Reactions were scored at 24 and 72 hours postapplication. It was concluded that the test material was not a primary dermal irritant under the conditions of this test (primary irritation index [PII] = 2.10).

Methyl glucose sesquisteate. Methyl glucose sesquisteate was evaluated in a skin irritation study involving rabbits, using the OECD 405 test protocol. Additional study details were not included. The test substance was classified as a nonirritant.³⁹

Human

Predictive testing. The skin irritation and sensitization potential of a body and hand cream containing 0.59% methyl glucose dioleate was evaluated in a repeated insult patch test (double-blind conditions) that initially involved 111 healthy participants (64 males, 47 females; 18-74 years old).⁴⁰ Of the 111, 109 completed the induction phase and 101 completed the challenge phase. The test procedure comprised 9 sequential 24-hour induction applications and 2 concurrently conducted 24-hour challenge applications (1 at induction site and 1 at naive site). The product was applied using a partially occlusive patching device consisting of a 2 cm × 2 cm absorbent pad (immersed with 150 µL of product), centered on the adhesive-coated surface of a 2 cm × 4 cm plastic film. The product was neither a clinically significant skin irritant nor a sensitizer under the conditions of this study.

Methyl glucose sesquisteate

Animal. Undiluted methyl glucose sesquisteate was evaluated in a Draize dermal corrosion (tissue destruction) test using 6 New Zealand albino rabbits (3 males, 3 females).²⁹ The test material (0.5 mL) was applied, under a 1" × 1" occlusive patch, to clipped areas of intact or abraded skin. The trunk was then covered with an impermeable occlusive wrapping for 4 hours. Test sites were scored for erythema/edema reactions at 4 and 48 hours postapplication. It was concluded that the test material was not corrosive (PII = 0).

The skin irritation potential of undiluted methyl glucose sesquisteate was evaluated in a Draize skin irritation test using 6 New Zealand albino rabbits (3 males, 3 females).²⁹ The test protocol was similar to the one in the preceding study, except that occlusive patches remained in place for 24 hours and reactions were scored at 24 and 72 hours postapplication. It was concluded that the test material had a potential for mild irritation (PII = 1.13).

The skin irritation/corrosive potential of methyl glucose sesquisteate in rabbits was evaluated according to the OECD 404 test protocol. Additional study details were not included. The test substance was classified as nonirritating.³⁹

Methyl glucose sesquisteate was evaluated in a skin sensitization study involving guinea pigs, using the OECD 406 test

Table 8. Skin Irritation and Sensitization Studies.

Test substance	Animals/participants	Doses/concentrations tested	Procedure	Results
Animal studies				
Methyl glucose dioleate (Glucate DO, as 20% gravimetric solution)	6 New Zealand albino rabbits	0.5 mL under 2.5 cm ² occlusive patch	Application to sites (abraded or intact) on opposite sides of vertebral column for 24 hours	Nonirritant (PII = 2.10) ²⁸
Methyl glucose sesquistearate (Glucate SS, undiluted)	6 New Zealand albino rabbits	0.5 mL under 1" × 1" occlusive patch	Application to sites (abraded or intact) for 4 hours	Not corrosive (PII = 0) ²⁹
Methyl glucose sesquistearate (Glucate SS, undiluted)	6 New Zealand albino rabbits	0.5 mL under 1" × 1" occlusive patch	Application to sites (abraded or intact) for 24 hours	Potential for mild irritation (PII = 1.13) ²⁹
PPG-10 methyl glucose ether (Glucam P-10 humectant, undiluted)	6 rabbits (strain not stated)	0.5 mL under 1" × 1" occlusive patch	Application to sites (abraded or intact) for 24 hours	Nonirritant ³⁰
PPG-20 methyl glucose ether (Glucam P-20 humectant, undiluted)	6 rabbits (strain not stated)	0.5 mL under 1" × 1" occlusive patch	Application to sites (abraded or intact) for 24 hours	Nonirritant ³¹
PPG-20 methyl glucose ether distearate (Glucam P-20 distearate emollient, undiluted)	Rabbits (number and strain not stated)	Not stated	Not stated	Nonirritant ³²
PEG-120 ethyl glucose dioleate (Glucam DOE-120 Thickener, undiluted)	Rabbits (number and strain not stated)	Not stated	Not stated	PII = 0.45 ³³
PEG-20 methyl glucose sesquistearate (Glucamate SSE-20, undiluted)	6 New Zealand albino rabbits	0.5 mL under 1" × 1" occlusive patch	Application to sites (abraded or intact) for 4 hours	Not corrosive (PII = 0) ³⁴
PEG-20 methyl glucose sesquistearate (Glucamate SSE-20, undiluted)	6 New Zealand albino rabbits	0.5 mL under 1" × 1" occlusive patch	Application to sites (abraded or intact) for 24 hours	Potential for mild irritation (PII = 1.08) ³⁴
PEG-120 methyl glucose trioleate (and) propylene glycol (and) water (Glucamate LT Thickener, contains 34-43% active PEG-120 methyl glucose trioleate)	Rabbits (number and strain not stated)	0.5 mL applied under semi-occlusive conditions	Application period not stated	Slightly irritating (PII = 0.3) ³⁵
PEG-120 methyl glucose trioleate (and) propylene glycol (and) water (Glucamate LT Thickener)	Guinea pigs (number and strain not stated)	Various doses (not stated, induction and challenge)	Maximization test	Nonsensitizer (sensitization index = 0) ³⁵
Predictive tests				
Methyl glucose dioleate (0.59% in body and hand cream)	111 Healthy participants initially, 109 completed induction phase; 101 completed challenge phase	150 µL under 2 cm × 2 cm partially occlusive patch	HR IPT: 24-hour induction and challenge applications	Nonirritant and nonsensitizer ⁴⁰
Methyl glucose sesquistearate (Glucate SS, up to 100%)	55 Healthy Participants	Test concentrations = 20% aqueous (12 participants), 40% aqueous (11 participants), 60% aqueous (11 participants), 80% aqueous (10 participants), and 100% (11 participants). 0.1 mL/cm ² under occlusive patch	HR IPT: 24-hour induction and challenge applications. Due to absence of skin irritation, undiluted material applied from fifth induction application through challenge in all participants	Nonirritant and nonsensitizer ⁴¹

(continued)

Table 8. (continued)

Test substance	Animals/participants	Doses/concentrations tested	Procedure	Results
Methyl glucose sesquistearate (4% in night cream)	51 Participants	Standard amount, equivalent to amount generally used	In use test, application to face once daily for 28 days	No evidence of an intolerance reaction or significant clinical aggravation (ie, erythema, dryness, scaling, roughness, or retentive and inflammatory lesions) ⁴²
Methyl glucose sesquistearate (4% in night cream)	110 Volunteers initially, 103 completed induction and challenge phases	15 μ L on filter paper disk in Finn chamber	HR IPT: 48-hour induction applications on Mondays and Wednesdays; 72-hour induction application on Fridays; 48-hour challenge application	Nonirritant and nonsensitizer ⁴³
PPG-10 methyl glucose ether (Glucam P-10, up to 100%)	53 Healthy participants	Test concentrations = 20% aqueous (12 participants), 40% aqueous (10 participants), 60% aqueous (11 participants), 80% aqueous (10 participants), and 100% (10 participants). 0.1 mL/cm ² under occlusive patch	HR IPT: 24-hour induction and challenge applications. Due to absence of skin irritation, undiluted material applied from fifth induction application through challenge in all participants	Nonirritant and nonsensitizer ⁴⁵
PPG-10 methyl glucose ether (0.8% in a face cream)	54 Participants	20 μ L on filter paper disk in Finn chamber (8-mm cup)	HR IPT: 48-hour induction applications on Mondays and Wednesdays; 72-hour induction application on Fridays; 48-hour challenge application	Nonirritant and nonsensitizer ⁴⁶
PPG-20 methyl glucose ether (Glucam P-20, up to 100%)	55 (5 groups of 11) Healthy participants initially; 53 completed study, 2 withdrew prior to study initiation (affected groups not stated)	Test concentrations = 20% aqueous (~11 participants), 40% aqueous (~11 participants), 60% aqueous (~11 participants), 80% aqueous (~11 participants), and 100% (~11 participants). 0.1 mL/cm ² under occlusive patch	HR IPT: 24-hour induction and challenge applications. Due to absence of skin irritation, undiluted material applied from fifth induction application through challenge in all participants	Nonirritant and nonsensitizer ⁴⁷
Methyl gluceth-10 (Glucam E-10, up to 100%)	53 Healthy participants	Test concentrations = 20% aqueous (10 participants), 40% aqueous (12 participants), 60% aqueous (10 participants), 80% aqueous (10 participants), and 100% (11 participants). 0.1 mL/cm ² under occlusive patch	HR IPT: 24-hour induction and challenge applications. Due to absence of skin irritation, undiluted material applied from fifth induction application through challenge in all participants	Nonirritant and nonsensitizer ⁴⁸
Methyl gluceth-20 (Glucam E-20, up to 100%)	56 Healthy participants	Test concentrations = 20% aqueous (10 participants), 40% aqueous (12 participants), 60% aqueous (12 participants), 80% aqueous (13 participants), and 100% (9 participants). 0.1 mL/cm ² under occlusive patch	HR IPT: 24-hour induction and challenge applications. Due to absence of skin irritation, undiluted material applied from fifth induction application through challenge in all participants	Nonirritant and nonsensitizer ⁴⁹

(continued)

Table 8. (continued)

Test substance	Animals/participants	Doses/concentrations tested	Procedure	Results
PEG-120 methyl glucose dioleate (25% aqueous)	51 Participants	0.15 mL on occlusive patch (1.5" × 2")	HRIPT: 24-hour induction and challenge applications	Nonirritant and nonsensitizer ⁵¹
PEG-20 methyl glucose sesquistearate (Glucamate SSE-20, up to 100%)	55 Healthy participants	Test concentrations = 20% aqueous (11 participants), 40% aqueous (10 participants), 60% aqueous (11 participants), 80% aqueous (11 participants), and 100% (12 participants). 0.1 mL/cm ² under occlusive patch	HRIPT: 24-hour induction and challenge applications. Due to absence of skin irritation, undiluted material applied from fifth induction application through challenge in all participants	Classified as skin fatiguing agent due to skin irritation in 3 participants tested at 100% concentration; not a primary skin irritant. Nonsensitizer ⁵²
PEG-20 methyl glucose sesquistearate (5.2% in exfoliant scrub)	42 Healthy participants	Not stated	In use test, application to face twice daily for 28 days.	No skin reactions/clinical signs related to product application ⁵³
PEG-20 methyl glucose sesquistearate (5.2% in exfoliant scrub). Product diluted to 10% aqueous (effective ingredient concentration = 0.52%)	54 Healthy participants	0.2 mL applied, under occlusive patch, to 50 mm ² area	HRIPT: 48 ± 4-hour application (induction days 1 through 8) and 72 ± 4-hour application (induction days 3, 6, and 9); 48 ± 4-hour challenge application	Nonirritant (mean irritation index = 0.010) and nonsensitizer ⁷³
Provocative tests				
Methyl glucose sesquistearate	475 Contact allergy patients	Not stated	Retrospective European survey of allergic contact reactions to cosmetics. Patients observed over 4-month period. Test protocol not stated	Allergic reaction in 1 patient ⁴⁴
PEG-120 methyl glucose dioleate (5% in face and body wash). Product diluted to 10% aqueous (effective ingredient concentration = 0.5%)	53 Atopic volunteers	20 µL on occlusive patch in Finn chamber (inner diameter = 8 mm; surface = 50 mm ²)	HRIPT: details relating to test protocol not included	Slight erythema in 12 patients during induction; slight erythema in 3 during challenge. Moderate skin compatibility classification based on irritation reactions observed. No allergic reactions ⁵⁰

Abbreviations: HRIPT, human repeated insult patch test; PI, primary irritation index; PEG, polyethylene glycol; PPG, polypropylene glycol.

protocol. Additional study details were not included. The test substance was classified as a nonsensitizer.³⁹

Human

Predictive testing. In a human skin irritation and sensitization study, methyl glucose sesquisteate was evaluated undiluted (100%, as supplied; 11 participants) and at the following concentrations in water: 20% (12 participants), 40% (11 participants), 60% (11 participants), and 80% (10 participants).⁴¹ Participants (55 total, all healthy) comprising the 5 groups collectively were >18 years old. During induction, the test material (0.1 mL/cm², under occlusive patch) was applied for 24 hours, and this procedure was repeated for a total of 4 consecutive exposures per week for 3 weeks. Because there was no visible evidence of skin irritation up to the fourth patch application in any of the test groups, undiluted test material was applied for the remainder of induction and during the challenge phase. For patch applications 5 through 12, visible irritation (1+ reaction) was observed in one participant. This 1+ reaction was not considered significant. During challenge, initiated after a 2-week nontreatment period, an occlusive patch was applied for 24 hours to a new test site. Reactions were scored at 24, 48, and 72 hours postremoval. There was no visible evidence of skin sensitization. The test material did not act as a primary irritant or sensitizer in this study.

The cutaneous (by clinical evaluation and self-assessment) and cosmetic (using a questionnaire) acceptability of a night cream containing 4% methyl glucose sesquisteate was evaluated using 51 female participants.⁴² Each was instructed to apply a standard amount of the product (equivalent to amount generally used) to the face once daily for 28 days (\pm 2 days). Facial skin of the participants were clinically examined by the investigating dermatologist on days 1 and 29, a daily self-evaluation card was completed by each participant on days 1 to 28, and an acceptability questionnaire was completed by each participant on day 29. There was no evidence of an intolerance reaction or significant clinical aggravation (ie, erythema, dryness, scaling, roughness, or retentive and inflammatory lesions in clinical examinations) in any of the participants. Additionally, none of the participants presented subjective signs that were deemed relevant and probably caused by product application. It was concluded that the product was well-tolerated, and, based on questionnaire results, that the product was judged favorably by the participants.

The skin sensitization potential of a night cream containing 4% methyl glucose sesquisteate was studied using a human repeated insult patch test (HRIPT) involving 110 adult volunteers (between 18 and 70 years of age).⁴³ Seven of the participants started, but did not complete, the induction phase and were not involved in the challenge phase for reasons unrelated to conduct of the study. During the 3-week induction period, the product (15 μ L on filter paper disc in Finn chamber) was applied for 48 hours (Mondays and Wednesdays) and 72 hours (Fridays) to the left upper back 3 times per week. Reactions were scored 15 to 20 minutes after patch removal. The induction phase was followed by a 2-week nontreatment period.

During the challenge phase, 1 Finn chamber containing a fresh filter paper disc immersed with the product (15 μ L) was applied for 48 hours to the area used for induction (left upper back). A second chamber was applied for 48 hours to a new site on the right upper back. Reactions were scored 30 to 35 minutes after patch removal. Follow-up examinations were performed 24 and 48 hours later. No adverse effects were observed in any of the 110 participants during induction, and the same was true for the 103 participants who completed the challenge phase. It was concluded that the product was neither a skin irritant nor a sensitizer.

Provocative testing. A retrospective European survey of allergic contact reactions to cosmetics was conducted using data on 475 patients with contact allergy to cosmetic ingredients.⁴⁴ The patients, treated at 5 European dermatology centers, were observed during a 4-month period (January–April 1996). The test protocol was not stated. One patient, at a center in Belgium, had an allergic reaction to methyl glucose sesquisteate (test concentration not stated).

Isostearic acid, esters with methyl α -D-glucoside. A primary dermal irritation study was performed according to OECD guideline 404 using 3 young adult, male New Zealand white rabbits.⁷ Isostearic acid, esters with methyl α -D-glucoside (0.5 g) was applied, under a semi-occlusive dressing, to the skin for 4 hours. The dermal application period was followed by a 14-day observation period. Very slight erythema was observed at the application sites of all 3 animals at 60 minutes postapplication. In 2 rabbits, the reaction had resolved within 24 hours. The reaction had resolved within 7 days in the remaining animal. Scaliness at the application site was observed in 1 animal at 72 hours and 7 days postapplication, but had resolved within 14 days. It was concluded that the test material was not a dermal irritant.

Isostearic acid, esters with methyl α -D-glucoside (100% UVCB substance, defined as substances of unknown or variable composition, complex reaction products or biological materials) was evaluated in the maximization test using Dunkin Hartley guinea pigs (number of animals not stated).⁷ The test material was evaluated at concentrations of 0.5% and 75% in sesame oil during induction, and the challenge concentration was 15% in sesame oil. 2-Mercaptobenzothiazole served as the positive control. Slight skin reactions were observed after induction. However, neither erythema nor edema was observed in test or control animals during the challenge phase. It was concluded that the test material was not a dermal sensitizer.

Polypropylene glycol-10 methyl glucose ether

Animal. The skin irritation potential of 100% PPG-10 methyl glucose ether was evaluated according to an occlusive patch test procedure involving at least 6 rabbits (strain not stated).³⁰ Patches (1" \times 1") containing the test substance (0.5 mL) were applied for 24 hours to abraded and intact sites that had been clipped free of hair. The patches were secured with adhesive tape, and the entire trunk of each animal was wrapped with an

impervious material. The test substance was classified as a nonirritant.

Human

Predictive testing. In a human skin irritation and sensitization study, PPG-10 methyl glucose ether was evaluated, using 53 participants, undiluted (100%, as supplied; 10 participants) and at 20% (12 participants), 40% (10 participants), 60% (11 participants), and 80% (10 participants) in water.⁴⁵ During induction, the test material (0.1 mL/cm², under occlusive patch) was applied for 24 hours, and this procedure was repeated for a total of 4 consecutive exposures per week for 3 weeks. Because there was no visible evidence of skin irritation up to the fourth patch application in any of the test groups, undiluted test material was applied for the remainder of induction and during the challenge phase. During challenge, initiated after a 2-week nontreatment period, an occlusive patch was applied for 24 hours to a new test site. Reactions were scored at 24, 48, and 72 hours postremoval. There was no visible evidence of skin irritation or sensitization during the study.

The skin sensitization potential of a face cream containing 0.8% PPG-10 methyl glucose ether was evaluated using 54 healthy male and female participants in an HRIPT using occlusive patches.⁴⁶ A Finn chamber (8 mm aluminum cup, affixed to Scanpor tape) containing a filter disk immersed with the product (20 μ L) was used for patch testing. Test sites were either to the left or right side of the infrascapular area of the back. During induction, patches were applied for 48 hours (on Mondays, and Wednesdays) and 72 hours (on Fridays) during 3 consecutive weeks. Reactions were scored by a dermatologist at 15 to 30 minutes after patch removal according to International Contact Dermatitis Research Group (ICDRG) criteria. The challenge phase was initiated following a 2-week nontreatment period. Challenge patches were applied to the original site and a new site for 48 hours. Reactions were scored at 30 minutes and 48 hours after patch removal. The product did not induce skin irritation or sensitization.

Polypropylene glycol-20 methyl glucose ether

Animal. The skin irritation potential of 100% PPG-20 methyl glucose ether was evaluated according to the preceding occlusive patch test procedure involving at least 6 rabbits (strain not stated).³¹ The test substance was classified as a nonirritant.

Human

Predictive testing. In a human skin irritation and sensitization study, PPG-20 methyl glucose ether was evaluated undiluted (as supplied) and at the following concentrations in water: 20%, 40%, 60%, and 80%. Five groups of 11 healthy participants were tested.⁴⁷ Two of the initial 55 participants withdrew prior to study initiation; the assigned test group for each was not stated. During induction, the test material (0.1 mL/cm², under occlusive patch) was applied for 24 hours, and this procedure was repeated for a total of 4 consecutive exposures per week for 3 weeks. Because there was no visible evidence of skin irritation up to the fourth patch application in any of the

test groups, undiluted test material was applied for the remainder of induction and during the challenge phase. During challenge, initiated after a 2-week nontreatment period, an occlusive patch was applied for 24 hours to a new test site. Reactions were scored at 24, 48, and 72 hours postremoval. There was no evidence of skin irritation or sensitization during the study, and it was concluded that no visible evidence of skin damage was observed in any of the participants tested.

Polypropylene glycol-20 methyl glucose ether distearate. Undiluted PPG-20 methyl glucose ether distearate was classified as a nonirritant in a skin irritation test involving rabbits (number and strain not stated).³² Details relating to the test protocol were not stated.

Methyl gluceth-10. In a human skin irritation and sensitization study, methyl gluceth-10 was evaluated undiluted (as supplied, 11 participants) and at 20% (10 participants), 40% (12 participants), 60% (10 participants), and 80% (10 participants, 53 total) in water.⁴⁸ During induction, the test material (0.1 mL/cm², under occlusive patch) was applied for 24 hours, and this procedure was repeated for a total of 4 consecutive exposures per week for 3 weeks. Because there was no visible evidence of skin irritation up to the fourth patch application in any of the test groups, undiluted test material was applied for the remainder of induction and during the challenge phase. During challenge, initiated after a 2-week nontreatment period, an occlusive patch was applied for 24 hours to a new test site. Reactions were scored at 24, 48, and 72 hours postremoval. There was no visible evidence of skin irritation or sensitization during the study.

Methyl gluceth-20. Methyl gluceth-20 was evaluated using 5 groups (56 total participants) according to an irritation and sensitization study.⁴⁹ The following concentrations (in distilled water) and participants were evaluated in the study: 20% (10 participants), 40% (12 participants), 60% (12 participants), 80% (13 participants), and 100% (undiluted, as supplied; 9 participants). Each concentration was applied at a dose of 0.1 mL/cm². There was no evidence of skin irritation or sensitization during the study, and it was concluded that no visible evidence of skin damage was observed in any of the participants tested.

Polyethylene glycol-120 methyl glucose dioleate

Animal. The skin irritation potential of 100% PEG-120 methyl glucose dioleate was evaluated using rabbits (number and strain not stated).³³ Details relating to the test protocol were not included. A primary irritation index of 0.45 (range = 0-8) was reported.

Human

Provocative testing. The skin sensitization potential of a face and body wash containing 5% PEG-120 methyl glucose dioleate was evaluated in an HRIPT (occlusive patches) involving 53 atopic volunteers.⁵⁰ The product was diluted with water to a concentration of 10% (effective concentration = 0.5%), and a 20 μ L volume of diluted product was applied to the skin using

a Finn chamber (inner diameter = 8 mm; surface = 50 mm²). Reactions were scored according to ICDRG criteria. Additional details relating to the patch test procedure were not included. Slight erythema was observed in 12 participants during induction; however, these reactions were considered normal for the product type class evaluated. Slight erythema was observed in 3 participants during the challenge phase. The authors concluded that the product had moderate skin compatibility, based on the irritation reactions observed, but that repeated applications did not induce any allergic reactions.

Predictive testing. In a study involving 51 adult participants, the skin irritation and sensitization potential of PEG-120 methyl glucose dioleate was evaluated.⁵¹ An occlusive patch (1.5" × 2") containing a 25% aqueous solution of the test material (0.15 mL) was applied to the upper back, between the scapulae, for 24 hours. This procedure was repeated 3 times per week for a total of 10 induction applications. Following a 2-week nontreatment period, a 24-hour challenge patch was applied to the original site and to a new site (volar forearm). Sites were evaluated at 24 and 48 hours postapplication. It was concluded that, under the conditions of this study, the test material did not have skin irritation or sensitization potential.

Polyethylene glycol-20 methyl glucose sesquisteate

Animal. Undiluted PEG-20 methyl glucose sesquisteate was evaluated in a Draize dermal corrosion (tissue destruction) test using 6 New Zealand albino rabbits (3 males, 3 females).³⁴ The test material (0.5 mL) was applied, under a 1" × 1" occlusive patch, to clipped areas of intact or abraded skin. The trunk was then covered with an impermeable occlusive wrapping for 4 hours. Reactions were scored for erythema/edema reactions at 4 and 48 hours postapplication. It was concluded that the test material was not corrosive (PII = 0).

The skin irritation potential of undiluted PEG-20 methyl glucose sesquisteate was evaluated in a Draize skin irritation test using 6 New Zealand albino rabbits (3 males, 3 females).³⁴ The test protocol was similar to the one in the preceding study, except that occlusive patches remained in place for 24 hours and reactions were scored at 24 and 72 hours postapplication. It was concluded that the test material had a potential for mild irritation (PII = 1.08).

Human

Predictive testing. The skin irritation and sensitization potential of PEG-20 methyl glucose sesquisteate was evaluated on methyl gluceth-20 in an earlier section of this report.⁵² The following concentrations (in distilled water) were tested on a total of 55 healthy participants: 20% (11 participants), 40% (10 participants), 60% (11 participants), 80% (11 participants), and 100% (undiluted, as supplied; 12 participants). Each concentration was applied at a dose of 0.1 mL/cm². Because the 80% concentration induced only very slight erythema (only induction reactions observed; patch applications 2 through 4) during induction, all subsequent patch applications (all participants) were at a concentration of 100%. The reaction classified as very slight erythema (to 80% concentration) was not deemed

significant irritation. For patch applications 5 through 12, skin irritation was observed in 3 participants tested with 100%, classifying the material as a skin fatiguing agent at that concentration. Challenge reactions were not observed in any of the participants. The test material did not cause primary skin irritation or sensitization in this study.

A 4-week use test was performed to assess the acceptability (ie, the good tolerance under normal use conditions) of an exfoliant scrub containing 5.2% PEG-20 methyl glucose sesquisteate.⁵³ Forty-two healthy female volunteers (19-65 years old; Fitzpatrick skin types I to IV) participated in the study. On day 1, the product was applied to wet skin of the face and neck, followed by rinsing, at the investigating center. Subsequent applications were made at home twice per week for 28 ± 2 consecutive days. Acceptability was evaluated daily at home by each volunteer, and visual examinations of application areas (face and neck) were performed by the investigating dermatologist (before day 1 and on day 29). Volunteers also completed a questionnaire at the end of the study. None of the participants had skin reactions/clinical signs that were related to product application. However, the sensation described as very slight pulling in one participant was attributed to product application, and 2% of the volunteers experienced discomfort that was related to product application. It was concluded that the product had "good acceptability" after application under normal conditions of use.

Polyethylene glycol-120 methyl glucose trioleate

Animal. A skin irritation test on PEG-120 methyl glucose trioleate (and) propylene glycol (and) water containing 34% to 43% active PEG-120 methyl glucose trioleate was performed using rabbits (number and strain not stated).³⁵ A 0.5-mL test solution was applied under semi-occlusive conditions, and additional details relating to the test protocol were not included. None of the animals died. A primary irritation index of 0.3 (range = 0-8) was reported, and the test substance was classified as slightly irritating.

The skin sensitization potential of PEG-120 methyl glucose trioleate (and) propylene glycol (and) water was evaluated in the maximization test using guinea pigs (number and strain not stated).³⁵ Induction and challenge applications at various doses were made, and additional details relating to the test protocol were not included. None of the animals died. A sensitization index of 0 was reported and the test substance was classified as a nonsensitizer.

Case Reports

Methyl glucose dioleate. A 27-year-old female presented with widespread eczema of the legs, arms, and face, approximately 8 hours after application of an insect repellent.⁵⁴ Methyl glucose dioleate is the main component of an ingredient of the repellent that is a water-in-oil emollient and emulsifier. Patch testing with the repellent yielded a positive reaction after 3 days (+D2/+D3). Patch testing with a 3% solution (in paraffin oil) yielded positive reactions after

2 and 3 days ++D2/+++D3). Results were negative for a 3% in paraffin test solution that was used in a patch test on 10 control participants.

Allergic contact dermatitis (widespread, persistent itching dermatitis [erythema and edema]) was observed in a 39-year-old male a day after using the same insect repellent mentioned in the preceding case report.⁵⁵ In an open patch test of the repellent, an itching erythematous reaction was observed a few hours (exact time not stated) after patch application. Patch testing with methyl glucose dioleate (10% in petrolatum) revealed positive reactions after 2 and 3 days (+++D2/+++D3).

After self-medication with a paste containing methyl glucose dioleate for treatment of a suspected interdigital mycosis (left foot), a 30-year-old female presented with an itchy dermatitis (erythema and edema) of the legs and abdomen.⁵⁶ Patch testing with the paste revealed positive reactions after 2 and 3 days (++D2/+++D3). Patch testing with methyl glucose dioleate (10% in petrolatum) revealed a positive reaction only on day 3 (++D3); results were negative in 5 control participants.

A 60-year-old presented with erythematovesicular lesions on both legs and itch after using a topical antibiotic, for treatment of leg ulcers, for 15 days.⁵⁷ After patch testing with individual ingredients of the antibiotic, only the 5% methyl glucose dioleate in petrolatum yielded a positive reaction (++) after 2 and 3 days. In another test (repeated open application test [ROAT]), the patient had a strongly positive reaction to methyl glucose dioleate (5% in petrolatum) after 4 days. This reaction was said to have increased for 2 days after discontinuation at day 4. Test results (ROAT) were negative in 5 control participants.

A 4-day history of a pruritic, erythematovesicular dermatitis of the legs, trunk, and face was reported for a 72-year-old female who used an ointment for treatment of a traumatic leg ulcer.⁵⁸ The dermatitis began on the left leg 5 days after initial treatment with the ointment and spread to the other leg, trunk, and face. Patch testing with the ointment yielded a strong positive reaction, which led to further spread of the dermatitis to the face, ears, and upper trunk. Subsequent patch testing identified an ingredient (contains methyl glucose dioleate and oleic acid) of the ointment as the source of the reaction. Patch testing with methyl glucose dioleate (5% in petrolatum) yielded positive reactions after 2 days (+ reaction) and 3 days (++) reaction); reactions were negative in 10 control participants.

A healthy 26-year-old woman, without atopic or contact dermatitis history, presented with a very itchy erythematous papulovesicular eruption on the breast, arms, and the upper part of the abdomen.⁵⁹ She had applied a nursing comfort balm on the breasts, and allergic contact dermatitis was suspected. Patch testing was performed using IQ Ultra chambers. Patches were removed prior to the end of the 24-hour application period due to itching, and a positive reaction (+ at day 1) to the balm was observed. This reaction increased in severity (++) at days 2 and 3. Further patch testing with the individual ingredients of the nursing balm revealed a positive reaction only to 5% methyl

glucose dioleate in petrolatum (++) on days 2 and 4). Negative patch test results (excluding irritancy) were reported for the 5 control participants tested with methyl glucose dioleate.

Methyl glucose sesquisteate, methyl glucose dioleate, methyl gluceth-20, and PPG-20 methyl glucose ether. A 22-year-old woman presented with a papular/vesicular eruption after using a lotion or facial cream that contained methyl glucose sesquisteate. When the patient was patch tested with this ingredient (5% in petrolatum), results were positive at 96 or 48 hours.⁶⁰ Patch-test results for methyl glucose sesquisteate (5% in petrolatum) in 20 control participants were negative. Positive patch-test results were also reported when the patient was patch tested with methyl glucose dioleate (5% in petrolatum). Methyl gluceth-20 and PPG-20 methyl glucose ether (each at 5% in petrolatum) yielded negative patch-test results in this patient.

Reproductive and Developmental Toxicity

Isostearic Acid, Esters With Methyl α -D-Glucoside

A combined repeated dose toxicity study with a reproduction/developmental toxicity screening test was performed according to the OECD 422 test protocol.⁷ Isostearic acid, esters with methyl α -D-glucoside (in 1% aqueous carboxymethyl cellulose) was administered orally (gavage) to 10 male and 10 female Han rats/dose group at 50, 150, and 1,000 mg/kg body weight per day. The fourth group served as the negative control. The males were dosed for 2 weeks prior to mating, during mating, and up to termination (30 days total). Females were dosed for 2 weeks prior to mating, during mating, during post coitum, and for at least 4 days of lactation (42-44 days total). Ten litters per dose group were delivered. There were also no treatment-related changes in reproduction, breeding, or pup development. The reproduction, breeding, and developmental NOAEL was defined as $\geq 1,000$ mg/kg/d. Results relating to repeated dose toxicity in adult rats are included in that section of the report.

Genotoxicity

Bacterial Cells

Methyl glucose sesquisteate. The mutagenicity of methyl glucose sesquisteate was evaluated in the Ames test. Details relating to the test protocol were not included. The test substance was classified as nonmutagenic.³⁹

Isostearic acid, esters with methyl α -D-glucoside. Isostearic acid, esters with methyl α -D-glucoside was evaluated in a reverse gene mutation assay using the following bacterial strains: *Salmonella typhimurium* strains TA98, TA100, TA1535, and TA1537, and *Escherichia coli* strain WP2 uvrA.⁷ The test material was evaluated at doses up to 3,330 μ g/plate both with and without metabolic activation. For each strain tested, dosing did not result in a significant dose-related increase in the number of revertant colonies, with or without metabolic activation. There was no evidence of cytotoxicity. Precipitation was

observed at doses of 1,000 and 3,330 $\mu\text{g}/\text{plate}$. The positive controls induced the appropriate responses in the corresponding strains. It was concluded that the test material was not mutagenic in any of the tester strains used in this study.

PEG-120 methyl glucose dioleate. In the Ames plate incorporation test, the genotoxicity of PEG-120 methyl glucose dioleate (in ethanol) was evaluated at doses up to 5,000 $\mu\text{g}/\text{plate}$, with or without metabolic activation, using *E coli* strain WP2 *uvrA* and the following *S typhimurium* strains: TA98, TA100, TA1535, and TA1537.⁶¹ Appreciable toxicity was not observed. It was concluded that PEG-120 methyl glucose dioleate was not genotoxic in any of the bacterial strains tested, with or without metabolic activation.

PEG-120 methyl glucose trioleate. The genotoxicity of PEG-120 methyl glucose trioleate (doses up to 5,000 $\mu\text{g}/\text{plate}$) in water was evaluated with or without metabolic activation using *E coli* strain WP2 *uvrA* and the following *S typhimurium* strains: TA98, TA100, TA1535, and TA1537.⁶² The positive controls without activation were: 2-(2-furyl)-3-(5-nitro-2-furyl)acrylamide (AF-2, for strains TA98, TA100, and WP2*uvrA*), sodium azide (for strain TA1535), and 9-aminoacridine (9-AA, for strain TA1537). With activation, 2-aminoanthracene (2-AA) served as the positive control for all 5 strains. Cytotoxicity was not observed over the range of doses tested. It was concluded that, under the conditions of this test, PEG-120 methyl glucose trioleate was nongenotoxic. All positive controls were genotoxic.

Methyl- α -D-glucopyranoside (methyl glucoside). The potential of methyl- α -D-glucopyranoside as an inhibitor of spontaneous mutagenesis in plate incorporation assays was investigated using *E coli* strains derived from the K12 subline.⁶³ Methyl- α -D-glucopyranoside is known to depress intracellular cyclic AMP (cAMP) levels more effectively than glucose. Stationary phase *E coli* k12 *trp* (amber) cells supplied (by conjugation) with the *Muc*⁺ mutation-enhancing IncP plasmid pKM101 were exposed to ultraviolet (UV) light. When compared to cultures grown on a defined minimal medium, the numbers of spontaneous *Val*^r and *Lac*⁺ mutations appearing on the selective plates tended to be lowest in cultures that had been supplemented with methyl- α -D-glucopyranoside (0.2% w/v). Thus, methyl- α -D-glucopyranoside had an antigenotoxic effect.

Mammalian Cells

Isostearic acid, esters with methyl α -D-glucoside. The genotoxicity of isostearic acid, esters with methyl α -D-glucoside (100% UVCB-substance [80% methyl glucoside isostearate esters (mainly di-), 16% isostearic acid, and 4% methyl glucoside]) in dimethyl sulfoxide (DMSO) was evaluated in the mouse lymphoma assay using L5178Y mouse lymphoma cells.⁷ In the first experiment, the test material was evaluated at concentrations up to 500 $\mu\text{g}/\text{mL}$ (with metabolic activation) and 300 $\mu\text{g}/\text{mL}$ (without metabolic activation). In the second experiment, the test material was evaluated at concentrations up to 375 $\mu\text{g}/$

mL (with metabolic activation) and 240 $\mu\text{g}/\text{mL}$ (without metabolic activation). In both experiments, the test material did not induce a significant increase in the mutation frequency with or without metabolic activation. The positive controls induced the appropriate response. The spontaneous mutation frequencies in the solvent-treated control cultures were between the minimum and maximum values of the historical control data range. Under the conditions of this test, it was concluded that the test material was not genotoxic.

Isostearic acid, esters with methyl α -D-glucoside (80% methyl glucoside isostearate esters [mainly di-], 16% isostearic acid, and 4% methyl glucoside) in DMSO was evaluated in a cytogenetics assay using peripheral human lymphocyte cultures.⁷ In the first assay, the test material was evaluated at concentrations up to 333 $\mu\text{g}/\text{mL}$ with and without metabolic activation. In the second assay, the test material was evaluated at concentrations up to 300 $\mu\text{g}/\text{mL}$ (with metabolic activation) and 800 $\mu\text{g}/\text{mL}$ (without metabolic activation). In both assays, the test material did not induce a statistically significant or biologically relevant increase in the number of cells with chromosome aberrations either with or without metabolic activation. The positive controls induced the appropriate response. The number of cells with chromosome aberrations in solvent control cultures was within the laboratory historical control data range.

Carcinogenicity

Studies on the carcinogenicity of methyl glucose polyethers and esters were not found in the published literature and unpublished data were not provided.

Summary

The safety of methyl glucose polyethers and esters as cosmetic ingredients is reviewed in this report. The methyl glucose polyethers function as skin and hair-conditioning agents, whereas, the methyl glucose esters function only as skin-conditioning agents in cosmetic products. Ingredients classified as both methyl glucose polyethers and esters based on their chemical structures function as skin-conditioning agents, surfactants, and viscosity-increasing agents in cosmetic products.

Data reported to the FDA by industry as part of the VCRP in 2012 indicate that the following methyl glucose polyethers and esters are being used in cosmetic products: methyl glucose dioleate, methyl glucose sesquioleate, methyl glucose sesquistearate, PPG-10 methyl glucose ether, PPG-20 methyl glucose ether, PPG-20 methyl glucose ether distearate, methyl gluceth-10, methyl gluceth-20, PEG-120 methyl glucose dioleate, PEG-20 methyl glucose distearate, PEG-20 methyl glucose sesquistearate, and PEG-120 methyl glucose trioleate.

Results from surveys of ingredient use concentrations provided by the Council in 2012 and 2013 indicate that the polyethers and esters are being used at concentrations up to 15% and 4%, respectively. The 15% maximum use concentration in rinse-off products relates to methyl gluceth-10 and methyl

gluceth-20 in skin-cleansing products. For leave-on products, the 15% maximum use concentration relates to methyl gluceth-10 in face and neck creams, lotions, and powders (not sprays).

The survey results provided by the Council also included a use concentration for the newly reported VCRP use(s) of methyl glucose sesquistearate (13 products—1% maximum use concentration), but not PEG-20 methyl glucose sesquistearate (1 product), in lipsticks. Additionally, a maximum use concentration of 0.05% for PEG-20 methyl glucose distearate in lipsticks was reported. Uses of methyl glucose sesquistearate and PEG-20 methyl glucose sesquistearate, but not PEG-20 methyl glucose distearate, in lipsticks were also reported in FDA's VCRP.

The following ingredients are used in cosmetic aerosol/pump sprays: PEG-20 methyl glucose sesquistearate, methyl gluceth-10, and methyl gluceth-20. Additionally, the following ingredients may be used in face/body powders: methyl glucose dioleate (up to 0.6%), PPG-10 methyl glucose ether (up to 0.8%), PPG-20 methyl glucose ether (up to 0.4%), methyl gluceth-10 (up to 15%), methyl gluceth-20 (up to 10%), PEG-120 methyl glucose dioleate (up to 4%), PEG-20 methyl glucose sesquistearate (up to 10%), and PEG-120 methyl glucose trioleate (up to 0.5%). Because these ingredients are used in aerosol/pump hair sprays or powders, they could possibly be inhaled.

Toxicokinetic data on methyl glucose polyethers and esters reviewed in this safety assessment were not found in the published literature. However, the Expert Panel (Panel) expected most of these ingredients to have low potential for skin penetration, based on their molecular weights, log K_{ow} s, and other properties.

In a study evaluating the pulmonary absorption of α -methyl-D-[U- 14 C]glucoside, the test material was injected into the trachea of rats. After 3 hours, the lungs and trachea were removed and assayed for unabsorbed radioactivity. The amount of test material absorbed was directly proportional to the concentration administered.

Acute oral toxicity data (rats) on methyl glucose polyethers and esters (trade name materials) suggest that these ingredients are relatively nontoxic, based on reported LD₅₀ values of >2g/kg or >5 g/kg. In an acute dermal toxicity study (rats) on a trade name material identified as PEG-120 methyl glucose trioleate (and) propylene glycol (and) water (Glucamate LT Thickener), an LD₅₀ of >12 g/kg was reported. Additional acute dermal toxicity data on this ingredient group were not available.

In ocular irritation tests involving rabbits, the following ingredients (all trade name materials) induced no-to-mild ocular irritation: methyl glucose sesquistearate, PPG-10 methyl glucose ether, PPG-20 methyl glucose ether, PPG-20 methyl glucose ether distearate, PEG-120 methyl glucose dioleate, PEG-20 methyl glucose sesquistearate, and PEG-120 methyl glucose trioleate (sold as 34% to 43% active). Methyl glucose dioleate was also nonirritating to the eyes of rabbits at a concentration of 20% or 25%, and PEG-20 methyl glucose sesquistearate was minimally irritating at a concentration of 25%.

In animal (rabbit) studies, methyl glucose dioleate (20% mineral oil suspension), undiluted PPG-10 methyl glucose ether, undiluted PPG-20 methyl glucose ether, undiluted PPG-20 methyl glucose distearate, and undiluted PEG-120 methyl glucose dioleate were classified as nonirritants. Methyl glucose sesquistearate was classified as a nonsensitizer in guinea pigs. Additionally, undiluted methyl glucose sesquistearate was classified as noncorrosive/nonirritating in 2 studies involving rabbits, whereas, in another study (rabbits), it was classified as having mild skin irritation potential. The same was true for undiluted PEG-20 methyl glucose sesquistearate in similar studies involving rabbits. PEG-120 methyl glucose trioleate (sold as 34% to 43% active) was classified as slightly irritating to the skin of rabbits. It was also classified as a nonsensitizer in a guinea pig maximization test; the test concentration was not stated.

A night cream containing 4% methyl glucose sesquistearate was well-tolerated (ie, no erythema or inflammatory lesions) in a 4-week cosmetic use test. This product was also neither a skin irritant nor a sensitizer in an HRIPT. In another 4-week cosmetic use test, an exfoliant scrub containing 5.2% PEG-20 methyl glucose sesquistearate was classified as having good acceptability, that is no skin reactions/clinical signs that were related to product application. The following ingredients were classified as nonirritants and nonsensitizers in human repeated insult patch tests: methyl glucose dioleate (0.59% in body and hand cream), methyl glucose sesquistearate (up to 100%), PPG-10 methyl glucose ether (up to 100%), PPG-20 methyl glucose ether (up to 80% aqueous), methyl gluceth-10 (up to 100%), methyl gluceth-20 (up to 100%), PEG-120 methyl glucose dioleate (25% aqueous), and PEG-20 methyl glucose sesquistearate (up to 100%). A retrospective European survey of allergic contact reactions to cosmetics was conducted using data on 475 patients with contact allergy to cosmetic ingredients. One patient, at a center in Belgium, had an allergic reaction to methyl glucose sesquistearate (test concentration not stated).

Positive patch-test reactions to methyl glucose dioleate were observed in various case reports. An insect repellent (main component of 1 ingredient = methyl glucose dioleate) induced contact dermatitis in 2 patients. Patch-test results for the repellent were positive in the 2 patients, but negative in 10 control participants. One of the 2 patients was patch tested with methyl glucose dioleate (10% in petrolatum), and results were negative. Dermatitis was observed in 2 additional patients after application of a paste (to treat suspected mycosis) and a topical antibiotic (for leg ulcer), both containing methyl glucose dioleate, respectively. Patch-test results for methyl glucose dioleate (10% in petrolatum) were positive in one patient, but negative in 5 control patients. For the other patient, similar patch-test results at a lower concentration (5% in petrolatum) were reported. A positive patch-test reaction to methyl glucose dioleate (5% in petrolatum) was observed in another patient who had used an ointment containing methyl glucose dioleate to treat a leg ulcer. Patch test results were negative in 10 control participants.

Dermatitis was also observed in a patient after using a lotion or facial cream containing methyl glucose sesquistearate.

Patch-test results for the ingredient (5% in petrolatum) were positive, but negative in 20 control participants. Additional patch tests revealed a positive reaction to methyl glucose dioleate (5%) in petrolatum in the patient, and negative reactions to PPG-20 methyl glucose ether and methyl gluceth-20 (both at 5% in petrolatum). Allergic contact dermatitis was also observed in a patient who had used a nursing comfort balm containing methyl glucose dioleate. Patch-test results were positive for 1 ingredient in the product, methyl glucose dioleate (5% in petrolatum). Negative patch-test results were reported for 5 control participants patch tested with methyl glucose dioleate.

Methyl glucose sesquistearate was classified as nongenotoxic in the Ames test. Also, PEG-120 methyl glucose dioleate and PEG-120 methyl glucose trioleate were not genotoxic in the Ames test (*S typhimurium* and *E coli* strains) at doses up to 5,000 µg/plate with or without metabolic activation. Negative Ames test (*S typhimurium* and *E coli* strains) results were also reported for isostearic acid, esters with methyl α -D-glucoside at doses up to 3,330 µg/plate, with and without metabolic activation. As a defined minimal medium supplement, methyl- α -D-glucopyranoside (0.2% w/v) had antigenotoxic activity in stationary phase *E coli* k12 *trp* (amber) cells, supplied (by conjugation) with the Muc⁺ mutation-enhancing IncP plasmid pKM101, exposed to UV light.

Repeated dose toxicity, reproductive and developmental toxicity, or carcinogenicity data on the methyl glucose polyethers and esters reviewed in this safety assessment were not identified in the published literature. However, a mixture (registered with the ECHA) containing on isostearic acid, esters with methyl α -D-glucoside (80% methyl glucoside isostearate esters [mainly di-], 16% isostearic acid, and 4% methyl glucoside) was practically nontoxic in an acute oral toxicity study (rats), was neither a skin irritant in rabbits nor a sensitizer in guinea pigs, and was nongenotoxic in bacterial and mammalian cell assays. The following results were reported in a repeated dose oral toxicity study with a reproduction/developmental toxicity screening test (rats): parental NOEL (150 mg/kg/d), parental NOAEL ($\geq 1,000$ mg/kg/d), and reproduction, breeding, and developmental toxicity NOAEL ($\geq 1,000$ mg/kg/d). Specifically, the repeated dose oral toxicity data were used by the Cosmetic Ingredient Review (CIR) Expert Panel for read-across in evaluating the safety of methyl glucose sesquistearate, PEG-20 methyl glucose sesquistearate, and PEG-20 methyl glucose distearate in lipsticks.

Discussion

There were limited genotoxicity data; however, robust dermal irritation and sensitization data were available in this assessment. After reviewing the available data, including the molecular weights, log K_{ow} s, and toxicity data, the Panel concluded that these ingredients, as used in cosmetics, would not result in significant systemic exposures. The Panel also concluded that the interrelationships between molecular structures and physicochemical and biological characteristics (ie, structure–

property and structure–activity relationships), in conjunction with their functions and concentrations in cosmetics, allow grouping these ingredients together and extending the available toxicological data to support the safety of each of the ingredients in the group.

The use of methyl glucose sesquistearate, PEG-20 methyl glucose sesquistearate, and PEG-20 methyl glucose distearate in lipsticks raised the concern about repeated ingestion as a route of exposure. Methyl glucose sesquistearate and PEG-20 methyl glucose distearate are being used in lipsticks at concentrations of 1% and 0.05%, respectively. Use concentration data on PEG-20 methyl glucose sesquistearate in lipsticks were not provided; however, it is assumed that this ingredient is being used at concentrations no greater than 1%. The Panel subsequently agreed that repeated dose oral toxicity data on isostearic acid, esters with methyl α -D-glucoside (80% methyl glucoside isostearate esters [mainly di-], 16% isostearic acid, and 4% methyl glucoside; registered with the ECHA) could be used for read-across, thereby satisfying the initial request for these data on the 3 ingredients. The use concentrations reported (up to 1%) are considered low, such that systemic toxicity would not result from cosmetic use in lipsticks. This prediction is supported by negative results from a combined repeated dose toxicity study with a reproductive and developmental toxicity screening test, in which rats received repeated oral doses of up to 1,000 mg/kg body weight isostearic acid, esters with methyl α -D-glucoside.

The Panel considered the potential effect that methyl glucose would have on glucose metabolism, were these ingredients to be absorbed and metabolized. As previously noted, however, for most of these ingredients, no significant systemic exposure would result from dermal use. The potential for complete deesterification of these ingredients to produce methyl glucose was considered insignificant, and, therefore, should not interfere with glucose metabolism. Regarding the extent of esterification of the methyl glucose esters, the *International Cosmetic Ingredient Dictionary and Handbook* states that, by convention, esters are monoesters unless stated otherwise.

The Panel discussed the issue of incidental inhalation exposure from aerosol and pump hair sprays and foot powders and sprays. Inhalation toxicity data were not available. However, the Panel considered pertinent data indicating that incidental inhalation exposures to these ingredients in such cosmetic products would not cause adverse health effects, including data characterizing the potential for these ingredients to cause acute oral toxicity, and ocular or dermal irritation or sensitization. The Panel noted that 95% to 99% of droplets/particles produced in cosmetic aerosols would not be respirable to any appreciable amount. 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 CIR Expert Panel concluded that the following methyl glucose polyethers and esters are safe in the present practices of use and concentration, described in this safety assessment, in cosmetics.

Esters

methyl glucose caprylate/caprinate*
 methyl glucose dioleate
 methyl glucose isostearate*
 methyl glucose laurate*
 methyl glucose sesquicaprylate/sesquicaprate*
 methyl glucose sesquicoate*
 methyl glucose sesquiosostearate
 methyl glucose sesquilaurate*
 methyl glucose sesquioleate
 methyl glucose sesquistearate

Polyethers

PPG-10 methyl glucose ether
 PPG-20 methyl glucose ether
 PPG-25 methyl glucose ether*
 methyl gluceth-10
 methyl gluceth-20

Esters and polyethers

PEG-120 methyl glucose dioleate
 PEG-20 methyl glucose distearate
 PEG-80 methyl glucose laurate*
 PEG-20 methyl glucose sesquicaprylate/ sesquicaprate*
 PEG-20 methyl glucose sesquilaurate*
 PEG-20 methyl glucose sesquistearate
 PEG-120 methyl glucose triisostearate*
 PEG-120 methyl glucose trioleate
 PPG-20 methyl glucose ether acetate*
 PPG-20 methyl glucose ether distearate

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

Authors' Note

Unpublished sources cited in this report are available from the Director, Cosmetic Ingredient Review, Washington, DC, USA.

The 2013 Cosmetic Ingredient Review Expert Panel members are Chair, Wilma F. Bergfeld, MD, FACP; Donald V. Belsito, MD; Curtis D. Klaassen, PhD; Daniel C. Liebler, PhD; Ronald A. Hill, PhD James G. Marks, Jr, MD; Ronald C. Shank, PhD; Thomas J. Slaga, PhD; and Paul W. Snyder, DVM, PhD The CIR Director is Lillian J. Gill, DPA. This report was prepared by Wilbur Johnson, Jr, MS, Senior Scientific Analyst and Bart Heldreth, PhD, Chemist.

Author Contributions

W. Johnson contributed to conception and design, contributed to acquisition, analysis, and interpretation, and drafted the manuscript.

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

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: The articles in this supplement were sponsored by the Cosmetic Ingredient Review.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: The articles in this supplement were sponsored by the Cosmetic Ingredient Review. The Cosmetic Ingredient Review is financially supported by the Personal Care Products Council.

References

1. Gottschalck TE, Breslawec HP. *International Cosmetic Ingredient Dictionary and Handbook*. 14th ed. Washington, DC: Personal Care Products Council; 2012.
2. Seldner A. Methyl glucoside ethers and esters in cosmetic creams and lotions. *Cosmet Toiletries*. 1980;95(3):85-86.
3. Organization for Economic Co-operation Development (OECD). Ecological categorization results from the Canadian Domestic Substance List. D-Glucopyranoside, methyl, 2,6-di-9-octadecenoate, (Z,Z)-. Web site. <http://webnet.oecd.org/ccrweb/ChemicalDetails.aspx?ChemicalID=DFFEF87E-5124-44C8-8FD6-02C305065E69>. Accessed May 3, 2012.
4. Anonymous. Methyl glucose sesquistearate. Statement on skin penetration and bioaccumulation potential. Unpublished data submitted by the Personal Care Products Council on 10-16-2012. 2012.
5. Food and Drug Administration (FDA). Food additives permitted for direct addition to food for human consumption. Methyl glucoside-coconut oil ester. 21 CFR 172.816. 2011.

6. Lubrizol, Inc. Methyl Glucoside Derivatives. Web site. <http://www.lubrizol.com/personalcare/products/methylglucosidederivatives/default.html>. Accessed May 11, 2012.
7. Evonik Industries. Summary of product data with reference to toxicology and ecology: Isolan[®] IS (methyl glucose isostearate). Web site. <http://echa.europa.eu/>. Accessed May 21, 2013.
8. European Patent Office. DE4040655. Web site. <http://translation.portal.epo.org/emtp/translate/?ACTION=description-retr>. Accessed February 14, 2012.
9. Wei Y, Huang H, Li X. Synthesis and analysis of methyl glucoside stearate. *Jing Xi Hua Gong Zhong Jian Ti*. 2004; 34(6):55-57.
10. Jia S, Wang Y, Wang R, Su X. Synthesis of methyl glucoside stearate and methyl glucoside stearate polyoxypropylene ether. *Huaxue Yanjiu Yu Yingyong*. 2009;21(8):1114-1118.
11. Li CJ, Anastas P. Green chemistry: present and future. *Chem Soc Rev*. 2012;41(4):1413-1414.
12. Behler A, Biermann M, Hill K, Raths HC, Saint Victor ME, Uphues G. Chap. 1. Industrial surfactant synthesis. In: Texter J, ed. *Reactions and Syntheses in Surfactant Systems*. Philadelphia, PA: Taylor and Francis; 2001:1-44.
13. Mutua LN, Akoh CC. Synthesis of alkyl glucoside fatty acid esters in non-aqueous media by *Candida sp.* lipase. *JAOCS*. 1993;70(1):43-46.
14. Desai N, Wisotzki K. Fatty acid esters of methylglucoside derivatives. *Off Gaz US Pat Trademark Off Pat*. 1996;1184(4):2377.
15. Gibbons JP, Swanson CJ. Methyl glucoside fatty acid diesters. *JAOCS*. 1959;36(11):553-555.
16. Conrad LI. New glucose derivatives in skin lotions. *Cosmet Perfum*. 1974;89(Mar):33-34.
17. Food and Drug Administration (FDA). *Frequency of Use of Cosmetic Ingredients*. Washington, DC: FDA; 2013.
18. Personal Care Products Council. Concentration of use by FDA product category. Methyl glucose polyethers and esters. Unpublished data submitted by the Personal Care Products Council on 4-24-2013. 2013.
19. Personal Care Products Council. Concentration of use by FDA product category. Methyl gluceth-10 and methyl gluceth-20. Unpublished data submitted by the Personal Care Products Council on 1-2-2013. 2013.
20. Rothe H, Fautz R, Gerber E, et al. Special aspects of cosmetic spray safety evaluations: principles on inhalation risk assessment. *Toxicol Lett*. 2011;205(2):97-104.
21. Bremmer HJ, Prud'homme de Lodder LCH, van Engelen JGM. Cosmetics Fact Sheet: To assess the risks for the consumer; Updated version for ConsExpo 4. Report No. RIVM 320104001/2006. 2006. Web site. <http://www.rivm.nl/bibliotheek/rapporten/320104001.pdf>. Accessed August 24, 2011:1-77.
22. Rothe H. Special aspects of cosmetic spray evaluation. Unpublished data presented at the 26 September CIR Expert Panel meeting. Washington DC; 2011.
23. Johnsen MA. The Influence of Particle Size. *Spray Technol Market*. 2004;14(11):24-27.
24. Food and Drug Administration (FDA). Indirect food additives: Adjuvants, production aids, and sanitizers. Methyl glucoside-coconut oil ester. 21 CFR 178.3600. 2011.
25. Lin YJ, Schanker LS. Short communication. Pulmonary absorption of glucose analogs in the rat. *Drug Metab Dispos*. 1983; 11(3):273-274.
26. Kopsidas G, MacPhee DG. Mutagenesis by 9-aminoacridine in *Salmonella typhimurium*: inhibition by glucose and other PTS class A carbon sources. *Mutat Res*. 1994;306(2):111-117.
27. Sellers T Jr, Bomball WA. Methyl glucoside as an extender/modifier for phenol-formaldehyde resin used to bond structural plywood. *Forest Prod J*. 1990;40(2):52-56.
28. Consumer Product Testing. Primary dermal irritation in rabbits, primary ocular irritation in rabbits, and acute oral toxicity in rats. Glucate DO (methyl glucose dioleate). Unpublished data submitted by the Personal Care Products Council on 10-16-2012. 1983:1-5.
29. Consumer Product Testing. Primary dermal irritation (rabbit), dermal corrosion (rabbit), ocular irritation (rabbit), acute oral toxicity (rat). Glucate SS (methyl glucose sesquisteate). Experiment Reference No. 77155-1. Unpublished data submitted by the Personal Care Products Council on 10-16-2012. 1977:1-17.
30. Lubrizol Advanced materials, Inc. Glucan[™] E-10 Humectant (PPG-10 Methyl Glucose Ether) summary of toxicology studies. Tox-156. Unpublished data submitted by the Personal Care Products Council on 4-16-2012. 2008:1.
31. Lubrizol Advanced materials, Inc. Glucam[™] P-20 Humectant (PPG-20 Methyl Glucose Ether) summary of toxicology studies. Tox-158. Unpublished data submitted by the Personal Care Products Council on 4-16-2012. 2008:1.
32. Lubrizol Advanced materials, Inc. Glucam[™] P-20 Distearate Emollient (PPG-20 Methyl Glucose Ether Distearate) summary of toxicology studies. ToX-157. Unpublished data submitted by the Personal Care Products Council on 4-16-2012. 2008. pp.1
33. Lubrizol Advanced materials, Inc. Glucamate[™] DOE-120 Thickener (PEG-120 Methyl Glucose Dioleate) summary of toxicology studies. Tox-159. Unpublished data submitted by the Personal Care Products Council on 4-16-2012. 2008:1.
34. Consumer Product Testing. Primary dermal irritation (rabbit), dermal corrosion (rabbit), ocular irritation (rabbit), acute oral toxicity (rat). PEG-20 methyl glucose sesquisterarate. Experiment Reference No. 77155-2. Unpublished data submitted by the Personal Care Products Council on 10-16-2012. 1977:1-19.
35. Lubrizol Advanced materials, Inc. Glucamate[™] LT Thickener (PEG-120 Methyl Glucose Trioleate and Propylene Glycol and Water) summary of toxicology studies. Tox-160. Unpublished data submitted by the Personal Care Products Council on 4-16-2012. 2008:1.
36. Personal Care Products Council. Comments on the draft report on methyl glucose polyethers and esters prepared for the September 2013 CIR Expert Panel Meeting. Unpublished data submitted by the Personal Care Products Council on 9-5-2013. 2013:1-2.
37. Alves EN, Presgrave Rde F, Presgrave OA, Sabagh FP, de Freitas JC, Corrado AP. A reassessment of the in vitro RBC hemolysis assay with defibrinated sheep blood for the determination of the ocular irritation potential of cosmetic products: comparison with the *In Vivo* Draize rabbit test. *Altern Lab Anim*. 2008;36(3):275-284.
38. Consumer Product Testing. Primary ocular irritation in rabbits. Glucamate SSE-20 (PEG-20 methyl glucose sesquisteate).

- Unpublished data submitted by the Personal Care Products Council on 10-16-2012. 1983. pp.1-10.
39. Evonik Industries. Summary of product data with reference to toxicology and ecology: Tego[®] Care PS (methyl glucose sesquistearate). Unpublished data submitted by the Personal Care Products Council on 4-24-2013. 2010.
 40. Product Investigations, Inc. Determination of the irritating and sensitizing propensities of a product (body and hand cream containing 0.59% methyl glucose dioleate) on human skin. Unpublished data submitted by the Personal Care Products Council on 10-15-2012. 2008. pp.1-12.
 41. Product Investigations, Inc. Evaluation of effects of Glucate SS (methyl glucose sesquistearate) during contact with human skin. Unpublished data submitted by the Personal Care Products Council on 10-16-2012. 1977. pp.1-13.
 42. Dermexpert. A study of cutaneous acceptability of a night cream containing 4% methyl glucose sesquistearate. Dermexpert Ref. AC052555. Unpublished data submitted by the Personal Care Products Council on 10-24-2012. 2006. pp.1-21.
 43. Product Investigations, Inc. Human repeated insult patch test of a night cream containing 4% methyl glucose sesquistearate. PII 20468. Unpublished data submitted by the Personal Care Products Council on 10-24-2012. 2006. pp.1-12.
 44. Goossens A, Beck MH, Hanek E, et al. Adverse cutaneous reactions to cosmetic allergens. *Contact Dermatitis*. 1999;40(2): 112-113.
 45. Product Investigations, Inc. Evaluation of Glucam P-10 (PPG-10 methyl glucose ether) during contact with human skin. Unpublished data submitted by the Personal Care Products Council on 10-16-2012. 1977. pp.1-13.
 46. TKL Research. Human repeated insult patch test with challenge: face cream containing 0.8% PPG-10 methyl glucose ether. TKL Study Report No. DS106108-9. Unpublished data submitted by the Personal Care Products Council on 10-24-2012. 2008. pp.1-26.
 47. Product Investigations, Inc. Evaluation of effects of Glucam P-20 (PPG-20 methyl glucose ether) during contact with human skin. Unpublished data submitted by the Personal Care Products Council on 10-16-2012. 1977. pp.1-10.
 48. Product Investigations, Inc. Evaluation of Glucam E-10 (methyl gluceth-10) during contact with human skin. Unpublished data submitted by the Personal Care Products Council on 10-16-2012. 1977. pp.1-13.
 49. Product Investigations, Inc. Evaluation of Glucam-20 (methyl gluceth-20) during contact with human skin. Unpublished data submitted by the Personal Care Products Council on 10-16-2012. 1976. pp.1-12.
 50. EVIC Portugal. Human repeat insult patch test with challenge on a face and body wash containing 5% PEG-120 methyl glucose dioleate. Unpublished data submitted by the Personal Care Products Council on 10-25-2012. 2002. pp.1-6.
 51. C.P.T.C., Inc. Repeated insult patch test of PEG-120 methyl glucose dioleate. Experiment Reference No. C-8-83. Unpublished data submitted by the Personal Care Products Council on 10-16-2012. 1983. pp.1-9.
 52. Product Investigations, 1977. Evaluation of effects of Glucamate SSE-20 (PEG-20 methyl glucose sesquistearate) during contact with human skin. Unpublished data submitted by the Personal Care Products Council on 10-16-2012. 1977. pp.1-13.
 53. EVIC France. Use test with clinical control by a dermatologist: Exfoliant scrub containing 5.2% PEG-20 methyl glucose sesquistearate. Unpublished data submitted by the Personal Care Products Council on 10-24-2012. 2009. pp.1-35.
 54. Rossi G, Steffens W. Allergic contact dermatitis from Autan spray: methyl glucose dioleate as sensitizing ingredient. *Contact Dermatitis*. 2004;50(5):324.
 55. Corazza M, Borghi A, Zampino MR, Virgili A. Allergic contact dermatitis due to an insect repellent: double sensitization to picaridin and methyl glucose dioleate. *Acta Derm Venereol*. 2005;85(3):264-265.
 56. Corazza M, Levratti A, Virgili A. Allergic contact dermatitis due to methyl glucose dioleate. *Contact Dermatitis*. 2001;45(5):308.
 57. Foti C, Vena GA, Mazzarella F, Angelini G. Contact allergy due to methyl glucose dioleate. *Contact Dermatitis*. 1995;32(5):303-304.
 58. Schianchi S, Calista D, Landi G. Widespread contact dermatitis due to methyl glucose dioleate. *Contact Dermatitis*. 1996;35(4):257-258.
 59. Deswysen AC, Dekeuleener V, Goossens A, Baeck M. Allergic contact dermatitis caused by a nursing comfort balm: methyl glucose dioleate as the sensitizing ingredient. *Contact Dermatitis*. 2013;68(5):315-316.
 60. Dooms-Goossens A, Vandekerckhove M, Verschave H, Degreef H. Cosmetic dermatitis due to methyl glucose sesquistearate. *Contact Dermatitis*. 1984;10(5):312-313.
 61. Microbiological Associates. Bacterial reverse mutation assay with an independent repeat assay of PEG-120 methyl glucose dioleate. Laboratory study number: G96CB43.502001. Unpublished data submitted by the Personal Care Products Council on 10-16-2012. 1997. pp.1-53.
 62. UBE Scientific Analysis Laboratory, Inc. Mutagenicity test of Glutamate LT (PEG-120 methyl glucose trioleate) by using microorganisms. Unpublished data submitted by the Personal Care Products Council on 10-16-2012. 2011. pp.1-11.
 63. Ambrose M, MacPhee DG. Catabolite repressors are potent antimutagens in *Escherichia coli* plate incorporation assays: experiments with glucose, glucose-6-phosphate and methyl-alpha-D-glucopyranoside. *Mutat Res*. 1998;398(1-2):175-182.
 64. Anonymous. Unpublished data: Methyl glucose dioleate. Statement on skin penetration potential. Unpublished data submitted by the Personal Care Products Council on 10-16-2012. 2012. pp.1
 65. American Chemical Society. Chemical Abstracts Service (CAS) Registry. PEG-120 methyl glucose dioleate. <http://www.cas.org>. Accessed September 24, 2012.
 66. Anonymous. Unpublished data: PEG-120 methyl glucose dioleate. Statement on skin penetration potential. Unpublished data submitted by the Personal Care Products Council on 10-16-2012. 2012. pp.1
 67. Anonymous. Unpublished data: PEG-20 methyl glucose sesquistearate. Statement on skin penetration potential. Unpublished data submitted by the Personal Care Products Council on 10-16-2012. 2012. pp.1
 68. Anonymous. Unpublished data: PEG-120 methyl glucose trioleate. Statement regarding skin penetration potential. Unpublished data submitted by the Personal Care Products Council on 10-16-2012. 2012. pp.1

69. Anonymous. Unpublished data: PPG-10 methyl glucose ether. Statement on skin penetration potential. Unpublished data submitted by the Personal Care Products Council on 10-16-2012. 2012. pp.1
70. Anonymous. Unpublished Data: PPG-20 methyl glucose ether. Statement on skin penetration potential. Unpublished data submitted by the Personal Care Products Council on 10-16-2012. 2012. pp.1
71. Anonymous. Unpublished data: Methyl gluceth-10 and methyl gluceth-20. Statement regarding skin penetration potential. Unpublished data submitted by the Personal Care Products Council on 10-16-2012. 2012. pp.1
72. Unilab Chemicals & Pharmaceuticals Pvt Ltd. Certificate of analysis and MSDS: Chlorphenesin BP (British Pharmacopoeia). Unpublished data submitted by the Personal Care Products Council on 7-13-2011. 2010. pp.1-4.
73. L.E.C.Bulgarie. Verification of the absence of sensitizing potential and of the good cutaneous compatibility of a cosmetic investigationsl product, by repeated epicutaneous applications under occlusive patch in healthy adult participants: exfoliant scrub containing 5.2% PEG-20 methyl glucose sesquistearate. Report No.: B090210RD12. Unpublished data submitted by the Personal Care Products Council on 10-24-2012. 2009. pp.1-12.