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

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All interested persons are provided 60 days from the above date to comment on this Tentative Report and to identify additional published data that should be included or provide unpublished data which can be made public and included. Information may be submitted without identifying the source or the trade name of the cosmetic product containing the ingredient. All unpublished data submitted to CIR will be discussed in open meetings, will be available at the CIR office for review by any interested party and may be cited in a peer-reviewed scientific journal. Please submit data, comments, or requests to the CIR Director, Dr. F. Alan Andersen.

The 2012 Cosmetic Ingredient Review Expert Panel members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; Ronald A Hill, Ph.D. James G. Marks, Jr., M.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Director is F. Alan Andersen, Ph.D. This report was prepared by Wilbur Johnson, Jr., M.S., Manager/Lead Specialist and Bart Heldreth, Ph.D., Chemist.

1101 17TH STREET, NW, SUITE 412 ◊ WASHINGTON, DC 20036-4702 ◊ PH 202.331.0651 ◊ FAX 202.331.0088 ◊

CININFO@CIR-SAFETY.ORG

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ABSTRACT: The methyl glucose polyethers and esters function as skin/hair conditioning agents, surfactants, and viscosity increasing agents, and are used at concentrations up to 15% in both rinse-off and leave-on cosmetic products. After reviewing data on molecular weights, the Panel determined that there likely would be no significant skin penetration of these ingredients. Thus, potential systemic exposure is unlikely. The Expert Panel concluded that the methyl glucose polyethers and esters are safe in the present practices of use and concentration.

INTRODUCTION

The safety of methyl glucose polyethers and esters is reviewed in this safety assessment. Relevant data on methyl glucoside (methyl α-D-glucopyranoside), backbone of methyl glucose polyether and ester structures, are also included for use in 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

Definitions and structures (with available molecular weight (m.w.) data) of the methyl glucose polyethers and esters reviewed in this safety assessment are found in Tables 1 and 2, respectively. The ingredients in this group are related in that they 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). The ingredients in this group vary by the identity and quantity of modifications at the other glucose alcohol functional groups, modified via traditional esterification or polyetherification techniques.

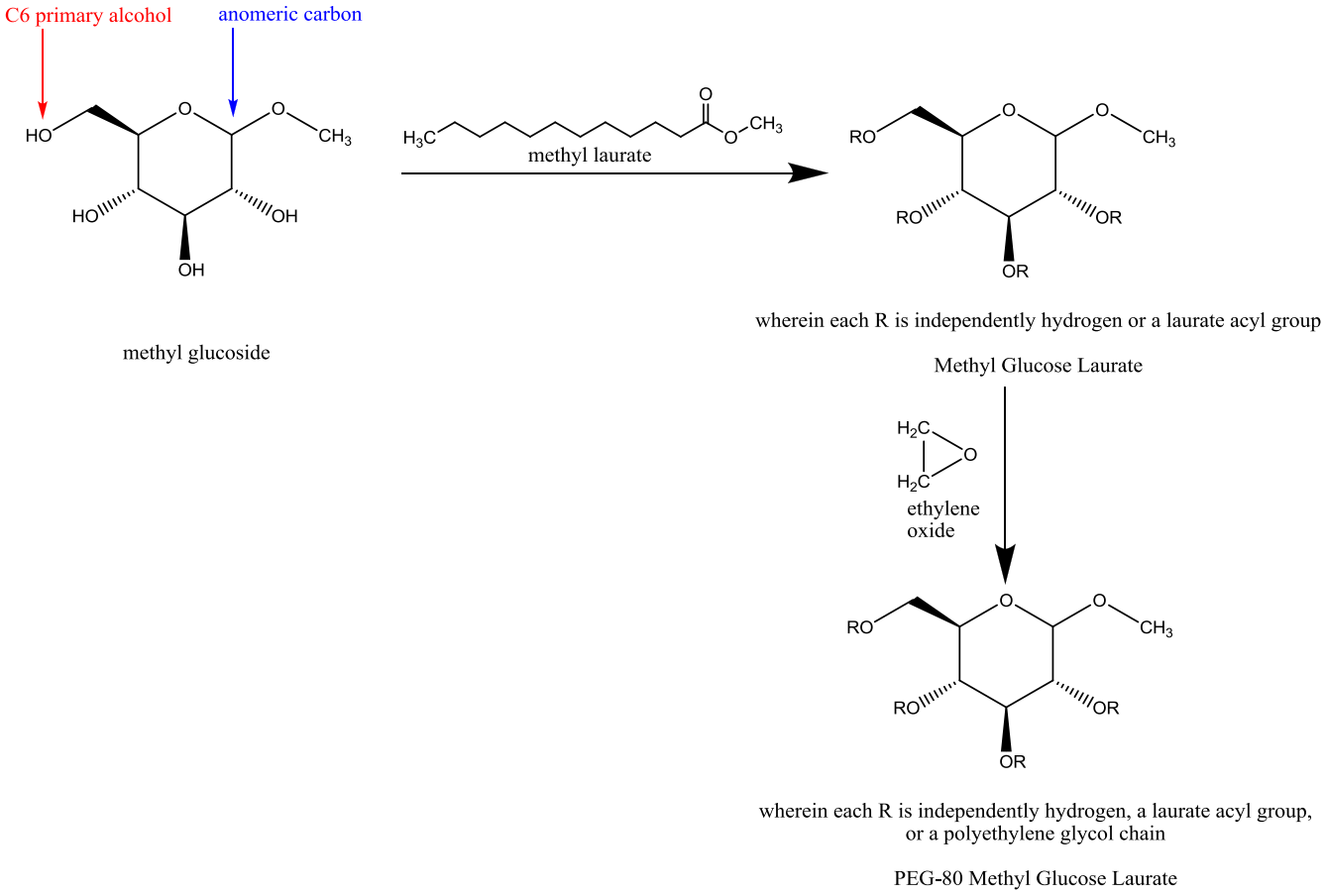


Figure 1. Methyl Glucose Laurate synthesis and PEG-80 Methyl Glucose Laurate synthesis

Physical and Chemical Properties

PPG-20 methyl glucose ether acetate (light color) 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)- (CAS No. 82933-91-3), another name for methyl glucose dioleate.[3]

Specifications for methyl glucoside-coconut oil ester (methyl glucose sesquicocoate) as a direct food additive are as follows:[4] acid number (10 to 20); hydroxyl number (200 to 300); pH (4.8 to 5.0, for 5% aqueous); and saponification number (178 to 190).

Physical properties associated with methyl glucose polyether and ester trade name materials are included in Tables 3, 4, and 5.[5] Studies on most of these trade name materials are included in the Toxicology section of this report.

Method of Manufacture

The pathways for methyl glucoside ester and polyether methyl glucoside synthesis are diagrammed in Figure 1.

Manufacture of methyl glucoside esters, such as Methyl Glucose Caprylate/Caprate, Methyl Glucose Dioleate, Methyl Glucose Isostearate, Methyl Glucose Laurate, Methyl Glucose Sesquicaprylate/Sesquicaprate, Methyl Glucose Sesquicocoate, 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).[6,7,8,9,10,11] 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.[12,13] 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.

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).[8] 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 two steps: 1) esterification of methyl glucoside with methyl laurate, followed by 2) polyetherification with ethylene oxide.

The following information on methyl glucoside (methyl α-D-glucopyranoside) is included because it forms the backbone of methyl glucose polyethers and esters reviewed in this safety assessment. Methyl glucoside, a cyclic or "internal" full acetal, is formed from one mole of methanol and one mole of glucose. It has been characterized as an unusually stable glucoside that exists in both alpha and beta forms.[14]

Impurities

Impurities data on methyl glucose polyethers and esters are included in Tables 4 and 5.

USE

Cosmetic

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. According to information supplied to the Food and Drug Administration (FDA) by industry as part of the Voluntary Cosmetic Registration Program (VCRP) in 2012, the following methyl glucose polyethers and esters are being used in cosmetic products:[15] 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 a survey of ingredient use concentrations provided by the Personal Care Products Council in 2012 indicate that, collectively, these ingredients and an additional ingredient, methyl glucose sesquiisostearate, are being used at concentrations up to 15% in rinse-off and leave-on products.[16] 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 data received on frequency and concentration of use in cosmetics for these ingredients are summarized in Table 6.

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

The following ingredients are used in products that are sprayed (highest maximum use concentration = 2%): PEG-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, moisturizing sprays, and indoor tanning aerosol preparations). Additionally, the following ingredients may be used in face/body powders (highest maximum use concentration = 15%): 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. 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 µm, with propellant sprays yielding a greater fraction of droplets/particles below 10 µm, compared with pump sprays .[17,18,19,20] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and bronchial regions and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.[17,18]

Non-Cosmetic

Methyl glucoside-coconut oil ester (methyl glucose sesquicocoate) is listed among the food additives permitted for direct addition to food for human consumption.[4] 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. Regarding use as an indirect food additive, methyl glucose sesquicocoate 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.[21]

TOXICOKINETICS

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

Methyl Glucoside

The pulmonary absorption of lipid-insoluble α-methyl-D-[U-^{14}C]glucoside (specific activity = 275 mCi/mmol) was studied using 5 to 6 male Sprague-Dawley rats.[22] The labeled compound + unlabeled compound (total concentration = 0.01 to 20 mM) was dissolved in phosphate solution (pH = 7.4), and 100 µl of solution was injected just above the point of tracheal bifurcation. After 3 h, the lungs and trachea were removed and assayed for unabsorbed radioactivity. When the 1-h pulmonary absorption of α-methyl-D-glucoside was measured over a 2000-fold range of the initial concentration (0.01 to 20 mM), the amount of compound absorbed was directly proportional to the concentration. The % 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 lipid-insoluble compounds of comparable molecular size.

It should be noted that methyl-D-glucoside has been described as a non-metabolizable glucose derivative[23] and a non-reducing derivative of glucose that does not undergo alkaline hydrolysis.[24]

TOXICOLOGY

Acute Toxicity

Oral

Methyl Glucose Dioleate

The acute oral toxicity of methyl glucose dioleate (Glucate DO; specific gravity = 1.01) was evaluated using 10 Wistar-derived albino rats (5 males, 5 females).[25] 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 (LD_{50} > 5 g/kg).

Methyl Glucose Sesquistearate

Methyl glucose sesquistearate (Glucate™ SS Emulsifier) was evaluated in an acute oral toxicity study involving albino rats (5 males, 5 females).[26] The animals were observed for 14 days after dosing. There was no evidence of gross pathology at necropsy of surviving animals. An LD_{50} of > 5 g/kg was reported.

PPG-10 Methyl Glucose Ether

The acute oral toxicity of PPG-10 methyl glucose ether (Glucam™ P-10 Humectant) was evaluated using rats (number and strain not stated).[27] Details relating to the test protocol were not stated. An LD_{50} of > 13.8 ml/kg was reported.

PPG-20 Methyl Glucose Ether

The acute oral toxicity of PPG-20 methyl glucose ether (Glucam™ P-20 Humectant) was evaluated using rats (number and strain not stated).[28] Details relating to the test protocol were not stated. An LD_{50} of > 3 ml/kg was reported.

PPG-20 Methyl Glucose Ether Distearate

An LD_{50} of > 5 g/kg was reported for PPG-20 methyl glucose ether distearate (Glucam™ P-20 Distearate Emollient) in a study involving rats (number and strain not stated).[29] Details relating to the test protocol were not stated.

PEG-120 Methyl Glucose Dioleate

An LD_{50} of > 5 g/kg was also reported for PEG-120 methyl glucose dioleate (Glucam™ DOE-120 Thickener) in a study involving rats (number and strain not stated).[30] Details relating to the test protocol were not stated.

PEG-20 Methyl Glucose Sesquistearate

The acute oral toxicity of PEG-20 methyl glucose sesquistearate (Glucamate® SSE-20) was evaluated using 10 Wistar-derived albino rats (5 males, 5 females).[31] 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 LD_{50} was > 5 g/kg.

PEG-120 Methyl Glucose Trioleate

The acute oral toxicity of PEG-120 methyl glucose trioleate (and) propylene glycol (and) water (Glucamate™ LT Thickener) was evaluated using rats (number and strain not stated).[32] None of the animals died, and the LD_{50} and NOEL (for systemic toxicity) were > 12 g/kg.

Dermal

PEG-120 Methyl Glucose Trioleate

The acute dermal toxicity of PEG-120 methyl glucose trioleate (and) propylene glycol (and) water (Glucamate™ LT Thickener) was evaluated using rats (number and strain not stated).[32] A single dose of the test substance (12 g/kg) was applied under occlusion. None of the animals died, and the LD_{50} and NOEL (for systemic toxicity) were > 12 g/kg.

Repeated Dose Toxicity

Repeated dose toxicity studies on methyl glucose polyethers and esters were not found in the published literature.

Antimicrobial Activity

The antimicrobial activity of the following methyl glucose esters of medium to long chain fatty acids was studied using *Zygosaccharomyces bailii* Y-7254 (yeast strain) and Lactobacillus fructivorans B-4000 (bacterial strain): lauric (C_{12}), myristic (C_{14}), palmitic (C_{16}), stearic (C_{18}), and oleic ($C_{18:1}$) acids.[33] Growth of these microorganisms was inhibited to various degrees by these methyl glucose monoesters (0.1, 0.5, and 1% (w/v) final concentrations in broth suspensions) using a modified broth dilution method. Generally, a dose-response effect was observed. Methyl glucose monoesters with lauric (C_{12}), or myristic acid (C_{14}) caused greater growth inhibition than those with longer chain fatty acids. The least inhibition was associated with methyl glucose oleate ($C_{18:1}$).

Ocular Irritation

Methyl Glucose Dioleate

The ocular irritation potential of methyl glucose dioleate (Glucate DO, as 20% gravimetric mineral oil suspension) was evaluated in the Draize test using 6 New Zealand albino rabbits.[25] The test material (0.1 ml) was instilled into one eye, and the contralateral eye served as the untreated control. The eyes were not rinsed after instillation. Reactions were scored for up to 72 h post-instillation. 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 sesquisteaerate (Glucate® SS) was evaluated in the Draize test using 6 New Zealand albino rabbits.[26] The preceding test procedure was used. It was concluded that the test material was non-irritating to the eyes of rabbits.

PPG-10 Methyl Glucose Ether

The ocular irritation potential of 100% PPG-10 methyl glucose ether (Glucam™ P-10 Humectant) was evaluated in rabbits (number and strain not stated) using the Draize test.[27] The test substance was classified as a mild transient irritant.

PPG-20 Methyl Glucose Ether

The ocular irritation potential of 100% PPG-20 methyl glucose ether (Glucam™ P-20 Humectant) was evaluated in rabbits (number and strain not stated) using the Draize test.[28] The test substance was classified as a mild transient irritant.

PPG-20 Methyl Glucose Ether Distearate

In another Draize test**,** PPG-20 methyl glucose ether distearate (Glucam™ P-20 Distearate Emollient) was classified as practically non-irritating in rabbits (number and strain not stated) when tested at a concentration of 100%.[29]

PEG-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.[35] The test substance (100 µl) was instilled into one eye of each animal. Instillation was

followed by massaging for 30 minutes. Untreated eyes served as controls. Reactions were scored at 24 h, 48 h, 72 h, and 7 days post-instillation, and maximum average Draize scores (MAS; range: 0 to 110) were determined. PEG-120 methyl glucose dioleate was classified as a slight irritant (maximum average Draize score = 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 (Glucamate™ DOE-120 Thickener) was evaluated in the Draize test using rabbits (number and strain not stated).[30] The test substance did not induce ocular irritation. In comparative irritation tests, Glucamate™ DOE-120 Thickener (concentrations not stated) 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.

PEG-20 Methyl Glucose Sesquistearate

The ocular irritation potential of undiluted PEG-20 methyl glucose sesquisteaerate (Glucamate® SSE-20) was evaluated in the Draize test using 9 New Zealand albino rabbits.[31] 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 h post-instillation. 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 sesquisteaerate (Glucamate® SSE-20) (as 25% gravimetric aqueous suspension) was evaluated using 6 New Zealand white rabbits (6 months old).[36] 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.

PEG-120 Methyl Glucose Trioleate

In an ocular irritation test on PEG-120 methyl glucose trioleate (and) propylene glycol (and) water (Glucamate™ LT Thickener), the test substance (0.1 ml, concentration not stated) was instilled into the eyes of rabbits (number and strain not stated) according to the Draize protocol.[32] None of the animals died. A total maximum average Draize score of 2 (range = 0 to 110) was reported at 1 h post-instillation, and a score of 0 was reported at 48 h post-instillation.

Skin Irritation and Sensitization

Animal and human skin irritation/sensitization studies are summarized in Table 7. Most of the results are classified as negative in these studies.

Methyl Glucose Dioleate

Animal

The skin irritation potential of methyl glucose dioleate (Glucate DO, as 20% gravimetric mineral oil suspension) was evaluated in a Draize skin irritation test using 6 New Zealand albino rabbits.[25] The test material (0.5 ml) was applied, under a 2.5 cm^2 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 h. Reactions were scored at 24 h and 72 h post-application. It was concluded that the test material was not a primary dermal irritant under the conditions of this test (PII =2.10).

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 subjects (64 males,

47 females; 18 to 74 years old).[37] Of the 111, 109 completed the induction phase and 101 completed the challenge phase. The test procedure comprised 9 sequential 24-h induction applications and 2 concurrently conducted 24-h 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 x 2 cm absorbent pad (immersed with 150 µl of product), centered on the adhesive-coated surface of a 2 cm x 4 cm plastic film. It was concluded that the product was neither a clinically significant skin irritant nor a sensitizer under the conditions of this study.

Methyl Glucose Sesquistearate

Animal

Undiluted methyl glucose sesquistearate (Glucate® SS) was evaluated in a Draize dermal corrosion (tissue destruction) test using 6 New Zealand albino rabbits (3 males, 3 females).[26] The test material (0.5 ml) was applied, under a 1" x 1" occlusive patch, to clipped areas of intact or abraded skin. The trunk was then covered with an impermeable occlusive wrapping for 4 h. Reactions were scored for erythema/edema reactions at 4 h and 48 h post-application. It was concluded that the test material was not corrosive (primary irritation index (PII = 0).

The skin irritation potential of undiluted methyl glucose sesquistearate (Glucate® SS) was evaluated in a Draize skin irritation test using 6 New Zealand albino rabbits (3 male, 3 females).[26] The test protocol was similar to the one in the preceding study, except that occlusive patches remained in place for 24 h and reactions were scored at 24 h and 72 h post-application. It was concluded that the test material had a potential for mild irritation (PII = 1.13).

Human

Predictive Testing

In a human skin irritation and sensitization study, methyl glucose sesquistearate (Glucate SS) was evaluated undiluted (100%, as supplied; 11 subjects) and at the following concentrations in water: 20% (12 subjects), 40% (11 subjects), 60% (11 subjects), and 80% (10 subjects).[38] Subjects (55 total, all healthy) comprising the 5 groups collectively were > 18 years old. During induction, the test material (0.1 ml/cm^2, under occlusive patch) was applied for 24 h, 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 4th patch application in any of the test groups, undiluted test material was applied for the reminder of induction and during the challenge phase. For patch applications 5 through 12, visible irritation (1+ reaction) was observed in one subject. This 1+ reaction was not considered significant. During challenge, initiated after a 2-week non-treatment period, an occlusive patch was applied for 24 h to a new test site. Reactions were scored at 24 h, 48 h, and 72 h post-removal. There was no visible evidence of skin sensitization. The test material did not act as a primary irritant or sensitizer in this study.

A use test was performed to estimate the cutaneous (by clinical evaluation and self-assessment) and cosmetic (using a questionnaire) acceptability of a night cream containing 4% methyl glucose sesquistearate.[39] Fifty-one female subjects (30 to 55 years old) participated in the study, and were instructed to apply a standard amount of the product (equivalent to amount generally used) to the face once daily for 28 days (+/- 2 days). The investigating dermatologist performed clinical examinations of facial skin on days 1 and 29. A daily self-evaluation card was completed by each subject on days 1 to 28. An acceptability questionnaire was completed by each subject on day 29. There was no evidence of an intolerance reaction or significant clinical aggravation (i.e., erythema, dryness, scaling, roughness, or retentive and inflammatory lesions in clinical examinations) in any of the subjects. Additionally, none of the subjects 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 subjects.

The skin sensitization potential of a night cream containing 4% methyl glucose sesquistearate was studied using a human repeated insult patch test (HRIPT) involving 110 adult volunteers (between 18 and 70 years of age).[40] Seven of the subjects 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 µL on filter paper disc in Finn chamber) was applied for 48 h (Mondays and Wednesdays) and 72 h (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 non-treatment period. During the challenge phase, one Finn chamber containing a fresh filter paper disc immersed with the product (15 µL) was applied for 48 h to the area used for induction (left upper back). A second chamber was applied for 48 h 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 h and 48 h

later. No adverse effects were observed in any of the 110 subjects during induction, and the same was true for the 103 subjects 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.[41] 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 sesquistearate (test concentration not stated).

PPG-10 Methyl Glucose Ether

Animal

The skin irritation potential of 100% PPG-10 methyl glucose ether (Glucam™ P-10 Humectant) was evaluated according to an occlusive patch test procedure involving at least 6 rabbits (strain not stated).[27] Patches (1" x 1") containing the test substance (0.5 ml) were applied for 24 h 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 non-irritant.

Human

Predictive Testing

In a human skin irritation and sensitization study, PPG-10 methyl glucose ether (Glucam P-10) was evaluated undiluted (100%, as supplied; 10 subjects) and at the following concentrations in water: 20% (12 subjects), 40% (10 subjects), 60% (11 subjects), and 80% (10 subjects).[42] Subjects (53 total, all healthy) comprising the 5 groups collectively were > 18 years old. During induction, the test material (0.1 ml/cm^2, under occlusive patch) was applied for 24 h, 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 4th patch application in any of the test groups, undiluted test material was applied for the reminder of induction and during the challenge phase. During challenge, initiated after a 2-week non-treatment period, an occlusive patch was applied for 24 h to a new test site. Reactions were scored at 24 h, 48 h, and 72 h post-removal. There was no visible evidence of skin irritation or sensitization during the study.

In an HRIPT using occlusive patches, the skin sensitization potential of a face cream containing 0.8% PPG-10 methyl glucose ether was evaluated using 54 healthy male and female subjects (18 to 65 years old).[43] The test protocol was a modified Draize procedure by Marzulli and Maibach. A Finn chamber (8 mm aluminum cup, affixed to Scanpor tape) containing a filter disk immersed with the product (20 µL) 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 h (on Mondays, and Wednesdays) and 72 h (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 non-treatment period. Challenge patches were applied to the original site and a new site for 48 h. Reactions were scored at 30 minutes and 48 h after patch removal. The product did not induce skin irritation or sensitization.

PPG-20 Methyl Glucose Ether

Animal

The skin irritation potential of 100% PPG-20 methyl glucose ether (Glucam™ P-20 Humectant) was evaluated according to the preceding occlusive patch test procedure involving at least 6 rabbits (strain not stated).[28] The test substance was classified as a non-irritant.

Human

Predictive Testing

In a human skin irritation and sensitization study, PPG-20 methyl glucose ether (Glucam P-20) was evaluated undiluted (as supplied) and at the following concentrations in water: 20%, 40%, 60%, and 80%. Five groups of 11 healthy subjects (> 18 years old) were tested.[44] Two of the initial 55 subjects withdrew prior to study initiation; the assigned test group for each was not stated. During induction, the test material (0.1 ml/cm^2, under occlusive patch) was applied for 24 h, 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 4th patch application in any of the test groups, undiluted test material was applied for the reminder of induction and during the challenge phase. During challenge, initiated after a 2-week non-treatment period, an occlusive patch was applied for 24 h to a new test site. Reactions were scored at 24 h, 48 h, and 72 h post-removal. 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 subjects tested.

PPG-20 Methyl Glucose Ether Distearate

PPG-20 methyl glucose ether distearate (Glucam^{TM} P-20 Distearate Emollient), undiluted, was classified as a non-irritant in a skin irritation test involving rabbits (number and strain not stated).[29] Details relating to the test protocol were not stated.

Methyl Gluceth-10

In a human skin irritation and sensitization study, methyl gluceth-10 (Glucam E-10) was evaluated undiluted (as supplied, 11 subjects) and at the following concentrations in water: 20% (10 subjects), 40% (12 subjects), 60% (10 subjects), and 80% (10 subjects).[45] Subjects (53 total, all healthy) comprising the 5 groups collectively were > 18 years old. During induction, the test material (0.1 ml/cm^2, under occlusive patch) was applied for 24 h, 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 4th patch application in any of the test groups, undiluted test material was applied for the reminder of induction and during the challenge phase. During challenge, initiated after a 2-week non-treatment period, an occlusive patch was applied for 24 h to a new test site. Reactions were scored at 24 h, 48 h, and 72 h post-removal. There was no visible evidence of skin irritation or sensitization during the study.

Methyl Gluceth-20

The skin irritation and sensitization potential of methyl gluceth-20 (Glucam E-20) was evaluated according to the preceding test procedure.[46] The following concentrations (in distilled water) were tested: 20% (10 subjects), 40% (12 subjects), 60% (12 subjects), 80% (13 subjects), and 100% (undiluted, as supplied; 9 subjects). Each concentration was applied at a dose of 0.1 ml/cm^2. Subjects (56 total, all healthy) comprising the 5 groups collectively were > 18 years old. 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 subjects tested.

PEG-120 Methyl Glucose Dioleate

Animal

The skin irritation potential of 100% PEG-120 methyl glucose dioleate (Glucam^{TM} DOE-120 Thickener) was evaluated using rabbits (number and strain not stated).[30] Details relating to the test protocol were not included. A primary irritation index of 0.45 (range: 0 to 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.[47] The product was diluted with water to a concentration of 10% (effective concentration = 0.5%), and a 20 µl volume of diluted product was applied to the skin using a Finn chamber (inner diameter = 8 mm; surface = 50 mm^2). Reactions were scored according to ICDRG criteria. Additional details relating to the patch test procedure were not included. Slight erythema was observed in 12 subjects during induction;

however, these reactions were considered normal for the product type class evaluated. Slight erythema was observed in 3 subjects 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 subjects , the skin irritation and sensitization potential of PEG-120 methyl glucose dioleate was evaluated.[48] An occlusive patch (1.5" x 2") containing a 25% aqueous solution of the test material (0.15 ml) was applied to the upper back, between the scapulae, for 24 h. This procedure was repeated 3 times per week for a total of 10 induction applications. Following a 2-week non-treatment period, a 24-h challenge patch was applied to the original site and to a new site (volar forearm). Sites were evaluated at 24 h and 48 h post-application. It was concluded that , under the conditions of this study, the test material did not have skin irritation or sensitization potential.

PEG-20 Methyl Glucose Sesquistearate

Animal

Undiluted PEG-20 methyl glucose sesquistearate (Glucamate® SSE-20) was evaluated in a Draize dermal corrosion (tissue destruction) test using 6 New Zealand albino rabbits (3 males, 3 females).[31] The test material (0.5 ml) was applied, under a 1" x 1" occlusive patch, to clipped areas of intact or abraded skin. The trunk was then covered with an impermeable occlusive wrapping for 4 h. Reactions were scored for erythema/edema reactions at 4 h and 48 h post-application. It was concluded that the test material was not corrosive (primary irritation index (PII = 0).

The skin irritation potential of undiluted PEG-20 methyl glucose sesquistearate (Glucamate® SSE-20) was evaluated in a Draize skin irritation test using 6 New Zealand albino rabbits (3 male, 3 females).[31] The test protocol was similar to the one in the preceding study, except that occlusive patches remained in place for 24 h and reactions were scored at 24 h and 72 h post-application. 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 sesquistearate (Glucamate® SSE-20) was evaluated according to the test procedure for the human skin irritation and sensitization study (repeated insult occlusive patch test) on methyl gluceth-20 in an earlier section of this report.[49] The following concentrations (in distilled water) were tested: 20% (11 subjects), 40% (10 subjects), 60% (11 subjects), 80% (11 subjects), and 100% (undiluted, as supplied; 12 subjects). Each concentration was applied at a dose of 0.1 ml/cm^2. Subjects (55 total, all healthy) comprising the 5 groups collectively were $\geq$ 18 years old. 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 subjects) 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 subjects tested with 100%, classifying the material as a skin fatiguing agent at that concentration. Challenge reactions were not observed in any of the subjects. 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 (i.e., the good tolerance under normal use conditions) of an exfoliant scrub containing 5.2% PEG-20 methyl glucose sesquistearate.[50] Forty-two healthy female volunteers (19 to 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 subjects had skin reactions/clinical signs that were related to product application. However, the sensation described as very slight pulling in one subject 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.

PEG-120 Methyl Glucose Trioleate

A skin irritation test on PEG-120 methyl glucose trioleate (and) propylene glycol (and) water (Glucamate™ LT Thickener) was performed using rabbits (number and strain not stated).[32] The test substance (0.5 ml, concentration not stated) 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 to 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 (Glucamate™ LT Thickener) was evaluated in the maximization test using guinea pigs (number and strain not stated).[32] 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 non-sensitizer.

Case Reports

Methyl Glucose Dioleate

A 27-year-old female presented with widespread eczema of the legs, arms, and face, approximately 8 h after application of an insect repellant.[51] Methyl glucose dioleate is the main component of an ingredient of the repellant, Isolan DO (a water-in-oil emollient and emulsifier). Patch testing with the repellant yielded a positive reaction after 3 days (?+D2/++ D3). Patch testing with Isolan DO (3% in paraffin oil) yielded positive reactions after 2 and 3 days ++D2/+++D3). Results were negative when Isolan DO (3% in paraffin) was patch tested on 10 control subjects.

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 repellant mentioned in the preceding case report.[52] In an open patch test of the repellant, 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.[53] 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 subjects.

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.[54] After patch testing with individual ingredients of the antibiotic, only one of the ingredients, methyl glucose dioleate (5% 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 subjects.

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.[55] 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 subjects.

Methyl Glucose Sesquistearate, 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 sesquistearate. When the patient was patch-tested with this ingredient (5% in petrolatum), results were positive at 96 h or 48 h.[56] However, patch test results for methyl glucose sesquistearate (5% in petrolatum) in 20 control subjects 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

Studies on the reproductive and developmental toxicity of methyl glucose polyethers and esters were not found in the published literature.

GENOTOXICITY

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 5000 µg/plate, with or without metabolic activation, using *Escherichia coli* strain WP2 *uvr*A and the following *Salmonella typhimurium* strains: TA98, TA100, TA1535, and TA1537.[57] 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 (Glutamate LT, doses up to 5000 µg/plate) in water was evaluated with or without metabolic activation using *Escherichia coli* strain WP2 *uvr*A and the following *Salmonella typhimurium* strains: TA98, TA100, TA1535, and TA1537.[58] The positive controls without activation were: 2-(2-furyl)-3-(5-nitro-2-furyl)acrylamide (AF-2, for strains TA98, TA100, and WP2*uvr*A), 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 non-genotoxic. 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 *Escherichia coli* strains derived from the K12 subline.[59] Methyl-α-D-glucopyranoside is known to depress intracellular cyclic AMP (cAMP) levels more effectively than glucose. Stationary phase *Escherichia coli* k12 *trp* (amber) cells supplied (by conjugation) with the Muc^+ mutation-enhancing IncP plasmid pKM101 were exposed to 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.

CARCINOGENICITY

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

SUMMARY

The safety of methyl glucose polyethers and esters in cosmetics 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.

According to information supplied to the Food and Drug Administration (FDA) by industry as part of the Voluntary Cosmetic Registration Program (VCRP) in 2012, the following methyl glucose polyethers and esters are being used in cosmetic products:[15] 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 a survey of ingredient use concentrations provided by the Personal Care Products Council in 2012 indicate that, collectively, the ingredients mentioned above and an additional ingredient, methyl glucose sesquiisostearate, are being used at concentrations up to 15% in rinse-off and leave-on products. 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 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 are used in face/body powders: 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. 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, based on the high molecular weights associated with many of these compounds, they are expected to have a low potential for skin penetration. 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 h, the lungs and trachea were removed and assayed for unabsorbed radioactivity. The amount of test material absorbed was directly proportional to the concentration injected.

Acute oral toxicity data (rats) on methyl glucose polyethers and esters (trade name materials) suggest that these ingredients are relatively non-toxic, based on reported LD_{50} values of > 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 LD_{50} of > 12 g/kg was reported. Additional acute dermal toxicity data on this ingredient group were not available.

The antimicrobial activity of the following methyl glucose esters of medium to long chain fatty acids was studied using Zygosaccharomyces bailii Y-7254 (yeast strain) and *Lactobacillus fructivorans* B-4000 (bacterial strain): lauric (C_{12}), myristic (C_{14}), palmitic (C_{16}), stearic (C_{18}), and oleic ($C_{18:1}$) acids. These esters were evaluated at concentrations of 0.1, 0.5, and 1% in broth suspensions. Methyl glucose monoesters with lauric (C_{12}), or myristic acid (C_{14}) caused greater growth inhibition than those with longer chain fatty acids. The least inhibition was associated with methyl glucose oleate ($C_{18:1}$).

In ocular irritation tests involving rabbits, the following ingredients (all tradename materials) induced no ocular irritation to mild ocular irritation when tested undiluted: 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. Methyl glucose dioleate was also non-irritating 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%.

The following tests were performed using trade name materials. 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 non-irritants. Undiluted methyl glucose sesquistearate was classified as non-corrosive in one study 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 (concentration not stated) was classified as slightly irritating to the skin of rabbits. It was also classified as a non-sensitizer in a guinea pig maximization test; the test concentration was not stated.

A night cream containing 4% methyl glucose sesquistearate was well-tolerated (i.e., no erythema or inflammatory lesions) in a 4-week cosmetic use test. In another 4-week cosmetic use test, an exfoliant scrub containing 5.2% PEG-20 methyl glucose sesquistearate was classified as having good acceptability, i.e., no skin reactions/clinical signs that were related to product application. The following ingredients (trade name materials and 1 product) were classified as non-irritants and non-sensitizers in human repeated insult patch tests: methyl glucose dioleate (0.59% in body and hand cream), methyl glucose sesquistearate (up to100%), PPG-10 methyl glucose ether (up to100%), 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 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 repellant (main component of 1 ingredient = methyl glucose dioleate) induced contact dermatitis in 2 patients. Patch test results for the repellant were positive in the 2 patients, but negative in 10 control subjects. 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 subjects.

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 in the patient, but negative in 20 control subjects. 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).

PEG-120 methyl glucose dioleate and PEG-120 methyl glucose trioleate were not genotoxic in the Ames test (*Salmonella typhimurium* and *Escherichia coli* strains) at doses up to 5,000 µg/plate with or without metabolic activation. As a defined minimal medium supplement, methyl-α-D-glucopyranoside had antigenotoxic activity in stationary phase *Escherichia 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 methyl glucose polyethers and esters were not identified in the published literature.

DISCUSSION

The Panel noted the absence of repeated dose toxicity, reproductive and developmental toxicity, and carcinogenicity data from this safety assessment. Limited genotoxicity data and robust dermal irritation and sensitization data were available. After reviewing data on molecular weights, the Panel determined that there likely would be no significant skin penetration of these ingredients. Thus, potential systemic exposure is unlikely and repeated dose toxicity, reproductive and developmental toxicity, or carcinogenicity data were not necessary to evaluate the safety of this group of ingredients.

The Panel discussed the potential effect that methyl glucose would have on glucose metabolism, were these ingredients to be absorbed and metabolized. As previously noted, however, significant dermal penetration of these ingredients was considered unlikely. While there were no available metabolism data, the complete deesterification of these ingredients to produce methyl glucose was considered highly unlikely. Overall, therefore, any impact of dermal application of these ingredients on glucose metabolism would be very unlikely. The Panel also discussed the apparent uncertainty in the definitions of esters reviewed, relating to the extent of esterification. That is, whether or not the esters are mono-, di-, tri, tetra-, or mixtures remains unknown. Additional data to document the extent of esterification that would result from the process of manufacturing these esters would be useful.

The Panel discussed the issue of incidental inhalation exposure from aerosol and pump hair sprays, body and hand sprays, and face/body powders. 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/dermal toxicity, ocular or dermal irritation or sensitization, and genotoxicity. The Panel noted that 95% – 99% of droplets/particles produced in cosmetic aerosols would not be respirable to any appreciable amount. The potential for inhalation toxicity is not limited to respirable droplets/particles deposited in the lungs. In principle, Inhaled droplets/particles deposited in the nasopharyngeal and thoracic regions of the respiratory tract may cause toxic effects depending on their chemical and other properties. However, coupled with the small actual exposure in the breathing zone and the concentrations at which the ingredients are used, the available information indicates that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic effects. A detailed discussion and summary of the Panel's approach to evaluating incidental inhalation exposures to ingredients in cosmetic products is available at http://www.cir-safety.org/cir-findings.

Although there are data gaps in this report, the Panel determined that the relatedness of molecular structures, physicochemical properties, and functions and concentrations in cosmetics allow grouping these ingredients together and interpolating the available toxicological data to support the safety of the entire group.

CONCLUSION

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

Esters
methyl glucose caprylate/caprate*
methyl glucose dioleate
methyl glucose isostearate*
methyl glucose laurate*
methyl glucose sesquicaprylate/ sesquicaprate*
methyl glucose sesquicocoate*
methyl glucose sesquiisostearate
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

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

Table 1. Definitions and functions of the ingredients in this safety assessment.[1]

(The italicized text below represents additions made by CIR staff.)

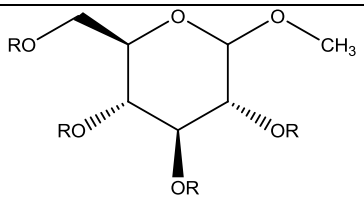
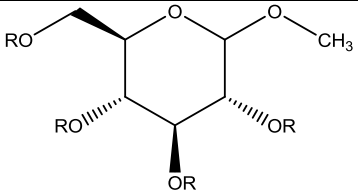
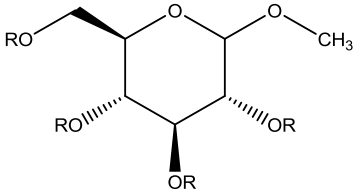
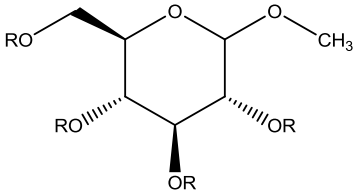
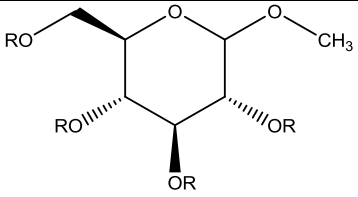
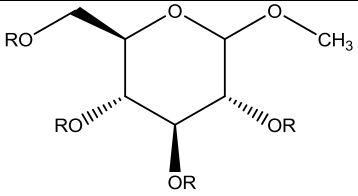
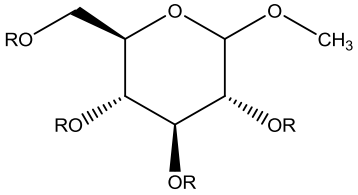
Ingredient CAS No.	Definition	Function
Esters		
Methyl Glucose Caprylate/Caprate [473802-96-9]	Methyl Glucose Caprylate/Caprate is the ester of methyl glucoside and a mixture of caprylic and capric acids.	Skin-Conditioning Agents - Emollient
Methyl Glucose Dioleate 122703-32-6 [82933-91-3]	Methyl Glucose Dioleate is the diester of a methyl glucoside and oleic acid.	Skin-Conditioning gents - 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.	
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 Sesquicocoate	Methyl Glucose Sesquicocoate is a mixture of mono- and diesters of a methyl glucoside and Coconut Acid.	Skin-Conditioning Agents - Emollient
Methyl Glucose Sesquiisostearate [138985-20-3]	Methyl Glucose Sesquiisostearate 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

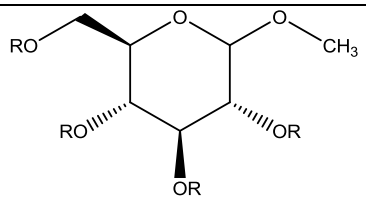
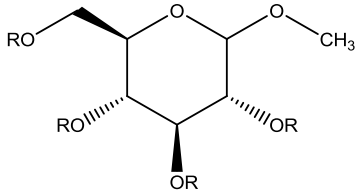
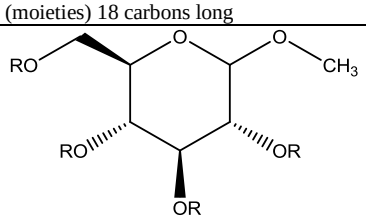
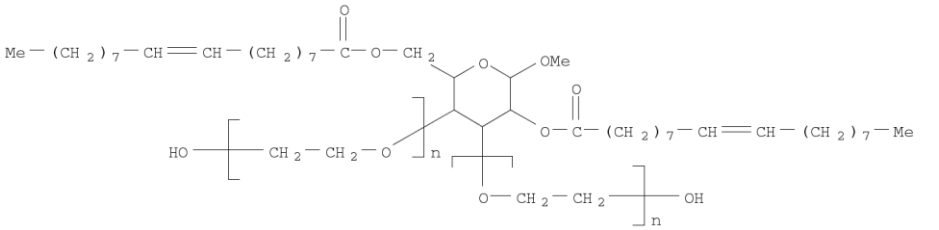
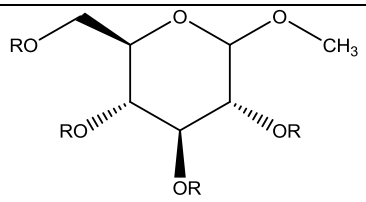
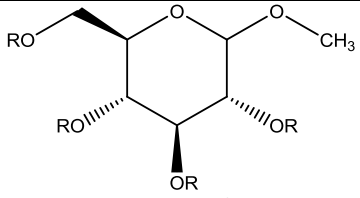
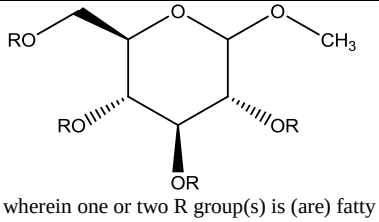
Table 1. Definitions and functions of the ingredients in this safety assessment.[1]

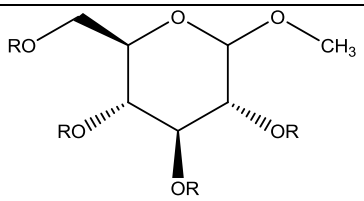
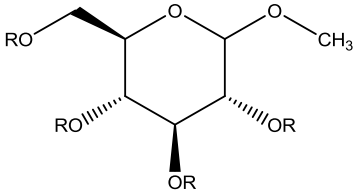
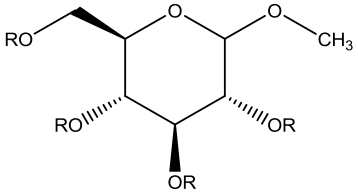
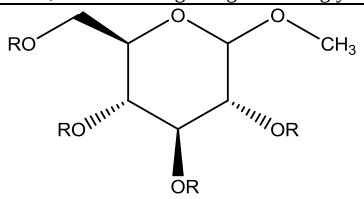
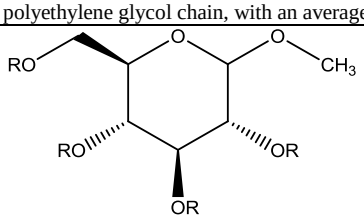
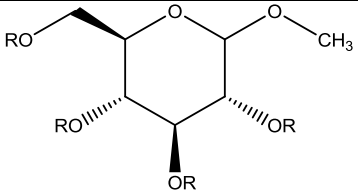
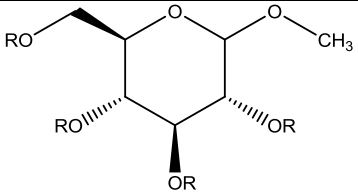
(The italicized text below represents additions made by CIR staff.)

Ingredient CAS No.	Definition	Function
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
Both Ester and Polyether		
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
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

Table 2. Idealized structures of the ingredients in this safety assessment.

Methyl Glucose Caprylate/Caprate	 wherein three R groups are hydrogen and one R group is a fatty acyl moiety 8 to 10 carbons long
Methyl Glucose Dioleate (m.w. = 722 daltons)[60]	 wherein two R groups are hydrogen and two R groups are Ω-9 unsaturated fatty acyl moieties18 carbons long
Methyl Glucose Isostearate	 wherein three R groups are hydrogen and one R group is a branched, fatty acyl moiety 18 carbons long
Methyl Glucose Laurate	 wherein three R groups are hydrogen and one R group is a fatty acyl moiety 12 carbons long
Methyl Glucose Sesquicaprylate/ Sesquicaprate	 wherein two or three R groups are hydrogen and the other R group(s) is (are) fatty acyl moiety (moieties) 8 to 10 carbons long
Methyl Glucose Sesquicocoate	 wherein two or three 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
Methyl Glucose Sesquiisostearate	 wherein two or three R groups are hydrogen and the other R group(s) is (are) branched, fatty acyl moiety (moieties) 18 carbons long

Methyl Glucose Sesquilaurate	 wherein two or three R groups are hydrogen and the other R group(s) is (are) fatty acyl moiety (moieties) 12 carbons long
Methyl Glucose Sesquioleate	 wherein two or three 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 (m.w. = 460 daltons; logKOW ≈ 7.09 [bioaccumulation not expected])[61]	 wherein two or three 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 file)[62] (m.w. = 6037 daltons)[63]	
PEG-20 Methyl Glucose Distearate	 wherein two R groups are fatty acyl moieties18 carbons long and two R groups are polyethylene glycol chains, with a combined average length of 20 glycol repeat units
PEG-80 Methyl Glucose Laurate	 wherein one R group is a fatty acyl moiety 12 carbons long and three R groups are polyethylene glycol chains, with a combined average length of 80 glycol repeat units
PEG-20 Methyl Glucose Sesquicaprylate/ Sesquicaprate	 wherein one or two R group(s) is (are) fatty acyl moiety (moieties) 8 to 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 one or two 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 (m.w. = 1265 daltons)[64]	 wherein one or two 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 three R group are fatty acyl moieties18 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 (m.w. = 6322 daltons)[65]	 wherein three 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
PPG-10 Methyl Glucose Ether (m.w. = 797 daltons)[66]	 wherein R is hydrogen or a polypropylene glycol chain, with an average length of 10 glycol repeat units
PPG-20 Methyl Glucose Ether (m.w. = 1300 daltons)[67]	 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

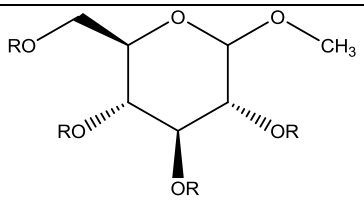
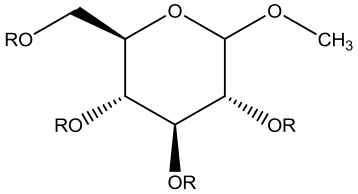
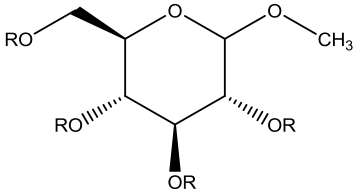
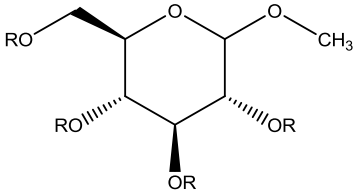
PPG-20 Methyl Glucose Ether Acetate	 wherein R is hydrogen, acetate, or a polypropylene glycol chain, with an average length of 20 glycol repeat units
PPG-20 Methyl Glucose Ether Distearate	 wherein two R groups fatty acyl moieties are 18 carbons long and the other R groups are hydrogen, or a polypropylene glycol chain, with an average length of 20 glycol repeat units
Methyl Gluceth-10 (m.w. = 634 daltons)[68]	 wherein R is hydrogen or a polyethylene glycol chain, with an average length of 10 glycol repeat units
Methyl Gluceth-20 (m.w. = 1074 daltons)[68]	 wherein R is hydrogen or a polyethylene glycol chain, with an average length of 20 glycol repeat units

Table 3. Physical Properties of Methyl Glucose Polyether and Ester Trade Name Materials[5]

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	GlucamTM E-10 Humectant **(TN6)**	Pale yellow medium viscosity liquid
Methyl gluceth-20	GlucamTM 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

Table 4. Properties From Technical Data Sheets on Methyl Glucose Polyether and Ester Trade Name Material[5]

Properties	TN1*	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		
Hydoxyl Value, mg/g	155	285	295	170	60	350-370	215	14-26		102		
Active Content											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 to 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		

*Full trade names for **TN#** abbreviations listed in Table 3; Charac. = characteristic

Table 5. Specifications For Methyl Glucose Polyether and Ester Trade Name Materials[5]

Specifications	TN1*	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	7 max.	6 max.
Active Content, % wt											37-43	68-72
Viscosity, mPa·s											5,000 max.	2,500-20,000
Melt Range, Class I, ˚C		48-55										
Turbidity, NTU Neat @ 25 ˚C												0-20
Cloud Point, ˚C										71-79		
Hydroxyl Value, mg/g	140-165		285-305	160-180	50-70	350-370	205-225	14-26		95-110		
Iodine Value	60-75		0-1	0-1		0-1		5 to 15	3 to 11	0-1		
Moisture, % weight	0-0.5	0.1	0-1	0-1	0-1	0-1				0-0.5		
Saponificafion Value, mg/g	145-160	125-140	0-1	0-1.5	58-72	0-1.5		14-26	9 to 20	40-50		
pH, aqueous solution						5.5-8.0		4.5-7.5	4.5-7.5	4.5-7.5	4.5-8.0	5.5-8.0
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 max.	< 2 ppm max.	< 2 ppm max.	< 2 ppm max.	< 2 ppm max.	< 2 ppm max.	< 2 ppm max.	< 2 ppm max.	< 2 ppm max.	< 2 ppm max.	< 2 ppm max.	< 2 ppm max.
Heavy Metals	< 20 ppm max.	< 20 ppm max.	< 20 ppm max.	< 20 ppm max.	< 20 ppm max.	< 20 ppm max.	< 20 ppm max.	< 20 ppm max.	< 20 ppm max.	< 20 ppm max.	< 20 ppm max.	< 20 ppm max.
Microbiological Count	TBC < 10/g	TBC < 10/g	TBC < 10/g	TBC < 10/g	TBC < 10/g	TBC < 10/g	TBC < 10/g	TBC < 10/g	TBC < 10/g	TBC < 10/g	TBC < 10/g	TBC < 10/g

*Full trade names for **TN#** abbreviations listed in Table 3

Table 6. Current Frequency and Concentration of Use According to Duration and Type of Exposure Provided in 2012.[15,16]

	MG Dioleate		**MG Sesquioleate**		**MG Sesquiisostearate**	
	# of Uses	Conc. (%)	# of Uses	Conc. (%)	# of Uses	Conc. (%)
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	12	0.2 to 0.6	1	NR	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	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					NR	NR
Leave-On	13	0.2 to 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	13	0.2 to 4	1	NR	NR	0.1
	MG Sesquistearate		**PPG-10 MG Ether**		**PPG-20 MG Ether**	
	# of Uses	Conc. (%)	# of Uses	Conc. (%)	# of Uses	Conc. (%)
Exposure Type						
Eye Area	29	0.3 to 2	1	NR	NR	0.5
Incidental Ingestion	14	1	NR	NR	NR	NR
Incidental Inhalation- Sprays	7	NR	2	NR	8	0.1 to 1
Incidental Inhalation- Powders	NR	0.5 to 4	NR	0.8	1	0.4
Dermal Contact	166	0.3 to 4	8	0.8	40	0.1 to 3
Deodorant (underarm)	NR	NR	NR	NR	5	0.1
Hair - Non-Coloring	2	0.5 to 2	11	2	14	NR
Hair-Coloring	NR	NR	1	0.5	NR	NR
Nail	NR	0.8	NR	NR	1	NR
Mucous Membrane	18	0.4 to 1	4	NR	2	NR
Baby Products	NR	NR	NR	NR	NR	NR
Duration of Use						
Leave-On	159	0.3 to 4	10	0.8 to 2	34	0.1 to 3
Rinse off	25	0.4 to 4	10	0.5	21	0.1 to 0.5
Diluted for (bath) Use	NR	NR	NR	NR	NR	NR
Totals/Conc. Range	184	0.3 to 4	20	0.5 to 2	55	0.1 to 3
	PPG-20 MG Ether Distearate		**Methyl Gluceth-10**		**Methyl Gluceth-20**	
	# of Uses	Conc. (%)	# of Uses	Conc. (%)	# of Uses	Conc. (%)
Exposure Type						
Eye Area	NR	NR	2	1 to 5	14	2 to 6
Incidental Ingestion	NR	NR	NR	NR	NR	NR
Incidental Inhalation- Sprays	NR	NR	1	1	11	0.5 to 2
Incidental Inhalation- Powders	NR	NR	NR	0.02 to 15	NR	1 to 10
Dermal Contact	2	4	60	0.02 to 15	358	0.3 to 15
Deodorant (underarm)	NR	NR	NR	NR	3	NR
Hair - Non-Coloring	NR	NR	9	NR	39	0.2 to 5
Hair-Coloring	NR	NR	NR	0.0003 to 11	NR	NR
Nail	NR	NR	NR	NR	3	2 to 5
Mucous Membrane	NR	NR	6	0.02	185	0.3 to 6
Baby Products	NR	NR	NR	NR	NR	NR
Duration of Use						
Leave-On	2	4	57	0.02 to 15	149	0.2 to 10
Rinse off	NR	NR	12	0.0003 to 15	244	0.3 to 15
Diluted for (bath) Use	NR	NR	NR	NR	7	1
Totals/Conc. Range	2	4	69	0.0003 to 15	400	0.2 to 15

Table 6. Current Frequency and Concentration of Use According to Duration and Type of Exposure Provided in 2012[16]

	PEG-120 MG Dioleate		PEG-20 MG Distearate		PEG-20 MG Sesquistearate	
	# of Uses	Conc. (%)	# of Uses	Conc. (%)	# of Uses	Conc. (%)
Exposure Type						
Eye Area	4	6	NR	NR	19	0.1 to 1
Incidental Ingestion	NR	NR	NR	0.05	NR	NR
Incidental Inhalation- Sprays	2	NR	NR	NR	2	0.9
Incidental Inhalation- Powders	NR	0.4 to 4	NR	NR	NR	1 to 10
Dermal Contact	356	0.2 to 6	2	NR	120	0.1 to 10
Deodorant (underarm)	1	NR	NR	NR	NR	NR
Hair - Non-Coloring	74	0.1 to 2	1	NR	2	0.9 to 3
Hair-Coloring	NR	NR	NR	NR	1	0.5
Nail	NR	NR	NR	NR	1	1 to 3
Mucous Membrane	276	0.2 to 4	NR	0.05	19	2 to 4
Baby Products	4	1	NR	NR	NR	NR
Duration of Use						
Leave-On	12	0.4 to 4	3	0.05	86	0.1 to 10
Rinse off	402	0.1 to 6	NR	NR	40	0.5 to 6
Diluted for (bath) Use	19	0.8 to 3	NR	NR	NR	2
Totals/Conc. Range	433	0.1 to 6	3	0.05	126	0.1 to 10
	PEG-120 MG Trioleate					
	# of Uses	Conc. (%)				
Exposure Type						
Eye Area	NR	NR				
Incidental Ingestion	NR	NR				
Incidental Inhalation- Sprays	NR	0.1				
Incidental Inhalation- Powders	NR	0.1 to 0.5				
Dermal Contact	3	0.1 to 0.5				
Deodorant (underarm)	NR	NR				
Hair - Non-Coloring	4	NR				
Hair-Coloring	NR	NR				
Nail	NR	NR				
Mucous Membrane	1	0.1 to 0.5				
Baby Products	NR	NR				
Duration of Use						
Leave-On	NR	0.1 to 0.5				
Rinse off	7	0.1 to 0.5				
Diluted for (bath) Use	NR	NR				
Totals/Conc. Range	7	0.1 to 0.5				

MG = Methyl Glucose; NR = Not Reported; Totals = Rinse-off + Leave-on Product Uses.

Note: Because 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.

Table 7. Skin Irritation and Sensitization Studies

Test Substance	Animals/Subjects	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 2.5cm^2 occlusive patch	Application to sites (abraded or intact) on opposite sides of vertebral column for 24 h	Non-irritant (primary irritation index [PII] = 2.10).[25]
Methyl Glucose Sesquistearate (Glucate® SS, undiluted)	6 New Zealand albino rabbits	0.5 ml under 1" x 1" occlusive patch	Application to sites (abraded or intact) for 4 h	Not corrosive (PII = 0).[26]
Methyl Glucose Sesquistearate (Glucate® SS, undiluted)	6 New Zealand albino rabbits	0.5 ml under 1" x 1" occlusive patch	Application to sites (abraded or intact) for 24 h	Potential for mild irritation (PII = 1.13).[26]
PPG-10 Methyl Glucose Ether (Glucam™ P-10 Humectant, undiluted)	6 rabbits (strain not stated)	0.5 ml under 1" x 1" occlusive patch	Application to sites (abraded or intact) for 24 h	Non-irritant.[27]
PPG-20 Methyl Glucose Ether (Glucam™ P-20 Humectant, undiluted)	6 rabbits (strain not stated)	0.5 ml under 1" x 1" occlusive patch	Application to sites (abraded or intact) for 24 h	Non-irritant.[28]
PPG-20 Methyl Glucose Ether Distearate (Glucam™ P-20 Distearate Emollient, undiluted)	Rabbits (number and strain not stated)	Not stated	Not stated	Non-irritant.[29]
PEG-120 Methyl Glucose Dioleate (Glucam™ DOE-120 Thickener, undiluted)	Rabbits (number and strain not stated)	Not stated	Not stated	PII = 0.45.[30]
PEG-20 Methyl Glucose Sesquistearate (Glucamate® SSE-20, undiluted)	6 New Zealand albino rabbits	0.5 ml under 1" x 1" occlusive patch	Application to sites (abraded or intact) for 4 h	Not corrosive (PII = 0).[31]
PEG-20 Methyl Glucose Sesquistearate (Glucamate® SSE-20, undiluted)	6 New Zealand albino rabbits	0.5 ml under 1" x 1" occlusive patch	Application to sites (abraded or intact) for 24 h	Potential for mild irritation (PII = 1.08).[31]
PEG-120 Methyl Glucose Trioleate (and) propylene glycol (and) water (Glucamate™ LT Thickener, concentration not stated)	Rabbits (number and strain not stated)	0.5 ml applied under semi-occlusive conditions	Application period not stated	Slightly irritating (PII = 0.3).[32]
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	Non-sensitizer (sensitization index = 0).[32]

Table 7. Skin Irritation and Sensitization Studies

Test Substance	Animals/Subjects	Doses/Concentrations Tested	Procedure	Results
		Predictive Tests		
Methyl Glcose Dioleate (0.59% in body and hand cream)	111 healthy subjects initially. 109 completed induction phase; 101 completed challenge phase	150 µl under 2 cm x 2 cm partially occlusive patch	HRIPT; 24 h induction and challenge applications	Non-irritant and non-sensitizer.[37]
Methyl Glucose Sesquistearate (Glucate® SS, up to 100%)	55 healthy subjects	Test concentrations = 20% aqueous (12 subjects), 40% aqueous (11 subjects), 60% aqueous (11 subjects), 80% aqueous (10 subjects), and 100% (11 subjects). 0.1 ml/cm^2 under occlusive patch.	HRIPT; 24 h induction and challenge applications. Due to absence of skin irritation, undiluted material applied from 5th induction application through challenge in all subjects	Non-irritant and non-sensitizer.[38]
Methyl Glucose Sesquistearate (4% in night cream)	51 subjects	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 (i.e., erythema, dryness, scaling, roughness, or retentive and inflammatory lesions).[39]
Methyl Glucose Sesquistearate (4% in night cream)	110 volunteers initially. 103 completed induction and challenge phases	15 µl on filter paper disk in Finn chamber	HRIPT: 48 h induction applications on Mondays and Wednesdays; 72 h induction application on Fridays; 48 h challenge application	Non-irritant and non-sensitizer.[40]
PPG-10 Methyl Glucose Ether (Glucam^{TM} P-10, up to 100%)	53 healthy subjects	Test concentrations = 20% aqueous (12 subjects), 40% aqueous (10 subjects), 60% aqueous (11 subjects), 80% aqueous (10 subjects), and 100% (10 subjects). 0.1 ml/cm^2 under occlusive patch.	HRIPT; 24 h induction and challenge applications. Due to absence of skin irritation, undiluted material applied from 5th induction application through challenge in all subjects	Non-irritant and non-sensitizer.[42]
PPG-10 Methyl Glucose Ether (0.8% in a face cream)	54 subjects	20 µl on filter paper disk in Finn chamber (8 mm cup)	HRIPT: 48 h induction applications on Mondays and Wednesdays; 72 h induction application on Fridays; 48 h challenge application	Non-irritant and non-sensitizer.[43]
PPG-20 Methyl Glucose Ether Glucam^{TM} P-20, up to 100%)	55 (5 groups of 11) healthy subjects initially; 53 completed study. 2 withdrew prior to study initiation (affected groups not stated)	Test concentrations = 20% aqueous (~11 subjects), 40% aqueous (~11 subjects), 60% aqueous (~11 subjects), 80% aqueous (~11 subjects), and 100% (~11 subjects). 0.1 ml/cm^2 under occlusive patch.	HRIPT; 24 h induction and challenge applications. Due to absence of skin irritation, undiluted material applied from 5th induction application through challenge in all subjects	Non-irritant and non-sensitizer.[44]
Methyl Gluceth-10 (Glucam E-10, up to 100%)	53 healthy subjects	Test concentrations = 20% aqueous (10 subjects), 40% aqueous (12 subjects), 60% aqueous (10 subjects), 80% aqueous (10 subjects), and 100% (11 subjects). 0.1 ml/cm^2 under occlusive patch.	HRIPT; 24 h induction and challenge applications. Due to absence of skin irritation, undiluted material applied from 5th induction application through challenge in all subjects	Non-irritant and non-sensitizer.[45]

Table 7. Skin Irritation and Sensitization Studies

Test Substance	Animals/Subjects	Doses/Concentrations Tested	Procedure	Results
Methyl Gluceth-20 (Glucam E-20, up to 100%)	56 healthy subjects	Test concentrations = 20% aqueous (10 subjects), 40% aqueous (12 subjects), 60% aqueous (12 subjects), 80% aqueous (13 subjects), and 100% (9 subjects). 0.1 ml/cm^2 under occlusive patch.	HRIPT; 24 h induction and challenge applications. Due to absence of skin irritation, undiluted material applied from 5th induction application through challenge in all subjects	Non-irritant and non-sensitizer.[46]
PEG-120 Methyl Glucose Dioleate (25% aqueous)	51 subjects	0.15 ml on occlusive patch (1.5" x 2")	HRIPT. 24 h induction and challenge applications.	Non-irritant and non-sensitizer.[48]
PEG-20 Methyl Glucose Sesquistearate (Glucamate® SSE-20, up to 100%)	55 healthy subjects	Test concentrations = 20% aqueous (11 subjects), 40% aqueous (10 subjects), 60% aqueous (11 subjects), 80% aqueous (11 subjects), and 100% (12 subjects). 0.1 ml/cm^2 under occlusive patch.	HRIPT; 24 h induction and challenge applications. Due to absence of skin irritation, undiluted material applied from 5th induction application through challenge in all subjects	Classified as skin fatiguing agent due to skin irritation in 3 subjects tested at 100% concentration; not a primary skin irritant. Non-sensitizer.[49]
PEG-20 Methyl Glucose Sesquistearate (5.2% in exfoliant scrub)	42 healthy subjects	Not stated	In use test, application to face twice daily for 28 days.	No skin reactions/clinical signs related to product application.[50]
PEG-20 Methyl Glucose Sesquistearate (5.2% in exfoliant scrub). Product diluted to 10% aqueous (effective ingredient concentration = 0.52%)	54 healthy subjects	0.2 ml applied, under occlusive patch, to 50 mm^2 area.	HRIPT; 48 ± 4 h application (induction days 1 through 8) and 72 ± 4 h application (induction days 3, 6, and 9); 48 ± 4 h challenge application	Non-irritant (mean irritation index = 0.010) and non-sensitizer.[69]
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.[41]
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.[47]

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