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Safety Assessment of Monoglyceryl Monoesters as Used in Cosmetics

Monice M. Fiume*, Wilma F. Bergfeld, Donald V. Belsito**, Ronald A. Hill**, Curtis D. Klaassen**, Daniel C. Liebler**, James G. Marks Jr**, Ronald C. Shank**, Thomas J. Slaga**, Paul W. Snyder**, Lillian J. Gill***, and Bart Heldreth†**

Abstract

The Expert Panel for Cosmetic Ingredient Safety (Panel) assessed the safety of 44 monoglyceryl monoesters that are structurally constituted as the esterification products of glycerin and carboxylic acids (the majority of which are fatty acids); 36 of these monoesters were previously reviewed by the Panel, and 8 are reviewed herein for the first time. Most of the monoglyceryl monoesters have several reported functions in cosmetics, but the most common function among the ingredients is skin conditioning agent; a few are reported to function only as surfactant–emulsifying agents. The Panel reviewed relevant new data, including frequency and concentration of use and considered the data from previous Cosmetic Ingredient Review reports. The Panel concluded that these ingredients are safe in cosmetics in the present practices of use and concentration described in this safety assessment.

Keywords

cosmetics, safety, monoglyceryl monoesters

Introduction

In 1982, the Expert Panel for Cosmetic Ingredient Safety (Panel) published the Final Report on the Safety Assessment of Glyceryl Stearate and Glyceryl Stearate SE; based on the data presented in that assessment, that Panel concluded that Glyceryl Stearate and Glyceryl Stearate SE are safe for topical application to humans.[1] In accordance with its Procedures, Panel evaluates the conclusions of previously issued reports every 15 years; therefore, a rereview was initiated.

Numerous additional monoglyceryl monoesters have also been previously reviewed by the Panel. These monoglyceryl monoesters are structurally constituted of the esterification products of glycerin and carboxylic acids, the vast majority of which are fatty acids. Additionally, according to the *International Cosmetic Ingredient Dictionary and Handbook* (*Dictionary*), almost all of these ingredients are reported to function as skin conditioning agents.[2] Therefore, because of the structural and functional similarities, the following previously reviewed monoglyceryl monoesters are also included in this safety assessment:

- Glyceryl Oleate—reviewed in 1986 and found to be safe as a cosmetic ingredient in the present practices of use and concentration[3]; a rereview was conducted in 2004, and the conclusion was reaffirmed.[4]
- Glyceryl Ricinoleate—first reviewed in 1988, and at that time the Panel concluded, the data were insufficient to determine safety[5]; in 2007, it was reviewed as part of a larger group of ingredients and found safe as a cosmetic ingredient in the practices of use and concentrations.[6]
- Glyceryl Ricinoleate SE—also reviewed as part of a larger group of ingredients in 2007 and found safe as a cosmetic ingredient in the practices of use and concentrations.[6]
- Glyceryl Monoesters—in 2004, the following glyceryl monoesters were determined to be safe as cosmetic ingredients in the present practices of use and concentration and are included in this report[7]:

Glyceryl Adipate
Glyceryl Arachidate
Glyceryl Behenate
Glyceryl Caprate
Glyceryl Caprylate
Glyceryl Caprylate/Caprate
Glyceryl Citrate/Lactate/Linoleate/Oleate

* Cosmetic Ingredient Review Senior Director
** Expert Panel for Cosmetic Ingredient Safety Member
*** Cosmetic Ingredient Review Former Director
† Cosmetic Ingredient Review Executive Director

Corresponding Author:
Bart Heldreth, Cosmetic Ingredient Review Executive Director, 1620 L Street, NW, Suite 1200, Washington, DC 20036, USA.
Email: cirinfo@cir-safety.org

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Glyceryl Cocoate
Glyceryl Erucate
Glyceryl Hydrogenated Rosinate
Glyceryl Hydrogenated Soyate
Glyceryl Hydroxystearate
Glyceryl Isopalmitate
Glyceryl Isostearate
Glyceryl Isotridecanoate/Stearate/Adipate
Glyceryl Lanolate
Glyceryl Laurate
Glyceryl Laurate SE
Glyceryl Laurate/Oleate
Glyceryl Linoleate
Glyceryl Linolenate
Glyceryl Montanate
Glyceryl Oleate SE
Glyceryl Oleate/Elaidate
Glyceryl Palmitate
Glyceryl Palmitate/Stearate
Glyceryl Palmitoleate
Glyceryl Pentadecanoate
Glyceryl Rosinate
Glyceryl Tallowate
Glyceryl Undecylenate

Several ingredients originally included in the 2004 safety assessment of glyceryl monoesters (ie, glyceryl alginate, glyceryl arachidonate, glyceryl collagenate, Glyceryl Isostearate/myristate, Glyceryl Isostearates, glyceryl myristate, glyceryl polyacrylate, glyceryl sesquioleate, glyceryl sorbitol oleate/hydroxystearate, glyceryl stearate/acetate, glyceryl thiodipropionate, and glyceryl stearate/maleate) are not included in this rereview for various reasons. The data were insufficient to support the safety of glyceryl arachidonate, and Panel does not routinely rereview ingredients that had insufficient data; that conclusion has since been reclassified as Use Not Supported. Glyceryl alginate, Glyceryl Isostearate/myristate, and glyceryl myristate are included in other Cosmetic Ingredient Review (CIR) safety assessments and hence not included here. Glyceryl collagenate, Glyceryl Isostearates, glyceryl polyacrylate, glyceryl sesquioleate, glyceryl sorbitol oleate/hydroxystearate, glyceryl stearate/acetate, and glyceryl thioglycolate are not appropriate for inclusion in this group and will be rereviewed at another time. And, glyceryl stearate/maleate is not a cosmetic ingredient but was mistakenly included in the *Dictionary* at the time of the 2004 assessment, leading to its inclusion in that report.

Furthermore, there are several monoglyceryl monoesters included in the *Dictionary* that have not yet been reviewed. These 8 ingredients are included in this safety assessment:

Glyceryl Acetate
Glyceryl Cocoate/Citrate/Lactate
Glyceryl Ethylhexanoate
Glyceryl Ethylhexanoate/Stearate/Adipate
Glyceryl Heptanoate
Glyceryl Hydrogenated Rapeseedate
Glyceryl Olivate
Glyceryl Stearate/Malate

An alphabetical listing of the 44 monoglyceryl monoesters included in this safety assessment is provided in Table 1, and these ingredients are defined in Table 2.

Excerpts from the summaries of the reports on the previously reviewed monoglyceryl monoesters are disseminated throughout the text of this rereview document, as appropriate. However, this information is not included in the tables or the summary section; only new data are included there.

As stated earlier, these monoesters all share a glycerin core. The Panel evaluated the safety of glycerin as used in cosmetics in 2014, concluding that glycerin is safe in cosmetics in the present practices of use and concentration described in the safety assessment.[8] Many of the acid components and related glyceryl esters of these monoesters have also been reviewed by the panel. Listings of those that have been reviewed, and the associated conclusions, are provided in Table 3. (The full reports can be found on the CIR website: https://www.cir-safety.org/ingredients).

Finally, much of the new data included in this safety assessment was found on the European Chemicals Agency (ECHA) website.[22-25] Please note that the ECHA website provides summaries of information generated by industry, and it is those summary data that are reported in this safety assessment when ECHA is cited.

Chemistry

Definition and Structure

The monoglyceryl monoesters are structurally constituted of the esterification products of one equivalent of glycerin and one equivalent of a carboxylic acid, usually a fatty acid (Figure 1). These ingredients vary only in the identity of those acids (eg, variable length, branching, and unsaturation of those acid residues). The definitions and idealized structures of the monoglyceryl monoesters are provided in Table 2.

Chemical Properties

Available molecular weights and log *P* values are provided in Table 4.[7,26] Please refer to the original reports on the previously reviewed monoglyceryl monoesters for additional property information.

Method of Manufacture

Glyceryl Oleate SE. In a pharmaceutical application, the self-emulsifying grade of Glyceryl Oleate can be formulated by mixing Glyceryl Oleate with 5% of an anionic surfactant.[27] According to the *Dictionary*, the cosmetic ingredient Glyceryl Oleate SE is a self-emulsifying grade of Glyceryl Oleate that contains some sodium and/or potassium oleate.[2]

Glyceryl Monoesters—general. Industrial monoglycerides can be prepared by the direct esterification of glycerol with a fatty acid, yielding mixtures of mono-, di-, and tri- glycerides, depending on the molar ratio of the reactants.[7]

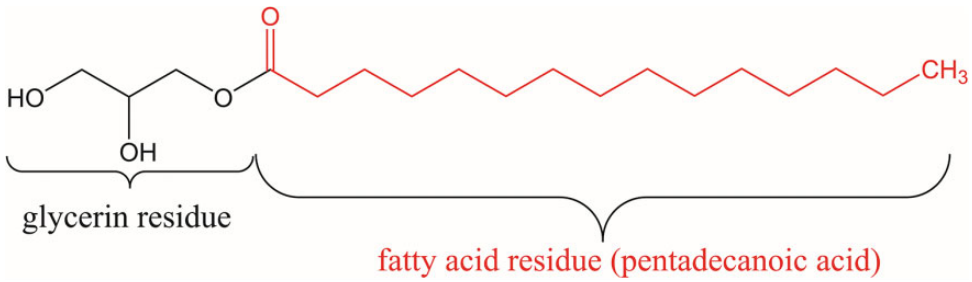

Figure 1. Glyceryl Pentadecanoate, a monoglyceryl monoester.

Glyceryl Oleate. Glyceryl Oleate is manufactured by the partial hydrolysis of corresponding tri- and diglycerides, by esterification of glycerol with oleic acid, or by glycerolysis of common fats and oils.[3] The glycerolysis of fats and oils, a transesterification reaction, is a commercial method for the preparation of monoglycerides.

Natural Occurrence

Glyceryl Acetate may be a natural component of tobacco or a product of pyrolysis (in tobacco smoke).[28]

Impurities/Constituents

Glyceryl Monoesters—general. According to one source, glyceryl monoesters are not pure monoesters but are mostly mixtures with mono-, di-, and tri-esters in a ratio of approximately 4:4:2, respectively.[7] Another source indicates that the guaranteed purity of commercial and conventional monoglyceride (glyceryl monoester) is a minimum of 90%, meaning that impurities account for a maximum of 10% of the composition. The results of impurities analyses of 14 glyceryl monoesters indicated that only one, glyceryl palmitate/ stearate, contained (mono)glycerol diester at a concentration of 1.2%.[7]

Glyceryl Stearate and Glyceryl Stearate SE. Glyceryl Stearate and Glyceryl Stearate SE may contain mono-, di-, and tri-glyceride impurities and fatty acid impurities.[1]

Ultraviolet Absorption

Glyceryl Ricinoleate. Glyceryl Ricinoleate absorbs ultraviolet light (UV), with a maximum absorbance at 270 nm.[6]

Use

Cosmetic

The safety of the cosmetic ingredients included in this assessment is evaluated on the basis of the expected use in cosmetics in accordance with data received from the US Food and Drug Administration (FDA) and from the cosmetics industry. The data received from the FDA are those collected from manufacturers on the use of individual ingredients in cosmetics by product category in its Voluntary Cosmetic Registration Program (VCRP). Data from the cosmetic industry are submitted in response to a survey of maximum use concentration by product category conducted by the Personal Care Products Council (Council).

Based on information from the VCRP and that received from the Council, 25 of the 44 ingredients included in this safety assessment are currently in use.[29-31] Of those, Glyceryl Stearate has the highest frequency of use; according to the 2015 VCRP data, Glyceryl Stearate is reported to be used in 5153 formulations, and 4229 of those uses are in leave-on formulations. Glyceryl Stearate SE has the next highest frequency of use, with 1420 reported uses[29] (Table 5).

The results of the concentration of use survey conducted by the Council in 2014 indicate that for the monoglyceryl monoesters in this group, Glyceryl Stearate has the highest maximum use concentration in leave-on formulations (17% in a deodorant), and Glyceryl Ricinoleate has the second highest maximum use concentration in leave-on formulations (15.2% in lipstick).[30,31] Overall, Glyceryl Rosinate is reported to have the greatest maximum reported used concentration, that is, 96% in a depilatory (Table 5).

Most of the in-use ingredients have been reviewed previously by the Panel. For the majority of these ingredients, the frequency of use has increased, but the concentration of use has remained the same or decreased. For example, in 1976 Glyceryl Stearate was reported to be used in 1371 cosmetic formulations at concentrations up to 50%[1]; currently, it is reported to be used in 5153 formulations at a maximum concentration of 18.9%. Additionally, for those ingredients that now have a higher concentration of use than what was reported historically that increase has been relatively small. However, Glyceryl Rosinate and Glyceryl Hydrogenated Rosinate are exceptions. The maximum concentration of use of Glyceryl Rosinate has increased from 12% in 1999 to 96% in 2014.[7] The primary reason for this increase is that Glyceryl Rosinate is now reported to be used at maximum concentrations of 72% to 96% in depilatories; yet, the next greatest concentration of use of Glyceryl Rosinate is 8% in mascara, which is a decrease from the 12% concentration of use in mascara reported in 1999. Glyceryl Hydrogenated Rosinate was not reported to be used in 1998, but now has 29 uses, with maximum use concentrations of 10% in leave-on products (lipstick) and 76.8% in rinse-off products (depilatories).

The 19 monoglyceryl monoester ingredients not currently reported to be in use, according to the VCRP and industry survey, are listed in Table 6.

Several of the monoglyceryl monoesters are used in products that can be incidentally ingested, used near the eye, or come in contact with mucous membranes. Glyceryl Ricinoleate is used at 11.6% in eyeliner and at 15.2% in lipstick (potential ingestion and mucous membrane exposure). (In the 2007 review of Glyceryl Ricinoleate, the use in lipstick was known, but a concentration of use was not reported.[6])

Additionally, some of the monoglyceryl monoesters are used in cosmetic sprays and could be incidentally inhaled; for example, Glyceryl Stearate is reported to be used at a maximum concentration of 14% in perfumes. 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 <10 μm compared with pump sprays.[32,33] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and thoracic regions of the respiratory tract and would not be respirable (ie, they would not enter the lungs) to any appreciable amount.[34,35] Some of the ingredients are used in spray deodorants; for example, glyceryl cocoate is used at a maximum concentration of 2% in a pump spray deodorant formulation. There is some evidence indicating that deodorant spray products can release substantially larger fractions of particulates having aerodynamic equivalent diameters in the range considered to be respirable.[34] However, the information is not sufficient to determine whether significantly greater lung exposures result from the use of deodorant sprays, compared to other cosmetic sprays. All of the monoglyceryl monoesters named in the report are not restricted from use in any way under the rules governing cosmetic products in the European Union.[36]

Non-Cosmetic

According to the US FDA, many of the monoglyceryl monoesters are direct food substances affirmed as generally recognized as safe (GRAS) for human and/or animal use, are permitted as direct food additives, or are permitted as indirect food additives. The food additive status of the monoglyceryl monoesters is provided in Table 7.

Glyceryl Acetate. Glyceryl Acetate is used as a gelatinizing agent for explosives, in leather tanning, and as a solvent for basic dyes.[28] It may be an additive for 1 or more types of tobacco products.

Glyceryl Oleate. Glyceryl Oleate has numerous applications in the pharmaceutical field.[27] Examples of these applications include emulsifier, solubilizer, absorption enhancer, oral drug delivery system, and vaginal drug delivery system.

Glyceryl Oleate can be used as a prior-sanctioned food ingredient and as a direct and indirect food additive. The pharmaceutical industry uses Glyceryl Oleate as an inert carrier compound and to enhance intestinal drug absorption.

Glyceryl Ricinoleate. Glyceryl Ricinoleate is listed by the FDA as an inactive ingredient in drug preparations.[5]

Glyceryl Stearate. Glyceryl Stearate is widely used in foods as a surfactant, emulsifier, and thickener. Glyceryl Stearate is an anti-scalant and dough conditioner in breads and is also used in pharmaceutical bases. Glyceryl Stearate has been granted regulatory status (by the FDA) as GRAS ingredient, an indirect food additive, a direct food additive, and as an over-the-counter substance.[1]

Toxicokinetics

Absorption, Distribution, Metabolism, and Excretion

Oral

Glyceryl Rosinate. Four groups of Fischer 344 rats were orally administered glycerol ester of wood rosin; the labeled compound was prepared using 1,3-[^{14}C] glycerol.[25] One group of 8 females was fed a diet containing 14000 ppm unlabeled ester for 18 hours, and 2 groups of 8 males were fed a diet containing 14000 ppm unlabeled ester for 20 hours or 10 days, respectively; 5 rats from each of the 3 groups was administered a single dose of 200 mg/kg bw [^{14}C]-glycerol ester of wood rosin by gavage after completion of dietary administration. The animals were then placed in metabolism cages, and expired carbon dioxide, urine, and feces were collected from each animal at 0 to 12 hours, 12 to 24 hours, and subsequent 24-hour intervals through 120 hours after dosing.

Less than 1% (males) to 2% (females) of the administered radioactivity was recovered in either expired carbon dioxide, urine, or the cage rinses with 120 hours of administration; the majority of the radioactivity was excreted in the feces. Small traces of radioactivity were detectable in the carcasses; this trace material was most likely residual radioactivity in the gastrointestinal tract. No metabolites were specifically identified; however, analysis of fecal extracts following dosing indicate that little hydrolysis occurred, and results were similar with 1-day and 10-day dietary administration.

In the fourth group, jugular vein cannulas were implanted in 9 male rats and the following day, 6 of these rats were also implanted with biliary cannulas. The 6 rats implanted with 2 cannulas were then dosed by gavage with 200 mg/kg bw [^{14}C] glycerol ester of wood rosin. Excreted bile was collected continuously, and samples were obtained at 4, 8, 12, and 24 hours after dosing, and blood samples were obtained from the jugular cannula at the same time intervals. The animals were killed 24 hours after dosing. Low levels of radioactivity were absorbed by the rats following dosing, and the radioactive species excreted in bile appeared to be a hydrolyzed product of the administered test substance; no intact test substance was present. Radioactivity was excreted in bile within 4 hours after dosing and was detectable in all samples collected for 24 hours post dose. The total amount of radioactivity excreted in bile during the 24-hour collection period ranged from 1.6% to 2.9% of the dose. Radioactivity content in the liver only accounted for 0.1% to 0.2% of the administered dose.

Glyceryl Monoesters—general. Lyceryl monoesters (monoglycerides) are metabolized to free fatty acids and glycerol, both of which are available for the resynthesis of triglycerides.[7]

Glyceryl Ricinoleate. Upon ingestion, Glyceryl Ricinoleate is digested and absorbed, and following emulsification in the small intestine and hydrolysis of the ester bond, the monoglyceride moieties are absorbed into the intestinal mucosa by passive diffusion.[5]

Penetration Enhancement

Monoglyceryl monoesters can act as penetration enhancers. Several studies demonstrating this behavior are summarized in Table 8.[37-41]

Glyceryl Laurate

Glyceryl Laurate enhanced the penetration of drugs as shown in animal in vitro models using cadaverous skin and hairless rat skin.[7]

Toxicological studies

Single Dose (Acute) Toxicity

Single dose (acute) toxicity studies are summarized in Table 9.

The dermal median lethal dose (LD_{50}) of Glyceryl Rosinate is >10 g/kg bw in rabbits in a 24-hour patch test.[25] In oral studies, LD_{50} values were reported to be >2 g/kg Glyceryl Behenate, >2 g/kg Glyceryl Hydrogenated Rosin, >5 g/kg Glyceryl Stearate, and >10 g/kg Glyceryl Rosinate.[22,23,25]

Dermal

Glyceryl Citrate/Lactate/Linoleate/Oleate. In an acute dermal toxicity study in rats, 2000 mg/kg Glyceryl Citrate/Lactate/Linoleate/Oleate did not induce toxicity in rats that received a single oral dose of 2000 mg/kg.[7]

Oral

Glyceryl Citrate/Lactate/Linoleate/Oleate. Glyceryl Citrate/Lactate/Linoleate/Oleate did not induce toxicity in rats that received a single oral dose of 2000 mg/kg.[7]

Glyceryl Isostearate. Glyceryl Isostearate did not induce toxicity in rats that received a single oral dose of 2000 mg/kg.[7]

Glyceryl Laurate. An LD_{50} of >20000 mg/kg was reported for rats dosed orally with Glyceryl Laurate.[7]

Glyceryl Oleate. Oral administration of a single 13 mL/kg dose of a sunscreen formulation containing 5% Glyceryl Oleate to rats produced no signs of toxicity and no lethality.[3]

Glyceryl Ricinoleate. Acute oral toxicity tests indicated that Glyceryl Ricinoleate has an LD_{50} greater than 25.0 mL/kg in mice and that products containing 5.6% Glyceryl Ricinoleate were not toxic when ingested.[5]

Glyceryl Rosinate. Undiluted, purified ester gum-2-octyldodecyl myristate (contains 50% Glyceryl Rosinate and 50% octyldodecyl myristate) was not toxic (LD_{50} >5 g/kg) when administered orally to fasted Wistar albino rats (5 males, 5 females).[7]

Glyceryl Stearate and Glyceryl Stearate SE. In acute oral toxicity studies in rats, Glyceryl Stearate and Glyceryl Stearate SE were nontoxic or mildly toxic.[1]

Repeated Dose Toxicity

Repeated dose toxicity studies are summarized in Table 10.

In a 90-day dietary study, the no-observable adverse effect level (NOAEL) for Glyceryl Hydrogenated Rosinate in rats was 10000 ppm. For Glyceryl Rosinate, the NOAEL for rats was 10000 ppm in one 90-day dietary study, and 2500 mg/kg bw/d in another. In a 28-day dietary study of glycerides, C8-18 and C18-unsaturated mono- and di-, acetates in rats, and the NOAEL were 1000 mg/kg bw/d.[22,25] Daily intravaginal dosing with 5% Glyceryl Oleate for 6 months in monkeys did not induce vaginal inflammation or mucosal lesions in cervical vaginal tissues.[42]

Animal

Dermal

Glyceryl Stearate. In subchronic and chronic dermal toxicity tests, 4% to 5% Glyceryl Stearate was nontoxic to rabbits but did cause moderate irritation (slight to moderate erythema, edema, atonia, desquamation, and/or fissuring).[1]

Oral

Glyceryl Laurate. No test substance–related gross or microscopic changes were observed in albino rats fed a mixture of mono-, di-, and tri-glycerides containing 40% to 45% Glyceryl Laurate for 2 days.[7] Neither gross nor microscopic lesions were noted in rats fed 25% Glyceryl Laurate in a 10-week study.

No test substance–related gross or microscopic changes were observed in albino rats fed a mixture of mono-, di-, and tri-glycerides containing 40% to 45% Glyceryl Laurate for 2 years.

Glyceryl Stearate. In chronic studies, 15% to 25% Glyceryl Stearate in the diet of rats for 3 consecutive generations had no adverse effects.[1] Rats fed a diet containing 25% Glyceryl Stearate for 2 years developed renal calcifications.

Inhalation

Glyceryl Laurate. A no-effect level of 280 mg/m^3 was reported for Glyceryl Laurate in a 3-week inhalation toxicity study involving rats.[7] Rats were subjected to 14 exposures, 1 hour in duration each.

Reproductive and Developmental Toxicity

Glyceryl Oleate

A reproduction/developmental toxicity screening test was conducted in male and female Sprague-Dawley rats for Glyceryl Oleate.[23] Both males and females were dosed by gavage with 0, 100, 300, or 1000 mg/kg bw/d Glyceryl Oleate in corn oil once daily for 14 days prior to mating; the males were dosed for an additional 28 days, and dosing of the females continued until day 4 of lactation. There were 12 females each in the control and each of 3 test groups, 7 males each in the control and high

dose groups, and 12 males each in the low- and mid-dose groups. A satellite group of 5 males and 5 females were dosed for 42 days, with a 14-day post-dosing observation period. The NOAELs for systemic toxicity (males and females), fertility (males and females), and development (F_1 generation) were 1000 mg/kg bw/d. No effects related to the administration of the test article were observed in parental animals or offspring.

For Read-Across

In the 28-day oral toxicity study in which rats were dosed with 0, 100, 300, and 1000 mg/kg/d glycerides, C8-18 and C18-unsaturated mono- and di-, acetates in polyethylene glycol (PEG) described in Table 10 (Repeated Dose Toxicity Studies), an additional 10 female Wistar Han rats were included in each group to assess reproduction and developmental toxicity.[22] After a minimum of 14 days of dosing, females of the reproduction study group were cohabitated with a male from the same treatment group. The test females were dosed for a total of 41 to 49 days, that is, during those 2 weeks prior to mating, during mating, during post-coitum, and during at least 4 days of lactation. No treatment-related effects were observed, and the NOAEL for parental fertility was 1000 mg/kg bw/d.

Glyceryl Hydrogenated Rosinate and Glyceryl Rosinate

Following the administration of hexane extracts of *Pinus ponderosa* needles to mice by stomach tube, increased embryonic resorptions were observed.[7] Glyceryl Rosinate and Glyceryl Hydrogenated Rosinate are esters of glycerin and acids derived from rosin, and rosin is obtained from trees of various species of *Pinus.*

Genotoxicity

Genotoxicity studies are summarized in Table 11.

Glyceryl Acetate was not mutagenic in an Ames test (≤10000 μg/plate) or chromosomal aberration assay (≤5000 μg/plate) with or without metabolic activation; in a sister chromatid exchange (SCE) assay, it was not genotoxic with metabolic activation, but without activation, a dose-dependent increase was observed in 2 studies, and a doubling of SCEs was produced with 5000 μg/mL.[43,44] Glyceryl Laurate was not mutagenic in an Ames test (≤5000 μg/plate), and Glyceryl Rosinate was not mutagenic in an Ames test (≤500 μg/plate), mammalian chromosome assay (≤507 μg/mL), or unscheduled DNA synthesis test (≤102 μg/mL).[24,45] Glycerides, C16-18 and C18-hydroxy mono- and di- (up to 10000 mg/kg bw), was not genotoxic in a mouse micronucleus test.[22]

In Vitro

Glyceryl citrate/lactate/linoleate/oleate. In the Ames plate incorporation and preincubation mutagenicity tests, Glyceryl Citrate/Lactate/Linoleate/Oleate was not mutagenic (with or without metabolic activation) to the following Salmonella typhimurium strains: TA98, TA100, TA1535, and TA1537.[7]

Glyceryl hydrogenated rosinate and glyceryl rosinate. In studies on the mutagenicity of resin acids, only neoabietic acid (component of rosin) was mutagenic in the Ames/Salmonella assay. Glyceryl Rosinate and Glyceryl Hydrogenated Rosinate are esters of glycerin and acids derived from rosin, which is composed of diterpene resin acids.[7]

Carcinogenicity

Oral and Dermal

Glyceryl Oleate. Glyceryl Oleate administration was associated with development of a few brain tumors (3 tumors in 63 mice) in a 2 generation study in mice of the TM strain whose feed was supplemented with 50 to 100 mg/mouse per day Glyceryl Oleate.[3] Digestive tract tumors were found in TM strain mice fed 200 mg/mouse per day Glyceryl Oleate (feed supplement) for 4 to 7 generations and were considered due to free fatty acid impurities.

Glyceryl ricinoleate. Glyceryl Ricinoleate was not a tumor promoter in a study involving groups of 10 mice.[6] However, the test substance induced slight epidermal hyperplasia in groups of 3 mice following the application of each to a small area of skin in the interscapular region.

Glyceryl stearate. Glyceryl Stearate, fed to mice in doses of 50 to 100 mg/d or 1.5% in the diet until they died, did not induce significant brain or gastric tumor formation, respectively. Five percent Glyceryl Stearate did not promote the carcinogenicity of 9,10 dimethylbenz[a]anthracene in mouse skin.[1]

Irritation and Sensitization

Dermal Irritation/Sensitization

Dermal irritation and sensitization studies are summarized in Table 12.

Undiluted Glyceryl Behenate, Glyceryl Hydrogenated Rosinate, and Glyceryl Rosinate were not irritating to rabbit skin. Glyceryl Hydrogenated Rosinate (challenge at up to 50%), Glyceryl Rosinate (challenge at 100%), and glyceride, C16-18 and C18 mono- and dihydroxy (25% at challenge) were not sensitizers in guinea pigs.[22,23,25]

In clinical testing, 5% Glyceryl Stearate was not irritating and Glyceryl Behenate (applied neat), Glyceryl Hydrogenated Rosinate, and Glyceryl Rosinate were not sensitizers in human repeated insult patch tests (HRIPTs).[23,25,46]

Non-Human

Glyceryl Citrate/Lactate/Linoleate/Oleate. Neither erythema nor edema was observed in rabbits after semiocclusive patches containing heated Glyceryl Citrate/Lactate/Linoleate/Oleate (single application) were applied to intact skin. In another study, Glyceryl Citrate/Lactate/Linoleate/Oleate (single application) induced clearly circumscribed erythema and very mild edema when applied to intact skin of rabbits.[7] All reactions had cleared by day 10 post application.

The sensitization potential of Glyceryl Citrate/Lactate/Linoleate/Oleate in 20 guinea pigs was evaluated using the Buehler method.[7] Following the dermal application of undiluted test substance during induction and challenge phases, no evidence of irritation or sensitization was observed.

Glyceryl Isostearate. Overall, Glyceryl Isostearate was classified as nonirritating to the skin of rabbits in a study in which single, semiocclusive patch applications were made to intact skin.[7] The most severe reaction (moderate irritation) did not clear until day 5 post removal. Glyceryl Isostearate was also classified as nonirritating to the skin of rabbits in another study in which single occlusive patch applications were made to intact and abraded skin sites.

Glyceryl Isostearate was also evaluated in the maximization test.[7] After induction, 10 guinea pigs were challenged with 50% Glyceryl Isostearate in PEG and microcrystalline cellulose. Two additional challenges were also conducted. The first challenge yielded 1 and 2 positive reactions (all slight reactions) at 24 and 48 hours, respectively. These results (allergic contact dermatitis) were confirmed by reactions observed after the third challenge.

Glyceryl Laurate. Undiluted Glyceryl Laurate induced minor erythema and edema when applied (occlusive patches, single application) to intact skin of rabbits.[7] In another study, single occlusive patch applications of 20% Glyceryl Laurate emulsion to abraded and intact skin caused moderate skin irritation in rabbits.

The skin sensitization potential of Glyceryl Laurate was evaluated in the maximization test.[7] Guinea pigs were subjected to 4 sensitizing injections of 2% Glyceryl Laurate and then challenged with intradermal injections of 0.8% Glyceryl Laurate and topical applications of 25% Glyceryl Laurate. No positive reactions were observed. In another maximization test, skin sensitization was induced in 2 of 10 guinea pigs challenged with a 10% dilution of 20% Glyceryl Laurate emulsion. When a second challenge was initiated 7 days after the first, positive reactions were observed in 5 animals. Positive reactions were also observed in 4 animals challenged with a 5% dilution of 20% Glyceryl Laurate emulsion. Because positive reactions were also noted in the control group after the first and second challenge, the results were attributed to skin irritation (but not sensitization) effects of the test substance.

Glyceryl Oleate. Undiluted and 50% concentrations of Glyceryl Oleate in corn oil used in dermal irritation studies in rabbits were found to be minimally irritating.[3] A volume of 0.5 mL of a sunscreen formulation containing 5% Glyceryl Oleate produced erythema and slight edema in rabbits.

Daily applications of 2.0 mL/kg of a 25.0% corn oil solution of a formulation containing Glyceryl Oleate for 20 days produced severe dermal irritation in rabbits.[3] In a 4-week dermal toxicity/phototoxicity study, product formulations containing varying concentrations of 2 sunscreen ingredients (containing 5% Glyceryl Oleate) produced slight, reversible dermal irritation.

Glyceryl Ricinoleate. Glyceryl Ricinoleate, when evaluated by a Draize skin test, was a mild irritant to rabbits.[5] In a primary skin irritation test in rabbits, Glyceryl Ricinoleate was classified as a nonirritant. When rabbits were tested with products containing 5.6% Glyceryl Ricinoleate in a single-insult occlusive patch test, the products had either no (4 of 5 tests) or mild (1 of 5 tests) irritation potentials.

Glyceryl Rosinate. A primary irritation index (PII) of 3.40 (potential for severe irritation-warning label may be considered) was reported in an occlusive patch test evaluating the skin irritation potential of undiluted, purified ester gum-2-octyldodecyl myristate (contains 50% Glyceryl Rosinate and 50% octyldodecyl myristate) in rabbits.[7] Follicular hyperkeratosis (comedone formation) was not observed in another study in which the same undiluted test substance was applied to the ears of rabbits.

The reaction of rosin with glycerol to form 2 esterification products (glyceryl triabietate [GTA] and glycerol esterified tall oil rosin [TORG]) reduced the allergenicity of rosin.[7] The GTA results from the esterification of glycerol with abietic acid, the major component of rosin.[7] The incidence of positive challenge reactions in 15 guinea pigs tested was as follows: 1 (8.3% GTA), 2 (10% TORG), 3 (0.93% and 2.8% GTA), and 9 (20% gum rosin). Glyceryl diabietate and glyceryl monoabietate induced either the same incidence or a higher incidence of sensitization in other experiments (similar test groups) in the same study.

Glyceryl Stearate and Glyceryl Stearate SE. Glyceryl Stearate and Glyceryl Stearate/SE at concentrations of up to 100% were reported to be mildly irritating or nonirritating to the skin of rabbits.[1] In 7 guinea pig sensitization studies, it was concluded that neither 0.1% Glyceryl Stearate nor 0.1% Glyceryl Stearate SE was capable of inducing sensitization.

Human

Glyceryl Caprylate. Glyceryl Caprylate (15%) did not induce skin irritation or sensitization in a repeated insult patch test (RIPT) involving 63 healthy subjects, 58 of whom completed the study.[7]

Glyceryl Hydrogenated Rosinate. Neither skin irritation nor sensitization was observed in any of the 51 subjects patch tested (semiocclusive patches) with a material consisting of 20% hydrogenated purified ester gum-2-octyldodecyl myristate and 80% white petrolatum.[7] (Because hydrogenated purified ester gum-2-octyldodecyl myristate is a trade mixture consisting of 50% Glyceryl Hydrogenated Rosinate and 50% octyldodecyl myristate, the effective concentration of Glyceryl Hydrogenated Rosinate in the test material is 10%.) The subjects were challenged at a new test site but not at the original site.

Glyceryl Laurate. Glyceryl Laurate was tested at a concentration of 50% wt/vol, in liquid paraffin, in an RIPT (Finn chambers) involving 91 healthy human subjects.[7] Glyceryl Laurate induced mild, erythematous reactions during induction in most of the subjects and questionable reactions in 7 subjects during

the challenge phase. Reactions ranged from mild to moderate erythema (score = 2) during induction and challenge phases.

The skin irritation and sensitization potential of Glyceryl Laurate was evaluated in a second RIPT (Finn chambers) using 107 healthy subjects, 93 of whom completed the study.[7] Glyceryl Laurate was tested at a concentration of 25% in liquid paraffin oil. Glycery1 laurate induced moderate erythema (score = 2) in 8 subjects during induction and in one subject during the challenge phase. Glyceryl Laurate was considered a sensitizer under the conditions of the study.

Glyceryl Linoleate. Glyceryl Laurate was tested at a concentration of 50% wt/vol, in liquid paraffin, in an RIPT (Finn chambers) involving 91 healthy human subjects.[7] Glyceryl Linoleate did not induce skin irritation or sensitization in the 74 subjects who completed the study.

Glyceryl Myristate. The skin irritation and sensitization potential of glyceryl myristate was evaluated in an RIPT (Finn chambers) using 107 healthy subjects, 93 of whom completed the study.[7] It was tested at a concentration of 50% in paraffin oil. Glyceryl myristate did not induce irritation or sensitization.

Glyceryl Oleate. Two aqueous Glyceryl Oleate preparations (15% and 30% concentrations) and a fragrance preparation containing 19.0% Glyceryl Oleate tested negative for cutaneous irritation when applied to human skin using single insult occlusive patch tests.[3]

Two sunscreen formulations containing 5% Glyceryl Oleate were considered mild compounds and caused no irritation in a cumulative occlusive patch test using human subjects.[3]

No signs of irritation or sensitization were observed in humans after repeated insult patch testing of a 15% aqueous Glyceryl Oleate preparation and a sunscreen formulation containing 5% Glyceryl Oleate.[3] A few subjects involved in simultaneous photoallergy and phototoxicity tests had slight, transient erythematous responses. No positive reactions were observed at any irradiated site during induction and challenge phases of the photoallergy test.

The skin irritation and sensitization potential of glycery1 oleate was evaluated in an RIPT (Finn chambers) using 107 healthy subjects, 93 of whom completed the study.[7] Glyceryl Oleate were tested at a concentration of 50% in paraffin oil. Glyceryl Oleate did not induce irritation or sensitization.

Glyceryl Rosinate. In human single-insult occlusive patch tests, no indication of skin irritation potential was observed in 2 products tested, each containing 5.6% Glyceryl Ricinoleate.[5]

Skin irritation was not observed in 12 healthy volunteers patch tested (occlusive patches) with a lipstick containing 1.0% Glyceryl Rosinate.[7] In an RIPT, neither skin irritation nor sensitization was observed in 78 healthy volunteers patch tested (occlusive patches) with the same product.

The contact sensitization potential of 3 product formulations containing Glyceryl Rosinate was evaluated in 3 maximization assays (healthy human subjects).[7] Results were negative for the following 3 study groups: foundation containing 4.0% Glyceryl Rosinate (25 subjects), blush containing 2.0% Glyceryl Rosinate (27 subjects), and lip gloss containing 2.0% Glyceryl Rosinate (27 subjects).

Skin irritation and sensitization were observed in 1 of 49 subjects patch tested (RIPT, semiocclusive patches) with a material consisting of 20% purified ester gum-2-octyldodecyl myristate and 80% white petrolatum.[7] (Because purified ester gum-2-octyldodecyl myristate is a trade mixture consisting of 50% Glyceryl Rosinate and 50% octyldodecyl myristate, the effective concentration of Glyceryl Rosinate in the test material is 10%.) The challenge reaction was observed at the original test site but not at the new site. It was concluded that the positive reaction observed was unique to that individual.

Glyceryl Stearate. When tested in single and RIPT to evaluate its skin irritation and sensitization in humans, Glyceryl Stearate used up to 20% was shown to be non-sensitizing and nonirritating.[1]

Allergenicity

Human

Glyceryl Rosinate. Data on 12 patients suspected of having gum rosin allergy indicated that sensitization to Portuguese gum rosin exhibited a dose-response relationship (0.001%-20%).[7] In the same study, the incidence of positive reactions to Portuguese gum rosin in a second group of 12 patients with gum rosin allergy was summarized as follows: 0.001% gum rosin (0-1 patient), 0.01% gum rosin (2-3 patients), 0.1% gum rosin (8 patients), 1% gum rosin (12 patients), and 10% gum rosin (10-12 patients). These data were based on patch tests with serial dilutions of Portuguese gum rosin in petrolatum.

The esterification of rosin with glycerol, in effect, reduced the allergenicity of rosin in dermatitis patients.[7] Five of 8 patients had positive reactions to 10% tall oil rosin in petrolatum, whereas 4 of 8 patients had positive reactions to 20% glycerol-esterified tall oil rosin in petrolatum. Additionally, 7 of 8 patients had positive reactions to 5% Portuguese gum rosin in petrolatum and 3 of 8 patients had positive reactions to 20% glycerol-esterified gum rosin in petrolatum.

Glyceryl-1-monoabietate was identified as a contact allergen in another study evaluating the allergenicity of rosin and its esterification products.[7] Abietic acid (esterified to form glyceryl-1-monoabietate) is a main component of rosin, and furthermore, clinical data indicate that it is easily oxidized to form contact allergens (eg, 15-hydroperoxyabietic acid and its methyl ester). It is also important to note that oxidation products of abietic acid and dehydroabietic acid (also a main component of rosin) that can be formed during storage have been found to be allergenic.

Phototoxicity

Glyceryl Isostearate. No evidence of significant cutaneous reactions, with or without UV irradiation, was found when the phototoxicity and photoallergenicity potential of Glyceryl Isostearate was evaluated using 20 guinea pigs.[7]

Glyceryl Rosinate. Phototoxicity was not induced in a group of 10 healthy volunteers tested with a lipstick containing 1.0% Glyceryl Rosinate. Patches were not applied to test sites.[7] Similarly, photoallergenicity was not induced in a group of 26 healthy volunteers patch tested (occlusive patches) with the same product in a repeat insult patch test.

Glyceryl Stearate. Products containing 2% Glyceryl Stearate were non-phototoxic and non-photoallergic.[1]

Ocular Irritation

Ocular irritation studies are summarized in Table 13. Undiluted Glyceryl Behenate and Glyceryl Palmitate/Stearate were nonirritating to rabbit eyes, and undiluted Glyceryl Rosinate was slightly irritating.[22,23,25]

Glyceryl Citrate/Lactate/Linoleate/Oleate. Glyceryl Citrate/Lactate/Linoleate/Oleate was not classified as ocular irritants in rabbits.[7]

Glyceryl Isostearate. Glyceryl Isostearate was not classified as ocular irritants in rabbits.[7]

Glyceryl Laurate. Glyceryl Laurate was not classified as ocular irritants in rabbits.[7]

Glyceryl Oleate. Minimal to moderate eye irritation was produced by undiluted Glyceryl Oleate, 50% Glyceryl Oleate in corn oil, and a fragrance preparation containing 19.0% Glyceryl Oleate when administered to rabbits.[3] A formulation containing 5% Glyceryl Oleate administered at a 0.1 mL dose to rabbit eyes induced slight conjunctivitis.

Glyceryl Ricinoleate. Glyceryl Ricinoleate was nonirritating to rabbit eyes in a primary eye irritation test, and in a Draize test, it was mildly irritating to rabbit eyes from which it was not rinsed but nonirritating to rabbit eyes from which it had been rinsed 2 and 4 seconds after instillation.[5] Various products containing Glyceryl Ricinoleate were tested for irritation potential in rabbit eyes. Of eight tests, 2 products demonstrated no irritation potential, 5 products had a minimal irritation potential, and 1 product had a mild irritation potential.

Glyceryl Rosinate. Undiluted, purified ester gum-2-octyldodecyl myristate (contains 50% Glyceryl Rosinate and 50% octyldodecyl myristate) was not irritating to the eyes of rabbits.[7]

Glyceryl Stearate. In primary eye irritation studies, Glyceryl Stearate and Glyceryl Stearate/SE at concentrations up to 100% were mildly irritating or nonirritating when instilled in the eyes of rabbits.[1]

Case Reports

Case reports of reactions to use of formulations containing several of the monoglyceryl monoesters are described in Table 14.[47-51]

Glyceryl Isostearate. Two case reports indicated skin reactions to 2 cosmetic products containing Glyceryl Isostearate as well as positive patch test reactions to this ingredient.[7]

Summary

In 1982, the Panel concluded that Glyceryl Stearate and Glyceryl Stearate SE are safe for topical application to humans. Since that time, the Panel has issued final reports on other monoglyceryl monoesters, finding them all to be safe as used in cosmetic products; an additional 8 monoglyceryl monoesters that have not been reviewed by the Panel have been identified to be used as cosmetic ingredients. In this report, we have compiled the safety data for 44 monoglyceryl monoesters (all of which are all esterification products of glycerin and aliphatic carboxylic acids, primarily fatty acids). Most of the monoglyceryl monoesters included in this safety assessment are reported to be used as skin conditioning agents.

Twenty-five of the 44 ingredients included in this safety assessment are currently used in cosmetic ingredients with Glyceryl Stearate having the highest frequency of use (it is found in 5153 formulations), the highest maximum use concentration in leave-on formulations (17% in a deodorant). Glyceryl Ricinoleate has the second highest maximum use concentration in leave-on formulations (15.2% in lipstick). Glyceryl Rosinate is reported to have the greatest maximum use concentration (96% in a depilatory). Most of the in-use ingredients have been reviewed previously by the Panel; for the majority of these ingredients, the frequency of use has increased but the concentration of use has remained the same or decreased.

According to the US FDA, many of the monoglyceryl monoesters are direct food substances affirmed as GRAS for human and/or animal use, are permitted as direct food additives, or are permitted as indirect food additives. Monoglyceryl monoesters can act as penetration enhancers for topical products.

Pharmacokinetics

In rats fed a diet containing radiolabeled glycerol ester of wood rosin, most of the radioactivity was excreted in the feces, primarily unchanged; results were similar with 1-day and 10-day dietary administration. In rats dosed by gavage, low levels of radioactivity were absorbed by rats following dosing, and the radioactive species excreted in bile appeared to be a hydrolyzed product of the administered test substance; no intact test substance was present in the excretions Radioactivity was excreted in bile within 4 hours after dosing and was detectable in all samples collected 24 hours post dose. The total amount of radioactivity excreted in bile during the 24-hour collection period ranged from 1.6% to 2.9% of the initial dose.

In a 24-hour patch test, the dermal LD_{50} of Glyceryl Rosinate and of glycerides, C16-18 and C18-hydroxy mono- and di-, were found to be >10 and >2 g/kg bw in rabbits, respectively. In oral studies, LD_{50} values were reported to be >2 g/kg

Glyceryl Behenate, >2 g/kg Glyceryl Hydrogenated Rosin, >5 g/kg Glyceryl Stearate, and >10 g/kg Glyceryl Rosinate. In a 90-day dietary study, NOAEL for Glyceryl Hydrogenated Rosinate in rats was 10000 ppm. For Glyceryl Rosinate, the NOAEL for rats was 10000 ppm in one 90-day study, and 2500 mg/kg bw/d in another. In a 28-day study in rats of glycerides, C8-18 and C18-unsatd. mono- and di-, acetates, the NOAEL was 1000 mg/kg bw/d.

Intravaginal dosing with 5% Glyceryl Oleate for 6 months in monkeys did not induce vaginal inflammation or mucosal lesions in cervical vaginal tissues. Glyceryl Oleate was not a reproductive or developmental toxin in rats. The NOAELs for systemic toxicity (males and females), fertility (males and females), and development (F_1 generation) were 1000 mg/kg bw/d. No effects related to the administration of the Glyceryl Oleate were observed in parental animals or offspring. In a reproductive and developmental toxicity study in which rats were dosed with 0, 100, 300, and 1000 mg/kg/d glycerides, C8-18 and C18-unsatd. mono- and di-, acetates in PEG, no treatment-related effects were observed, and the NOAEL for parental fertility was 1000 mg/kg bw/d.

Glyceryl Acetate was not mutagenic in an Ames test (≤10000 μg/plate) or chromosomal aberration assay (≤5000 μg/plate) with or without metabolic activation. In an SCE assay, Glyceryl Acetate was not genotoxic with metabolic activation; in the absence of metabolic activation, a dose-dependent increase in SCEs was observed in 2 separate studies; a doubling of SCEs was produced with 5000 μg/mL Gyceryl Acetate.

Glyceryl Laurate was not mutagenic in an Ames test (≤5000 μg/plate), and Glyceryl Rosinate was not mutagenic in an Ames test (≤500 μg/plate), mammalian chromosome assay (≤507 μg/mL), or unscheduled DNA synthesis test (≤102 μg/mL). Glycerides, C16-18 and C18-hydroxy mono- and di- (up to 10000 mg/kg bw), was not genotoxic in a mouse micronucleus test.

Undiluted Glyceryl Behenate, Glyceryl Hydrogenated Rosinate, and Glyceryl Rosinate were not irritating to rabbit skin. Glyceryl Hydrogenated Rosinate (challenge at up to 50%), Glyceryl Rosinate (challenge at 100%), and glyceride, C16-18 and C18 mono- and di-hydroxy (25% at challenge) were not sensitizers in guinea pigs.

In clinical testing, 5% Glyceryl Stearate was not irritating and Glyceryl Behenate (applied neat), Glyceryl Hydrogenated Rosinate, and Glyceryl Rosinate were not sensitizers in HRIPTs. Case reports of reactions to use of formulations containing several of the monoglyceryl monoesters have been described.

Undiluted Glyceryl Behenate and Glyceryl Palmitate/Stearate were nonirritating to rabbit eyes. Undiluted Glyceryl Rosinate was slightly irritating to rabbit eyes.

Discussion

In 1982, the Panel concluded that Glyceryl Stearate and Glyceryl Stearate SE are safe for topical application to humans. In accordance with its Procedures, the Panel evaluates the conclusions of previously issued reports every 15 years to determine whether the conclusion should be reaffirmed. Because it was determined that the time had elapsed and a rereview of Glyceryl Stearate had not been conducted, one was initiated. The Panel determined it was appropriate to reopen the safety assessment of Glyceryl Stearate and Glyceryl Stearate SE to include 34 previously reviewed monoglyceryl monoesters, and 8 additional cosmetic ingredients that had not yet been reviewed because all of these ingredients are esterification products of glycerin and carboxylic acids, the vast majority of which are fatty acids.

For many of the ingredients included in the report, the frequency of use has increased since the Panel's original review, but the concentration of use has not. However, there are a few ingredients for which the concentration of use has increased, but these increased concentrations of use did not cause concern for the Panel for several reasons:

- The maximum use concentration of Glyceryl Rosinate increased significantly in a rinse-off products whereas its current maximum leave-on concentration is less than that reported at the time of the original review.
- Glyceryl Hydrogenated Rosinate which was not reported to be in use when it was originally reviewed by the Panel but now reported to be used at a maximum use concentration of up to 10% in lipstick formulations and 76.8% in rinse-off products. Glyceryl Hydrogenated Rosinate is not an irritant when applied undiluted to rabbit skin and is not a sensitizer when used at a concentration of 50% in guinea pigs.
- The maximum leave-on use concentration of Glyceryl Ricinoleate has increased slightly (from 12% to 15.2%), and Glyceryl Ricinoleate SE, which was not in use when reviewed previously, is now reported to be used at up to 6.8% in leave-on formulations. Based on the clinical experience of members of the Panel with the routine use of 20% Glyceryl Ricinoleate in personal care products, absence of adverse effects in dermal screening results for sensitization testing, these reported increased concentrations of use were not of concern to the Panel.

The Panel recognized that some of the monoglyceryl monoesters can act as penetration enhancers. The Panel cautioned that care should be taken in formulating cosmetic products that may contain these ingredients in combination with any ingredients whose safety was based on their lack of dermal absorption data or when dermal absorption was a concern.

The Panel acknowledged that some of the monoglyceryl monoesters may be formed from plant-derived or animal-derived constituents. The Panel thus expressed concern regarding pesticide residues and heavy metals that may be present in botanical ingredients. They stressed that the cosmetics industry should continue to use the necessary procedures to sufficiently limit amounts of such impurities in an ingredient before blending them into cosmetic formulations. Additionally, the Panel considered the risks inherent in using animal-derived ingredients, namely the transmission of infectious agents. Although tallow may be used in the manufacture of glyceryl tallowate and is clearly animal-derived, the Panel notes that tallow is highly

processed, and tallow derivatives even more so. The Panel agrees with determinations by the US FDA that tallow derivatives are not risk materials for transmission of infectious agents.

Some of the monoglyceryl monoesters are used in products that could be incidentally inhaled; for example, Glyceryl Stearate is reported to be used at a maximum concentration of 14% in perfumes. However, the Panel did not find concern with the use of these ingredients in formulations that might be inhaled, and a no-effect level of 280 mg/m^3 was reported for Glyceryl Laurate in a 3-week inhalation toxicity study in rats subjected to 1-hour exposures. The Panel also noted that in aerosol products, 95% to 99% of droplets/particles would not be respirable to any appreciable amount. Furthermore, droplets/particles deposited in the nasopharyngeal or bronchial regions of the respiratory tract present no toxicological concerns based on the chemical and biological properties of these ingredients. Coupled with the small actual exposure in the breathing zone and the concentrations at which the 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 https://www.cir-safety.org/cir-findings.

Conclusion

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

Glyceryl Acetate*
Glyceryl Adipate*
Glyceryl Arachidate*
Glyceryl Behenate
Glyceryl Caprate
Glyceryl Caprylate
Glyceryl Caprylate/caprate
Glyceryl Citrate/Lactate/Linoleate/Oleate
Glyceryl Cocoate
Glyceryl Cocoate/Citrate/Lactate*
Glyceryl Erucate*
Glyceryl Ethylhexanoate*
Glyceryl Ethylhexanoate/Stearate/Adipate
Glyceryl Heptanoate*
Glyceryl Hydrogenated Rapeseedate*
Glyceryl Hydrogenated Rosinate
Glyceryl Hydrogenated Soyate*
Glyceryl Hydroxystearate
Glyceryl Isopalmitate*
Glyceryl Isostearate
Glyceryl Isotridecanoate/Stearate/Adipate
Glyceryl Lanolate
Glyceryl Laurate
Glyceryl Laurate SE*
Glyceryl Laurate/oleate*
Glyceryl Linoleate
Glyceryl Linolenate
Glyceryl Montanate*
Glyceryl Oleate
Glyceryl Oleate SE*
Glyceryl Oleate/Elaidate
Glyceryl Olivate*
Glyceryl Palmitate
Glyceryl Palmitate/Stearate*
Glyceryl Palmitoleate*
Glyceryl Pentadecanoate*
Glyceryl Ricinoleate
Glyceryl Ricinoleate SE
Glyceryl Rosinate
Glyceryl Stearate
Glyceryl Stearate SE
Glyceryl Stearate/Malate
Glyceryl Tallowate*
Glyceryl Undecylenate

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

Author Contribution

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

Author's Note

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Table 1. Monoglyceryl Monoesters.

Glyceryl Acetate[#]
Glyceryl Adipate
Glyceryl Arachidate
Glyceryl Behenate
Glyceryl Caprate
Glyceryl Caprylate
Glyceryl Caprylate/Caprate
Glyceryl Citrate/Lactate/Linoleate/Oleate
Glyceryl Cocoate
Glyceryl Cocoate/Citrate/Lactate[#]
Glyceryl Erucate
Glyceryl Ethylhexanoate[#]
Glyceryl Ethylhexanoate/Stearate/Adipate[#]
Glyceryl Heptanoate[#]
Glyceryl Hydrogenated Rapeseedate[#]
Glyceryl Hydrogenated Rosinate
Glyceryl Hydrogenated Soyate
Glyceryl Hydroxystearate
Glyceryl Isopalmitate
Glyceryl Isostearate
Glyceryl Isotridecanoate/Stearate/ Adipate
Glyceryl Lanolate
Glyceryl Laurate
Glyceryl Laurate SE
Glyceryl Laurate/Oleate
Glyceryl Linoleate
Glyceryl Linolenate
Glyceryl Montanate
Glyceryl Oleate
Glyceryl Oleate SE
Glyceryl Oleate/Elaidate
Glyceryl Olivate[#]
Glyceryl Palmitate
Glyceryl Palmitate/Stearate
Glyceryl Palmitoleate
Glyceryl Pentadecanoate
Glyceryl Ricinoleate
Glyceryl Ricinoleate SE
Glyceryl Rosinate
Glyceryl Stearate
Glyceryl Stearate SE
Glyceryl Stearate/Malate[#]
Glyceryl Tallowate
Glyceryl Undecylenate

[#]Not previously reviewed by the Panel.

Table 2. Definitions, Idealized Structures, and Reported Functions of the Ingredients in this Safety Assessment. [2; CIR Staff]

Ingredient CAS No.	Definition & Structure	Function(s)
Glyceryl Acetate 26446-35-5	The ester of acetic acid and glycerin	Skin conditioning agent–misc
Glyceryl Adipate 26699-71-8	The ester of glycerin and adipic acid that conforms to the formula:	Skin conditioning agent–emollient
Glyceryl Arachidate 30208-87-8 50906-68-8	The monoester of glycerin and arachidic acid. It conforms generally to the formula	Skin conditioning agent–emollient; surfactant–emulsifying agent; viscosity increasing agent–non-aq
Glyceryl Behenate 6916-74 -1 77538-19-3 30233-64-8	The monoester of glycerin and behenic acid. It conforms generally to the formula	Skin conditioning agent–emollient; surfactant–emulsifying agent
Glyceryl Caprate 11139-88 -1 26402-22-2	The monoester of glycerin and capric acid. It conforms to the formula	Skin conditioning agent–emollient; surfactant–emulsifying agent
Glyceryl Caprylate 26402-26-6	The monoester of glycerin and caprylic acid. It conforms to the formula	Skin conditioning agent–emollient; surfactant–emulsifying agent
Glyceryl Caprylate/Caprate	A monoester of glycerin esterified with a mixture of caprylic and capric acids. Wherein RC(O)- represents the residue of caprylic or capric acid	Skin conditioning agent–emollient; surfactant–emulsifying agent
Glyceryl Citrate/Lactate/Linoleate/Oleate	Glycerin esterified with a blend of citric, lactic, linoleic, and oleic acids Wherein RC(O)- represents the residue of citric, lactic, linoleic, or oleic acid	Skin conditioning agent–emollient
Glyceryl Cocoate 61789-05-7	The monoester of glycerin and coconut fatty acids. It conforms generally to the formula: where RC(O)- represents the fatty acids derived from coconut oil	Skin conditioning agent–emollient; surfactant–emulsifying agent
Glyceryl Cocoate/Citrate/Lactate	Glycerin esterified with a blend of coconut, citric and lactic acids Wherein RC(O)- represents the residue of coconut, citric, or lactic acid	Skin conditioning agent–emollient
Glyceryl Erucate 28063-42-5	The monoester of glycerin and erucic acid. It conforms generally to the formula	Skin conditioning agent–emollient; surfactant–emulsifying agent
Glyceryl Ethylhexanoate	The ester of glycerin and ethylhexanoic acid that conforms to the formula	Skin conditioning agent–emollient
Glyceryl Ethylhexanoate/Stearate/Adipate	Glycerin esterified with a blend of 2-ethylhexanoic acid, stearic acid, and adipic acid Wherein RC(O)- represents the residue of 2-ethylhexanoic, stearic, or adipic acid	Skin conditioning agent–occlusive
Glyceryl Heptanoate 26402-24-4	The glyceryl ester of heptanoic acid that conforms to the formula:	Skin conditioning agent–emollient; surfactant–emulsifying agent
Glyceryl Hydrogenated Rapeseedate	The monoester of glycerin and the fatty acids derived from hydrogenated rapeseed oil Wherein RC(O)- represents the residue of the fatty acids derived from hydrogenated rapeseed oil (<1% myristic acid; 3%-5% palmitic acid; 38%-42% stearic acid; 1% oleic acid; <1% linoleic acid; 8%-10% arachidic acid; <1% eicosenoic acid; 42%-50% behenic acid; <1% erucic acid; 1%-2% lignoceric acid)	Skin conditioning agent–emollient; surfactant–emulsifying agent
Glyceryl Hydrogenated Rosinate	The monoester of glycerin and hydrogenated mixed long chain acids derived from rosin Wherein RC(O)- represents the residue of the hydrogenated mixed long chain acids derived from rosin	Skin conditioning agent–emollient; surfactant–emulsifying agent
Glyceryl Hydrogenated Soyate	The monoester of glycerin and hydrogenated mixed long chain acids derived from soy Wherein RC(O)- represents the residue of the hydrogenated mixed long chain acids derived from soy (total fatty acid composition of glycine soja (soybean) oil is 11.5%-60% oleic acid; 2.9%-12.1% linolenic acid)	Skin conditioning agent–emollient
Glyceryl Hydroxystearate 1323-42-8	The monoester of glycerin and hydroxystearic acid. It conforms generally to the formula	Skin conditioning agent–emollient; surfactant–emulsifying agent

(continued)

Table 2. (continued)

Ingredient CAS No.	Definition & Structure	Function(s)
Glyceryl Isopalmitate	The monoester of glycerin and a branched chain 16 carbon aliphatic acid. It conforms to the formula *one example of an "iso"*	Skin conditioning agent–emollient; surfactant–emulsifying agent
Glyceryl Isostearate 61332-02-3 66085-00-5	The monoester of glycerin and isostearic acid. It conforms generally to the formula *one example of an "iso"*	Skin conditioning agent–emollient; surfactant–emulsifying agent
Glyceryl Isotridecanoate/Stearate/Adipate 473452-89-0	Glycerin esterified with a blend of isotridecanoic acid, stearic acid and adipic acid Wherein RC(O)- represents the residue of isotridecanoic, stearic, or adipic acid	Skin conditioning agent–emollient; surfactant–emulsifying agent
Glyceryl Lanolate	The monoester of glycerin and lanolin acid Wherein RC(O)- represents the residue of lanolin acid	Hair conditioning agent; skin conditioning agent–emollient; surfactant–emulsifying agent
Glyceryl Laurate 142-18-7 27215-38-9 37318-95-9	The monoester of glycerin and lauric acid. It conforms generally to the formula:	Skin conditioning agent–emollient; surfactant–emulsifying agent
Glyceryl Laurate SE	A self-emulsifying grade of Glyceryl Laurate that contains some sodium and/or potassium laurate	Surfactant–emulsifying agent
Glyceryl Laurate/Oleate	The monoester of glycerin esterified with a blend of lauric and oleic acids Wherein RC(O)- represents the residue of lauric or oleic acid	Skin conditioning agent–emollient; surfactant–emulsifying agent
Glyceryl Linoleate 2277-28-3 26545-74-4 37348-65-5	The monoester of glycerin and linoleic acid. It conforms to the formula:	Skin conditioning agent–emollient; surfactant–emulsifying agent
Glyceryl Linolenate 18465-99 -1 56554-41-7	The monoester of glycerin and linolenic acid. It conforms to the formula:	Skin conditioning agent–emollient; surfactant–emulsifying agent
Glyceryl Montanate 68476-38-0 71035-02-4	The monoester of glycerin and montan acid wax Wherein RC(O)- represents the residue of montan acid wax	Skin conditioning agent–emollient; surfactant–emulsifying agent
Glyceryl Oleate 111-03-5 161403-66-3 25496-72-4 37220-82-9 68424-61-3	The monoester of glycerin and oleic acid. It conforms generally to the formula	Fragrance ingredient; skin conditioning agent–emollient; surfactant–emulsifying agent
Glyceryl Oleate SE	A self-emulsifying grade of Glyceryl Oleate that contains some sodium and/or potassium oleate	Surfactant–emulsifying agent
Glyceryl Oleate/Elaidate	A mixture of monoglycerides of oleic and elaidic acids Wherein RC(O)- represents the residue of elaidic or oleic acid	Skin conditioning agent–emollient; surfactant–emulsifying agent
Glyceryl Olivate	The monoester of glycerin and the fatty acids derived from olive oil. It conforms generally to the formula: Wherein RC(O)- represents the fatty acids derived from olive oil (7.5%-20% palmitic acid; 0.3%-3.5% palmitoleic acid; 0.5%-3.5% stearic acid; 53%-86% oleic acid; 3.5%-20% linoleic acid; 0%-1.5% linolenic acid)	Skin conditioning agent–emollient; surfactant–emulsifying agent
Glyceryl Palmitate 26657-96-5 542-44-9	The monoester of glycerin and palmitic acid. It conforms to the formula:	Skin conditioning agent–emollient; surfactant–emulsifying agent
Glyceryl Palmitate/Stearate 68002-71-1	The monoester of glycerin esterified with a blend of palmitic and stearic acids Wherein RC(O)- represents the residue of palmitic or stearic acid	Skin conditioning agent–emollient; surfactant–emulsifying agent
Glyceryl Palmitoleate 37515-61-0	The monoester of glycerin and palmitoleic acid. It conforms to the formula:	Skin conditioning agent–emollient; surfactant–emulsifying agent
Glyceryl Pentadecanoate 122636-37-7	The monoester of glycerin and pentadecanoic acid. It conforms generally to the formula:	Surfactant–emulsifying agent
Glyceryl Ricinoleate		

(continued)

Table 2. (continued)

Ingredient CAS No.	Definition & Structure	Function(s)
1323-38-2 141-08-2	The monoester of glycerin and ricinoleic acid. It conforms generally to the formula:	Skin conditioning agent–emollient; surfactant–emulsifying agent
Glyceryl Ricinoleate SE	A self-emulsifying grade of Glyceryl Ricinoleate containing sodium and/or potassium stearate	Skin conditioning agent–emollient; surfactant–emulsifying agent
Glyceryl Rosinate 8050-31-5	The monoester of glycerin and mixed long chain acids derived from rosin Wherein RC(O)- represents the residue of mixed long chain acids derived from rosin	Depilating agent; fragrance ingredient; skin conditioning agent–emollient; surfactant–emulsifying agent
Glyceryl Stearate 11099-07-3 123-94-4 31566-31-1	The monoester of glycerin and stearic acid. It conforms generally to the formula:	Fragrance ingredient; skin conditioning agent–emollient; surfactant–emulsifying agent
Glyceryl Stearate SE 11099-07-3 85666-92-8	A self-emulsifying grade of Glyceryl Stearate that contains some sodium and/or potassium stearate	Surfactant–emulsifying agent
Glyceryl Stearate/Malate	The ester of glycerin esterified with a blend of stearic and malic acids Wherein RC(O)- represents the residue of stearic or malic acid	Skin conditioning agent–emollient; surfactant–emulsifying agent
Glyceryl Tallowate	The monoester of glycerin and tallow fatty acids. It conforms generally to the formula: wherein RC(O)- represents the residue of the fatty acids derived from tallow (37%-43% oleic acid; 24%-32% palmitic acid; 20%-25% stearic acid; 3%-6% myristic acid; 2%-3% linoleic acid[21])	Skin conditioning agent–emollient; surfactant–emulsifying agent
Glyceryl Undecylenate 123759-97-7 62285-15-8	The ester of glycerin and undecylenic acid that conforms to the formula:	Skin conditioning agent–emollient; surfactant–emulsifying agent

Table 3. Previously Reviewed Components and Related Glyceryl Esters.

Component	Conclusion	Reference
Glycerin	Safe in cosmetics in the present practices of use and concentration (was used in 15654 formulations, 10046 of which were leave-ons; the maximum use concentrations were 79.2% in leave-on products, 99.4% in rinse-off products, and 47.9% in products diluted for the bath	8
Acetic Acid	Safe in the present practices of use and concentration	9
Adipic Acid	Safe in the present practices of use and concentration	10
Caprylic/Capric/Coco Glycerides	Safe for use as a cosmetic ingredient	11
Citric Acid	Safe in the present practices of use and concentration	12
Coconut Acid	Safe for use as a cosmetic ingredient	11
Cocos Nucifera (Coconut) Oil	Safe for use as a cosmetic ingredient	11
Cocoglycerides	Safe for use as a cosmetic ingredient	11
Hydrogenated Coco-Glycerides	Safe for use as a cosmetic ingredient	11
Hydroxystearic Acid	Safe as a cosmetic ingredient in the present practices of use	13
Isostearic Acid	Safe as a cosmetic ingredient in the present practices of use	14
Lactic Acid	Safe for use in cosmetic products at concentrations $\leq$10%, at final formulation pH $\geq$3.5, when formulated to avoid increasing sun sensitivity or when directions for use include the daily use of sun protection. These ingredients are safe for use in salon products at concentrations $\leq$30%, at final formulation pH $\geq$3.0, in products designed for brief, discontinuous use followed by thorough rinsing from the skin, when applied by trained professionals, and when application is accompanied by directions for the daily use of sun protection	15
Lanolin Acid	Safe for topical application to humans in the present practice of use and concentration	16
Lauric Acid	Safe in the present practices of use and concentration	17
Malic Acid	Safe for use as a pH adjuster in cosmetic formulations; data are insufficient to determine the safety for any other functions	18

(continued)

Table 3. (continued)

Component	Conclusion	Reference
Montan Wax	Safe in the present practices of use and concentration	19
Oleic Acid	Safe in the present practices of use and concentration	17
Olive Acid	Safe in the present practices of use and concentration	20
Olea Europaea (Olive) Fruit Oil	Safe in the present practices of use and concentration	20
Palmitic Acid	Safe in the present practices of use and concentration	17
Rapeseed Acid	Safe in the present practices of use and concentration	20
Hydrogenated Rapeseed Oil	Safe in the present practices of use and concentration	20
Ricinoleic Acid	Safe in the present practices of use and concentration	6
Ricinus Communis (Castor) Seed Oil	Safe in the present practices of use and concentration	6
Hydrogenated Castor Oil	Safe in the present practices of use and concentration	6
Soy Acid	Safe in the present practices of use and concentration	20
Hydrogenated Soybean Oil	Safe in the present practices of use and concentration	20
Stearic Acid	Safe in the present practices of use and concentration	17
Tallow	Safe as a cosmetic ingredient in the present practices of use	21
Tallow Glyceride	Safe as a cosmetic ingredient in the present practices of use	21
Hydrogenated Tallow Glyceride	Safe as a cosmetic ingredient in the present practices of use	21
Tallow Glycerides	Safe as a cosmetic ingredient in the present practices of use	21
Hydrogenated Tallow Glycerides	Safe as a cosmetic ingredient in the present practices of use	21

Table 4. Molecular Weights and Log *P* values.

Ingredient	Molecular Weight (Da)	Log P (estimated)	Reference
Glyceryl Arachidate	386.61	8.105 ± 0.429	26
Glyceryl Laurate	274.4	n/a	7
Glyceryl Linoleate	354.53	n/a	7
Glyceryl Montanate	498.82	12.181 ± 0.429	26
Glyceryl Oleate	356.54	6.677 ± 0.435	26
Glyceryl Palmitate	330.50	6.067 ± 0.429	26
Glyceryl Palmitoleate	328.49	5.658 ± 0.435	26
Glyceryl Ricinoleate	372.54	4.863 ± 0.448	26
Glyceryl Stearate	358.56	7.086 ± 0.429	26
Glyceryl Undecylenate	258.35	3.111 ± 0.436	26

Table 5. Current and Historical Frequency and Concentration of Use According to Duration and Exposure.

	# of Uses		Max Conc of Use (%)		# of Uses		Max Conc of Use (%)	
	Glyceryl Behenate				Glyceryl Caprate			
	2015[29]	1998[7]	2014[30,31]	1999[7]	2015[29]	1998[7]	2014[30,31]	1999[7]
Totals*	90	NR	0.27-2.5	2-5	57	NR	1	NR
Duration of Use								
Leave-On	81	NR	0.3-2.5	2-5	46	NR	1	NR
Rinse-Off	9	NR	0.27	NR	11	NR	NR	NR
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR	NR	NR
Exposure Type								
Eye Area	20	NR	0.3 -1.5	2	4	NR	NR	NR
Incidental Ingestion	7	NR	NR	NR	7	NR	NR	NR
Incidental Inhalation-Spray	22[a]; 13[b]	NR	0.48[a]	5[a]	7[a]; 8[b]	NR	1	NR
Incidental Inhalation-Powder	13[b]	NR	0.45-2[c]	NR	8[b]; 1[c]	NR	NR	NR
Dermal Contact	65	NR	0.3-2.5	NR	50	NR	NR	NR
Deodorant (underarm)	NR	NR	NR	5	5[a]	NR	pump spray: 1	NR
Hair - Non-Coloring	3	NR	0.48	NR	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	2	NR	0.27	NR	NR	NR	NR	NR
Mucous Membrane	7	NR	NR	NR	7	NR	NR	NR
Baby Products	NR	NR	NR	NR	1	NR	NR	NR

	Glyceryl Caprylate				Glyceryl Caprylate/Caprate			
	2015[29]	1998[7]	2014[30,31]	1999[7]	2015[29]	1998[7]	2014[30,31]	1999[7]
Totals*	190	NR	0.001 -1.5	NR	2	1	NR	2
Duration of Use								
Leave-On	177	NR	0.001 -1.5	NR	1	1	NR	NR
Rinse-Off	13	NR	0.01 -1.5	NR	1	NR	NR	NR
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR	NR	NR
Exposure Type								
Eye Area	29	NR	0.03-1	NR	NR	NR	NR	NR
Incidental Ingestion	20	NR	0.3-1	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	33[a]; 37[b]	NR	1[a]	NR	1	NR	NR	2[b]
Incidental Inhalation-Powder	16; 37[b]	NR	0.98; 0.001-1[c]	NR	NR	NR	NR	2[b]
Dermal Contact	161	NR	0.001 -1.5	NR	NR	NR	NR	2
Deodorant (underarm)	2[a]	NR	1.5	NR	NR	NR	NR	NR
Hair—Non-Coloring	6	NR	0.01-1	NR	1	NR	NR	NR
Hair—Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	20	NR	0.3-1	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

(continued)

Table 5. (continued)

	# of Uses		Max Conc of Use (%)		# of Uses		Max Conc of Use (%)	
	Glyceryl Citrate/Lactate/Linoleate/Oleate				Glyceryl Cocoate			
	2015[29]	1998[7]	2014[30,31]	1999[7]	2015[29]	1998[7]	2014[30,31]	1999[7]
Totals*	NR	NR	0.0004-0.004	NR	14	1	1-2	0.3-5
Duration of Use								
Leave-On	NR	NR	NR	NR	11	NR	2	0.3-2
Rinse-Off	NR	NR	0.0004-0.004	NR	3	1	1-2	1-5
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR	NR	1
Exposure Type								
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	0.3-2
Incidental Inhalation-Spray	NR	NR	0.0004	NR	10[b]	NR	NR	NR
Incidental Inhalation-Powder	NR	NR	NR	NR	10[b]	NR	NR	NR
Dermal Contact	NR	NR	NR	NR	11	1	2	1-5
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	2 (pump spray)	NR
Hair - Non-Coloring	NR	NR	0.0004-0.004	NR	3	NR	1	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	NR	2	0.3-4
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

	Glyceryl Erucate				Glyceryl Ethylhexanoate/Stearate/Adipate			
	2015[29]	1998[7]	2014[30,31]	1999[7]	2015[29]	N/A	2014[30,31]	N/A
Totals*	NR	NR	NR	0.5	39		0.6-3	
Duration of Use								
Leave-On	NR	NR	NR	0.5	38		0.6-3	
Rinse-Off	NR	NR	NR	NR	1		NR	
Diluted for (Bath) Use	NR	NR	NR	NR	NR		NR	
Exposure Type								
Eye Area	NR	NR	NR	NR	21		0.8-3	
Incidental Ingestion	NR	NR	NR	NR	1		NR	
Incidental Inhalation-Spray	NR	NR	NR	0.5	1[a]		NR	
Incidental Inhalation-Powder	NR	NR	NR	0.5[b]	4		1 -1.4	
Dermal Contact	NR	NR	NR	0.5	37		0.8-3	
Deodorant (underarm)	NR	NR	NR	NR	NR		NR	
Hair—Non-Coloring	NR	NR	NR	NR	1		NR	
Hair—Coloring	NR	NR	NR	NR	NR		NR	
Nail	NR	NR	NR	NR	NR		NR	
Mucous Membrane	NR	NR	NR	NR	1		NR	
Baby Products	NR	NR	NR	NR	NR		NR	

(continued)

Table 5. (continued)

	# of Uses		Max Conc of Use (%)		# of Uses		Max Conc of Use (%)	
	Glyceryl Hydrogenated Rosinate				Glyceryl Hydroxystearate			
	2015[29]	1998[7]	2014[30,31]	1999[7]	2015[29]	1998[7]	2014[30,31]	1999[7]
Totals*	29	NR	3-76.8	NR	14	32	0.5-2	0.8-2
Duration of Use								
Leave-On	22	NR	3-10	NR	14	22	0.5-2	0.8-2
Rinse-Off	7	NR	65-76.8	NR	NR	10	NR	NR
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR	NR	NR
Exposure Type								
Eye Area	14	NR	3-4.8	NR	10	NR	1-2	2
Incidental Ingestion	6	NR	4-10	NR	4[a]	1	NR	NR
Incidental Inhalation-Spray	1[a]	NR	6.5[a]	NR	NR	10[a]; 8[b]	NR	0.8[a]; 2[b]
Incidental Inhalation-Powder	NR	NR	NR	NR	NR	8[b]	0.5-0.9[c]	2[b]
Dermal Contact	9	NR	65-76.8	NR	13	31	0.5-0.9	0.8-2
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	0.9 (not spray)	2[a]
Hair—Non-Coloring	NR	NR	6.5	NR	NR	NR	NR	NR
Hair—Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	6	NR	4-10	NR	NR	2	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

	Glyceryl Isostearate				Glyceryl Isotridecanoate/Stearate/Adipate			
	2015[29]	1998[7]	2014[30,31]	1999[7]	2015[29]	1998[7]	2014[30,31]	1999[7]
Totals*	104	53	0.3-2	0.3-6	1	NR	NR	NR
Duration of Use								
Leave-On	14	53	0.8-2	0.5-6	1	NR	NR	NR
Rinse-Off	90	NR	0.3-1.5	0.3-3	NR	NR	NR	NR
Diluted for (Bath) Use	NR	NR	NR	1	NR	NR	NR	NR
Exposure Type								
Eye Area	4	23	NR	0.5-2	NR	NR	NR	NR
Incidental Ingestion	1	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	5[a]	3[a]; 1[b]	NR	3[a]; 2[b]	1[a]	NR	NR	NR
Incidental Inhalation-Powder	NR	1; 1[b]	0.8-1[c]	2[b]	NR	NR	NR	NR
Dermal Contact	14	53	0.8-2	0.3-6	1	NR	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair—Non-Coloring	1	NR	0.3	NR	NR	NR	NR	NR
Hair—Coloring	78	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	1	NR	NR	1	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

(continued)

Table 5. (continued)

	# of Uses		Max Conc of Use (%)		# of Uses		Max Conc of Use (%)	
	Glyceryl Lanolate				Glyceryl Laurate			
	2015[29]	1998[7]	2014[30,31]	1999[7]	2015[29]	1998[7]	2014[30,31]	1999[7]
Totals*	1	3	NR	NR	210	29	0.000065-4.5	0.1-4
Duration of Use								
Leave-On	1	3	NR	NR	101	12	0.000065-0.5	0.4-4
Rinse-Off	NR	NR	NR	NR	106	17	0.000065-4.5	0.1-4
Diluted for (Bath) Use	NR	NR	NR	NR	3	NR	1	NR
Exposure Type								
Eye Area	NR	NR	NR	NR	9	3	0.000065-0.48	0.1
Incidental Ingestion	NR	NR	NR	NR	8	NR	NR	NR
Incidental Inhalation-Spray	1[a]	1[a]; 2[b]	NR	NR	1; 24[a]; 10[b]	1; 5[a]	0.2[a]	1; 0.4[a]
Incidental Inhalation-Powder	NR	2[b]	NR	NR	1; 10[b]; 3c	NR	0.1-0.5[c]	NR
Dermal Contact	1	3	NR	NR	176	20	0.000065-4.5	NR
Deodorant (underarm)	NR	NR	NR	NR	15[a]	4[a]	NR	0.1-4
Hair—Non-Coloring	NR	NR	NR	NR	26	9	0.088 -1.5	0.3-2
Hair—Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	72	7	0.000065-4.5	0.3
Baby Products	NR	NR	NR	NR	6	NR	NR	NR

	Glyceryl Linoleate				Glyceryl Linolenate			
	2015[29]	1998[7]	2014[30,31]	1999[7]	2015[29]	1998[7]	2014[30,31]	1999[7]
Totals*	87	17	0.000055-4.6	0.7-1	70	10	0.00045-0.4	0.7-1
Duration of Use								
Leave-On	70	13	0.000055-4.6	0.7-1	55	9	0.00045-0.4	0.7-1
Rinse-Off	17	4	NR	0.7-1	15	1	NR	0.7-1
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR	NR	NR
Exposure Type								
Eye Area	8	1	2.5	NR	7	1	0.2	NR
Incidental Ingestion	1	3	0.056-2.5	0.7	1	3	0.046-0.2	0.7
Incidental Inhalation-Spray	1; 16[a]; 30[b]	1; 2[a]; 2[b]	0.000055-0.0002[a]	1[b]	1; 12[a]; 20[b]	2[a]; 2[b]	0.00045[a]	1[b]
Incidental Inhalation-Powder	30[b]; 2[c]	1	0.003-0.75[b]	1[b]	20[b]; 2[c]	2[b]	NR	1[b]
Dermal Contact	64	14	0.0002-2.5	0.7-1	47	7	0.09-0.2	0.7-1
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair—Non-Coloring	17	NR	0.000055	NR	17	NR	0.00045	NR
Hair—Coloring	1	NR	NR	NR	1	NR	NR	NR
Nail	4	NR	0.019-4.6	NR	4	NR	0.001-0.4	NR
Mucous Membrane	2	3	NR	0.7	2	NR	0.046-0.2	0.7
Baby Products	2	NR	NR	NR	2	NR	NR	NR

(continued)

Table 5. (continued)

	# of Uses		Max Conc of Use (%)		# of Uses		Max Conc of Use (%)	
	Glyceryl Oleate				Glyceryl Oleate/Elaidate			
	2015[29]	2002[4]	2014[30,31]	2004[4]	2015[29]	1998[7]	2014[30,31]	1999[7]
Totals*	663	112	0.0001-3	0.00002-5	4	NR	NR	0.3-2
Duration of Use								
Leave-On	231	92	0.0001-3	0.00002-3	2	NR	NR	0.3-2
Rinse-Off	411	19	0.1-2.7	0.02-5	2	NR	NR	NR
Diluted for (Bath) Use	21	1	NR	0.2-3	NR	NR	NR	NR
Exposure Type								
Eye Area	87	7	0.0075-2.3	0.008-0.01	NR	NR	NR	NR
Incidental Ingestion	34	18	0.0001-0.075	0.01-0.3	NR	NR	NR	NR
Incidental Inhalation-Spray	2; 48[a]; 22[b]	1; 27[a]; 20[b]	1.4; 0.0092[a]	0.0003; 0.00002-0.5[a]; 0.1-2[b]	2[a]	NR	NR	2[a]; 2[b]
Incidental Inhalation-Powder	7; 22[b]; 2[c]	2; 20[b]	0.0028-3[c]	0.01-3; 0.1-2[b]	NR	NR	NR	2[b]
Dermal Contact	493	73	0.0075-3	0.00002-3	2	NR	NR	0.3-2
Deodorant (underarm)	NR	NR	0.1-2.7	NR	NR	NR	NR	NR
Hair—Non-Coloring	118	21	0.0092-2.7	0.08-0.2	2	NR	NR	NR
Hair—Coloring	5	NR	2	0.02	NR	NR	NR	NR
Nail	NR	NR	0.015	NR	NR	NR	NR	NR
Mucous Membrane	262	19	0.0001-2.4	0.01-5	NR	NR	NR	NR
Baby Products	13	2	NR	0.01-3	NR	NR	NR	NR

	Glyceryl Palmitate				Glyceryl Ricinoleate			
	2015[29]	1998[7]	2014[30,31]	1999[7]	2015[29]	1998[7]	2014[30,31]	1999[7]
Totals*	4	NR	NR	NR	42	16	1.5-15.2	2-12
Duration of Use								
Leave-On	3	NR	NR	NR	40	15	1.5-15.2	2-12
Rinse-Off	1	NR	NR	NR	2	1	NR	NR
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR	NR	NR
Exposure Type								
Eye Area	NR	NR	NR	NR	10	7	1.5-11.6	2-12
Incidental Ingestion	NR	NR	NR	NR	16	5	11.9-15.2	NR
Incidental Inhalation-Spray	3[b]	NR	NR	NR	6[a]	1[a]; 2[b]	NR	12[a]
Incidental Inhalation-Powder	3[b]	NR	NR	NR	NR	2[b]	NR	NR
Dermal Contact	4	NR	NR	NR	26	11	1.5-12.6	2-12
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair—Non-Coloring	NR	NR	NR	NR	NR	N	NR	NR
Hair—Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	18	5	11.9-15.2	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

(continued)

Table 5. (continued)

	# of Uses		Max Conc of Use (%)		# of Uses		Max Conc of Use (%)	
	Glyceryl Ricinoleate SE				Glyceryl Rosinate			
	2015[29]	2002[6]	2014[30,31]	2004[6]	2015[29]	1998[7]	2014[30,31]	1999[7]
Totals*	NR	NR	6.8	NR	50	4	0.018-96	0.06-12
Duration of Use								
Leave-On	NR	NR	6.8	NR	36	3	0.018-8	0.06-12
Rinse-Off	NR	NR	NR	NR	14	1	2.6-96	3
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR	NR	NR
Exposure Type								
Eye Area	NR	NR	6.8	NR	6	2	0.3-8	12
Incidental Ingestion	NR	NR	NR	NR	20	NR	0.48-0.5	6
Incidental Inhalation-Spray	NR	NR	NR	NR	2[a]	NR	NR	NR
Incidental Inhalation-Powder	NR	NR	NR	NR	1	NR	NR	NR
Dermal Contact	NR	NR	6.8	NR	23	2	0.018-96	0.6-10
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair—Non-Coloring	NR	NR	NR	NR	1	NR	2.6	NR
Hair—Coloring	NR	NR	NR	NR	2	NR	NR	3
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	20	NR	0.48-0.5	0.4-6
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR
	Glyceryl Stearate				Glyceryl Stearate SE			
	2015[29]	1976[1]	2014[30,31]	1976[1]	2015[29]	1976[1]	2014[30,31]	1976[1]
Totals*	5153	1371	0.0002-18.9	0.1-50	1420	217	0.001-10	0.1-25
Duration of Use								
Leave-On	4229	1086	0.0002-17	0.1-50	944	196	0.001-10	0.1-25
Rinse-Off	914	284	0.006-18.9	0.1-25	476	21	0.5-6	0.1-25
Diluted for (Bath) Use	10	1	1-10	0.1-1	NR	NR	6	NR
Exposure Type								
Eye Area	566	115	0.014-9	0.1-50	59	40	0.2-5	0.1-5
Incidental Ingestion	30	NR	0.0002-3	NR	1	NR	NR	NR
Incidental Inhalation-Spray	17; 1705[a]; 1380[b]	5; 308[a]; 212[b]	2-14; 0.5-4.8[a]; 2.3-6[b]	0.1-25; 0.1-25[a, b]	1; 565[a]; 253[b]	1; 36[a]; 24[b]	3; 0.001-3[a]; 2-3.9[b]	1-5; 0.1-25[a, b]
Incidental Inhalation-Powder	20; 1380[b]; 28[c]	137; 212[b]; 11[c]	0.05-3; 2.3-6[b]; 0.0083-10[c]	0.1-25	253[b]; 3[c]	24[b]	2-3.9[b]; 0.2-10[c]	0.1-25[b]
Dermal Contact	4346	1167	0.0083-18.9	0.1-25; 0.1-25[b]	1013	205	0.2-10	0.1-25
Deodorant (underarm)	42[a]	NR	0.25-17	NR	1[a]	NR	NR	NR
Hair—Non-Coloring	318	97	0.15-4.8	0.1-25	45	7	0.001-4	1-25
Hair—Coloring	200	29	0.9-7	0.1-10	340	NR	3-6	NR
Nail	11	15	0.006-6	1-50	1	NR	NR	NR
Mucous Membrane	182	36	0.0002-18	0.1-25	22	2	3-6	10-25
Baby Products	33	11	1.8	0.1-5	3	NR	NR	NR

(continued)

Table 5. (continued)

	# of Uses		Max Conc of Use (%)		# of Uses		Max Conc of Use (%)	
	Glyceryl Stearate/Malate				Glyceryl Undecylenate			
	2015[29]	N/A	2014[30,31]	N/A	2015[29]	1998[7]	2014[30,31]	1999[7]
Totals*	NR		0.25		17	2	1	NR
Duration of Use								
Leave-On	NR		0.25		15	2	1	NR
Rinse-Off	NR		NR		2	NR	1	NR
Diluted for (Bath) Use	NR		NR		NR	NR	NR	NR
Exposure Type								
Eye Area	NR		0.25		2	NR	NR	NR
Incidental Ingestion	NR		NR		NR	NR	NR	NR
Incidental Inhalation-Spray	NR		NR		7[a]; 6[b]	2[a]	NR	NR
Incidental Inhalation-Powder	NR		NR		6[b]	NR	NR	NR
Dermal Contact	NR		0.25		14	2	1	NR
Deodorant (underarm)	NR		NR		NR	NR	NR	NR
Hair—Non-Coloring	NR		NR		2	NR	NR	NR
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

*Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.
[a]Includes products that can be sprays, but it is not known whether the reported uses are sprays.
[b]Not specified whether this product is a spray or a powder or neither, but it is possible it may be a spray or a powder, so this information is captured for both categories of incidental inhalation.
[c]Includes products that can be powders, but it is not known whether the reported uses are powders.
NR – no reported use.
N/A – no information is reported in this column because this is the first review of this ingredient.

Table 6. Ingredients Currently not Reported to be Used.

Glyceryl Acetate
Glyceryl Adipate
Glyceryl Arachidate
Glyceryl Cocoate/Citrate/Lactate
Glyceryl Erucate (was in use in 1998)
Glyceryl Ethylhexanoate
Glyceryl Heptanoate
Glyceryl Hydrogenated Rapeseedate
Glyceryl Hydrogenated Soyate
Glyceryl Isopalmitate
Glyceryl Laurate SE
Glyceryl Laurate/Oleate
Glyceryl Montanate
Glyceryl Oleate SE
Glyceryl Olivate
Glyceryl Palmitate/Stearate
Glyceryl Palmitoleate
Glyceryl Pentadecanoate
Glyceryl Tallowate

Table 7. Food Additive Status.

Ingredient	CFR Citation
GRAS Ingredients for Human Use	
Glyceryl Behenate	21CFR184.1328
Glyceryl Laurate	21CFR184.1505
Glyceryl Linoleate	21CFR184.1505
Glyceryl Oleate	21CFR184.1323
Glyceryl Palmitate	21CFR184.1324
Glyceryl Palmitate/Stearate	21CFR184.1329
Glyceryl Stearate	21CFR184.1324
GRAS Ingredients for Animal Use	
Glyceryl Caprate	21CFR582.4505
Glyceryl Caprylate/Caprate	21CFR582.4505
Glyceryl Laurate	21CFR582.4505
Glyceryl Laurate/Oleate	21CFR582.4505
Glyceryl Palmitate/Stearate	21CFR582.4505
Glyceryl Stearate	21CFR582.4505
	21CFR582.1324
Direct Food Additives	
Glyceryl Hydrogenated Rapeseedate	21CFR172.736
Glyceryl Hydrogenated Rosinate	21CFR172.615
Glyceryl Hydrogenated Soyate	21CFR172.736
Glyceryl Rosinate	21CFR172.615; 21CFR172.735
Prior-Sanctioned Food Ingredients	
Glycerol Oleate	21CFR181.27
Indirect Food Additives	
Glyceryl Acetate	21CFR177.1200
Glyceryl Behenate	21CFR175.105; 21CFR176.210
Glyceryl Caprate	21CFR175.105; 21CFR176.180; 21CFR177.2800

(continued)

Table 7. (continued)

Ingredient	CFR Citation
GRAS Ingredients for Human Use	
Glyceryl Caprylate	21CFR175.105; 21CFR176.210
Glyceryl Caprylate/Caprate	21CFR175.105; 21CFR176.210; 21CFR177.2800
Glyceryl Cocoate	21CFR175.105; 21CFR176.210; 21CFR177.2800
Glyceryl Erucate	21CFR175.105
Glyceryl Hydrogenated Rosinate	21CFR178.3130
Glyceryl Hydroxystearate	21CFR175.105; 21CFR176.170; 21CFR176.200; 21CFR177.1200; 21CFR177.2800
Glyceryl Isopalmitate	21CFR175.105
Glyceryl Isostearate	21CFR175.105
Glyceryl Laurate	21CFR175.105; 21CFR176.210; 21CFR177.2800
Glyceryl Laurate/Oleate	21CFR175.105; 21CFR176.210; 21CFR177.2800
Glyceryl Linoleate	21CFR175.105
Glyceryl Linolenate	21CFR175.105
Glyceryl Oleate	21CFR175.105; 21CFR175.300; 21CFR175.320; 21CFR176.210; 21CFR177.2800
Glyceryl Palmitate	21CFR175.105
Glyceryl Palmitate/Stearate	21CFR175.105; 21CFR176.210; 21CFR177.2800
Glyceryl Palmitoleate	21CFR175.105
Glyceryl Ricinoleate	21CFR175.105; 21CFR176.170; 21CFR176.210; 21CFR178.3130
Glyceryl Rosinate	21CFR175.105; 21CFR175.300; 21CFR178.3120
Glyceryl Stearate	21CFR175.105; 21CFR175.210; 21CFR175.300; 21CFR176.200; 21CFR176.210; 21CFR176.210

Table 8. Penetration Enhancement.

Ingredient	Test Compound	Test System	Results	Reference
Glyceryl Caprylate/ Caprate	5-fluorouracil	Human abdominal skin samples ability to enhance skin penetration was determined in vitro by measuring skin permeability coefficients	10-fold increase in penetration, as compared to the buffer control (statistically significant)	37
Glyceryl Isostearate	5-fluorouracil	Human abdominal skin samples (same protocol as above)	Did not enhance penetration	37
Glyceryl Oleate 77.5% in a hexagonal gel phase	Vitamin K, 2.5%	Porcine ear skin in Franz diffusion cells was compared to vaseline as a vehicle	2.2-fold increase to the stratum corneum (9 hours); 3- and 2-fold increase to the epidermis + dermis after 3 and 12 hours, respectively	38
15% in a nanodispersion of a hexagonal phase			2.7-fold increase to the stratum corneum (9 hours); 3- and 3.7-fold increase to the epidermis + dermis after 3 and 12 hours, respectively	
Glyceryl Oleate 1:2 with PEG-40 hydrogenated castor oil	Lidocaine, 2.5%	Hairless mouse skin in Franz diffusion cells	Statistically significant increase in penetration	39
3:2 with PEG-40 stearate			Greater penetration than with above mixture	
Glyceryl Oleate, 5-20% in a propylene glycol solution	Cisplatin, 0.05%	Porcine ear skin in Franz diffusion cells; full thickness skin and tape-stripped skin (stratum corneum removed) was used	Did not act as a real penetration enhancer, but increased drug partition to the receptor solution, thereby improving transdermal penetration Only a small enhancement was observed in skin without the stratum corneum as compared to intact skin	40
Glyceryl Oleate, 0.1%-30% in propylene glycol	5-aminolevulinic acid, 5%	Full-thickness hairless mouse skin in diffusion cells	Significantly increased in vitro skin permeation/retention	41
5%-20% in propylene glycol		4-hour application to dorsal area of hairless mice	Concentration-dependent increase in protoporphyrin IX (conversion product of test substance)	

Table 9. Single Dose (Acute) Toxicity Studies.

Ingredient	Animals/Group	Concentration/Dose/ Vehicle	Procedure	LD_{50}/Results	Reference
			DERMAL		
Glyceryl Rosinate	4 male NZW rabbits	5 g/kg bw, in water	24-hour patch; it was not stated whether it was occlusive	>5 g/kg bw No irritation observed	25
Glyceryl Rosinate	5 male NZW rabbits	10 g/kg bw, in water	24-hour occlusive patch	>10 g/kg bw No irritation observed	25
Glycerides, C16-18 and C18-hydroxy mono- and di-	5 Wistar rats	2 g/kg bw, neat	24-hour occlusive patch	>2 g/kg bw No irritation observed	22
			ORAL		
Glyceryl Behenate	5 female Swiss mice	2 g/kg bw, neat	By gavage	>2 g/kg bw	23
Glycerol ester of partially hydrogenated gum rosin	5 male Sprague-Dawley rats	2 g/kg bw in olive oil	By gavage	>2 g/kg bw	25
Glycerol ester of partially hydrogenated gum rosin	5 male Sprague-Dawley rats	2 g/kg bw, neat	By gavage	>2 g/kg bw	25
Glyceryl Rosinate	Sprague-Dawley rats, 5/sex	2 g/kg bw in petrolatum	By gavage	>2 g/kg	25
Glyceryl Rosinate	10 male Sprague-Dawley rats	5 g/kg of a 10% wt/vol suspension in corn oil	By gavage	>5 g/kg; urinary and fecal staining, soft stool and decreased motor activity were observed for the first 48 hour	52
Glyceryl Rosinate	10 rats	5 g/kg of a 10% wt/vol suspension in corn oil	By gavage	>5 g/kg; urinary and fecal staining, soft stool, piloerection, and decreased motor activity were observed for 1 week, most notably for 24 hour	53
Glyceryl Rosinate	Male Hilltop-Wistar albino rats; 3 (low dose) or 10 (high dose)	5 or 10 g/kg in 0.25% agar and 0.10% Tween 80	By gavage	>10 g/kg	25
Glyceryl Stearate	5 female NMRI mice/sex	40 mL/kg bw; vehicle not stated	OECD guideline 401; given orally (details not provided)	>5 g/kg bw	22
Glyceryl Stearate	5 male NMRI mice	Not given	OECD guideline 401 (details not provided)	>5 g/kg bw	22

Abbreviation: OECD, Organisation for Economic Co-operation and Development.

Table 10. Repeated Dose Toxicity Studies.

Ingredient	Animals/Group	Study Duration	Dose/Concentration	Procedure	Results	Reference
				ORAL		
Glyceryl Hydrogenated Rosinate	Sprague-Dawley rats, 20/sex in low dose group; 25/sex in all other groups	90 days	mixed with corn oil (50:50); 2000, 5000, and 10000 ppm in feed	Dietary study; 5 control, mid- and high-dose animals/sex were killed at 30 days	NOAEL–10000 ppm No signs of toxicity	25
Glyceryl Rosinate	Sprague-Dawley rats, 10/sex	28 days	30% in 70% corn oil, given at 0.2% and 1.0%	Dietary study	NOEL–1% No effect on mortality, morbidity, clinical signs, food consumption, or body weight gain; no gross or microscopic lesions	25
Glyceryl Rosinate	Sprague-Dawley rats, 15/sex	90 days	0.2%, 1%, and 5% in corn oil	Dietary study	NOAEL–1% Decreased food consumption during the initial weeks of dosing in males an d females, increased liver weights in females, and increased relative liver-to-body weight in males in the high-dose group	25
Glyceryl Rosinate	Fischer 344 rats, 20/sex/group	90 days	625, 1250, and 2500 mg/kg/d	Dietary study	NOAEL–2500 mg/kg/d No toxic effects	25
Glycerides, C8-18 and C18-unsatd. mono- and di-, acetates	10 male and 5 female Wistar Han rats - Recovery group with an additional 5 males and females in the control and high dose group	28 days	0, 100, 300 and 1000 mg/kg/d; on polyethylene glycol	By gavage	NOAEL–1000 mg/kg bw/d No clinical signs of toxicity; no toxicologically relevant changes in hematology, clinical chemistry, organ weights, or gross or microscopic lesions	22
				MUCOUS MEMBRANE EXPOSURE		
Glycerol Oleate	12 female rhesus macaque monkeys	6 months	5% dissolved in a vaginal lubricant formulation	Intravaginal administration of 1 mL of gel containing 50 mg test article; administration was 2×/day for first 8 weeks; after a 3-week nontreatment period, dosing was 1×/day for 11 weeks	No vaginal inflammation or mucosal lesions in cervical vaginal tissues	42

Abbreviations: NOAEL, no-observable adverse effect level; NOEL, no-observed effect level.

Table 11. Genotoxicity Studies.

Test Article	Concentration/Vehicle	Test System	Procedure	Results	Reference
			IN VITRO		
Glyceryl Acetate	100-10000 μg/plate	*S typhimurium* TA100, TA1535, TA1537, or TA98	Ames test	Not mutagenic	43
Glyceryl Acetate (89% pure)	500-5000 μg/mL in deionized water	CHO cells	Chromosomal aberration assay, with or without metabolic	Not mutagenic	44
Glyceryl Acetate (89% pure)	501-5010 μg/mL, with metabolic activation 1500-5010 μg/mL, without metabolic activation Vehicle—deionized water	CHO cells	SCE assay	Not genotoxic with metabolic activation Positive results without metabolic activation; a dose-dependent increase was observed in 2 trials, and a doubling of SCEs was produced with 5000 μg/mL	44
Glyceryl Laurate	6.25-5000 μg/plate in Tween 80/ bidistilled water (0.1 mL/plate)	*S typhimurium* TA 1535, TA 1537, TA 1538, TA 98, and TA 100	Ames test, with and without metabolic activation (OECD Guideline 471)	Negative Positive controls gave expected results	24
Glyceryl Rosinate	2.5-500 μg/plate (vehicle not specified)	*S typhimurium* TA 1535, TA 1537, TA 1538, TA 98, and TA 100	Ames test, with and without metabolic activation (OECD Guideline 471)	Negative Positive controls gave expected results	45
Glyceryl Rosinate	50.7-507 μg/mL	CHO cells	Mammalian chromosome aberration test, with (2-hour incubation) and without (7.3-hour incubation) metabolic activation (OECD Guideline 473)	Not genotoxic Positive controls gave expected results	45
Glyceryl Rosinate	5.08-102 μg/mL	Rat hepatocyte primary cell cultures	UDS test (OECD Guideline 482)	Not genotoxic Positive controls gave expected results	45
Acetic and fatty acid esters of glycerol	0.61-78 μg/plate (all *S typhimurium* strains, without activation) 10-313 μg/plate (all *S typhimurium* strains, with activation) 313-5000 μg/plate (*E coli*, with and without activation) Vehicle–acetone	*S typhimurium* TA 1535, TA 1537, TA 98, and TA 100; *E. coli* WP2 UVR A	Ames test, with and without metabolic activation (OECD Guideline 471)	Negative Positive controls gave expected results	24
Glyceride, C14-18 and C16-22 unsaturated, mono- and di-	8-5000 μg/plate in Tween 80/ bidistilled water	*S typhimurium* TA 1535, TA 1537, TA1538, TA 98, and TA 100	Ames test, with and without metabolic activation (OECD Guideline 471)	Negative Positive controls gave expected results	22
Glycerides, C8-18 and C18-unsatd. mono- and di-, acetates	Six hours, with and without metabolic activation: 0.02, 0.39, 0.078, and 0.156 mg/mL 24 and 48 hours without activation: 0.078, 0.156, 0.313, 0.625, 1.25, 2.5, 5.0 mg/mL Vehicle: acetone	Chinese hamster lung fibroblasts	Mammalian chromosome aberration test (OECD Guideline 473)	Negative Positive controls gave expected results	22
			IN VIVO		
Glycerides, C16-18 and C18-hydroxy mono- and di-	1000, 5000 (24-hour analysis), or 10000 (24-, 48-, and 72-hour analysis) mg/kg bw	7 male and female CFW 1 mice	Micronucleus test; animals were dosed with a single 20 mL/kg bw by gavage	Negative Positive controls gave expected results	22

Abbreviations: CHO, Chinese hamster ovary; DMSO, dimethyl sulfoxide; OECD, Organisation for Economic Co-operation and Development; SCE, sister chromatid exchange; UDS, unscheduled DNA synthesis.

Table 12. Dermal Irritation and Sensitization.

Test Article	Concentration/Dose	# per Group	Procedure	Results	Reference
DERMAL IRRITATION					
NON-HUMAN					
Glyceryl Behenate	Neat	3 male NZW rabbits	4-hour semiocclusive patch applied to shaved and abraded skin; 0.5-mL applied; animals were observed for up to 7 days	Not irritating Slight erythema was observed in 1 animal at 24 hours; no edema was observed	23
Glycerol ester of partially hydrogenated gum rosin	Neat	NZW rabbits, 2 males and 1 female	4-hour occlusive patch applied to intact skin; 0.5 g applied; animals were observed for up to 72 hours	Not irritating No erythema or edema	25
Glyceryl Rosinate	No vehicle, but moistened with distilled water	3 NZW rabbits	4-hour semiocclusive patch applied to intact skin; 0.5 g applied; animals were observed for up to 72 hours	Not irritating No erythema or edema	25
Glyceryl Rosinate	Neat	3 NZW rabbits	4-hour semiocclusive patch applied to intact and abraded skin; 0.5 g applied; animals were observed for up to 72 hours	Not a primary irritant; at most, a minimal irritant Mean primary cutaneous irritation score was 0.6 Slight to well-defined erythema was observed in damaged skin; slight erythema in intact skin	25
Glyceryl Rosinate	Neat	3 NZW rabbits	4-hour semiocclusive; 0.5 g applied to intact and abraded skin; animals were observed for up to 72 hours	Not a primary irritant; at most, a minimal irritant Mean primary cutaneous irritation score was 0.3 Slight to well-defined erythema was observed in damaged skin; slight erythema in intact skin	25
Glyceryl Rosinate	No vehicle, but moistened with distilled water	NZW rabbits, 2 males and 1 female	24-hour occlusive patch applied to intact skin; 0.5 g applied; animals were observed for up to 72 hours	Not irritating No erythema or edema	25
Glyceryl Stearate	75% in vaseline	3 NZW rabbits	4-hour semiocclusive patch; 0.5 mL applied; animals were observed for 72 hours	No irritating No erythema or edema	22
HUMAN					
Glyceryl Stearate	5% emulsion in a mineral oil/water mixture (50:50)	20 subjects	A 12-mm Finn chamber containing 50 μL of the test article was applied for 48 hours to the volar forearm of each subject using adhesive tape; the test sites were evaluated 24 hours after patch removal on a scale of 0-3; TEWL) was measured using an evaporimeter	No difference in erythema between treated and control sites; the median value for clinical erythema was 0 at the Glyceryl Stearate–treated site (with 5% of the observations having a score >1, ie, slight erythema, spotty, o= diffuse) and 0.5 at the control site (with 10% of the observations having a score >1) No significant effect on TEWL when compared to the control	46
Glyceryl Stearate	5% emulsion in a mineral oil/water mixture (50:50)	27 subjects	SLS (15% for 7 hours) was used prior to application of the test article; 17-hour patches were then applied to the SLS-treated skin	No difference in the erythema between treated and control site; with application to irritated skin, the median value for clinical erythema was 1 both at the Glyceryl Stearate–treated site and control site; 22% of the observations at the test site and 15% of the observations at the control site had a score >1 No significant effect on TEWL	46

(continued)

Table 12. (continued)

Test Article	Concentration/Dose	# per Group	Procedure	Results	Reference
			SENSITIZATION		
			NON-HUMAN		
Glycerol ester of partially hydrogenated gum rosin	10% in corn oil 25% in petroleum jelly	5 male and 5 female Hartley guinea pigs	GPMT Intradermal induction: 3 pairs of intradermal injections: (1) FCA with an equal volume of water; (2) test article (10%) in vehicle; (3) test article (10%) in a 50:50 mixture of FCA and vehicle Topical induction: 6 days after intradermal induction, the test site was pretreated with 10% SLS; a 48-hour occlusive patch (25% test article) was applied the next day Challenge: Topical challenge with 24-hour occlusive patches (25% test article) was performed after a 2-week nontreatment period	Not an irritant or a sensitizer	25
Glycerol ester of partially hydrogenated gum rosin	Neat for induction 25% and 50% in in paraffin oil for challenge	Female Hartley guinea pigs	As above	Not an irritant or a sensitizer	25
Glyceryl Rosinate	Intradermal induction: 7.5% Topical induction: 83.3% Topical challenge: 83.3% and 41.65% In a coconut oil product	20 female Dunkin-Hartley guinea pigs	GPMT Intradermal induction: 3 pairs of intradermal injections: (1) FCA with an equal volume of water; (2)test article in vehicle; (3) test article in a 50:50 mixture of FCA and vehicle Topical induction: 6 days after intradermal induction, the test site was pretreated with SLS; a 48-hour occlusive patch was applied the next day Challenge: Topical challenge with 48-hour occlusive patches was performed after a 2-week nontreatment period	Not a sensitizer Slight to well-defined erythema was observed during the first 48 hours in both control and test article-treated animals challenged at 83.3%; all animals appeared normal after 72 hours	25
Glyceryl Rosinate	Induction: 100% Challenge: 6.25% and 12.5% in paraffin oil	15 female Dunkin-Hartley guinea pigs	GPMT Induction: On day 0, test animals received 2 injections of FCA, the skin was abraded, and a 498-hour semiocclusive patch was applied; on day 7, a second 48-hour semiocclusive patch was applied Challenge: Topical challenge with 24-hour semiocclusive patches was performed after a 2-week nontreatment period	Not an irritant or a sensitizer	25
Glyceride, C16-18 and C18 Mono- and Dihydroxy	Induction: 50% in paraffin oil Challenge: 25% in vaseline	20 female Pirbright white guinea pigs	Induction: 1 intradermal (day 0) and 1 occlusive 48-hour epicutaneous (day 7) exposure, with FCA Challenge: 24-hour occlusive patch applied 14 days after second induction exposure	Not a sensitizer	22

(continued)

Table 12. (continued)

Test Article	Concentration/Dose	# per Group	Procedure	Results	Reference
			HUMAN		
Glyceryl Behenate	Applied neat	93 subjects	HRIPT; 0.2 g applied with an occlusive patch Nine 24-hour patches induction patches were applied (3×/wk for 3 weeks); the challenge patch was applied to a previously untreated site after a 2-week nontreatment period	Not a sensitizer	23
Glycerol ester of partially hydrogenated gum rosin	Not stated, assumed neat	202 subjects	HRIPT Induction: 24-hour occlusive patches were applied 3×/wk for 3 weeks Challenge: Patches were applied to the original site and a previously untreated site after a 2-week nontreatment period	Not an irritant or a sensitizer	25
Glyceryl Rosinate	Not stated	25 male and 25 female subjects	HRIPT Induction: Patches were applied every other day, for a total of 15 applications Challenge: 24-hour patch was applied after a 2-week nontreatment period	Not an irritant or a sensitizer	25
Glyceryl Rosinate	Not stated	100 male and 100 female subjects	Schwartz patch test 5-day exposure for induction; challenge after a 6-week nontreatment period, a 48-hour patch was applied	Not an irritant or a sensitizer	25

Abbreviations: FCA, Freund's Complete Adjuvant; GPMT, guinea pig maximization test; HRIPT, human repeated insult patch test; ME, microemulsion; NZW, New Zealand White; TEWL, transepidermal water loss.

Table 13. Ocular Irritation Studies.

Test Article	Concentration	#/Animals/Grp	Method	Results	Reference
NON-HUMAN					
Glyceryl Behenate	Undiluted	3 male NZW rabbits	Single instillation; 0.1 mL Eyes were not rinsed	Not irritating; slight lacrimation in all animals at 1 hour and 1 animal at 24 hours; no other ocular effects were observed	23
Glyceryl Palmitate/ Stearate	Undiluted	6 NZW rabbits	Single instillation; 0.1 mL Eyes were not rinsed	Not irritating	22
Glyceryl Rosinate	Undiluted	6 NZW rabbits	Single instillation; 100 mg	Slightly irritating; mild irritation (of the conjunctiva was observed in 4 rabbits at 24 hours	25
Glyceryl Rosinate	Undiluted	6 NZW rabbits	Single instillation; 100 mg	Slightly irritating; slight signs of irritation to the cornea, iris, and the conjunctiva; conjunctival irritation did not fully reverse in 2 animals within 72 hours	25

Abbreviation: NZW, New Zealand White.

Table 14. Case Reports.

Ingredient	Case History	Patch Testing	Reference
Glyceryl Caprylate	Female with a history of facial eczema for several years that occurred after application of a skin care cream; the cream was composed of 90% Glyceryl Caprylate, 6% glyceryl dicaprylate, 4% free glycerol, and <0.1% glyceryl tricaprylate	- A 24-hour occlusive patch test with several allergen series and the patient's products resulted in positive reactions to several compounds at 72 hours - A subsequent ROAT with the patient's own products, applied 2×/day for 1 week, resulted in a distinct reaction (erythema and vesicles) with the product containing 90% Glyceryl Caprylate - Additional patch testing with 5% Glyceryl Caprylate in pet gave a +++ reaction - Further patch testing with 0.1% and 1.0% Glyceryl Caprylate (in pet) produced a + and +++ reaction, respectively - No reactions were observed in 3 control subjects patched tested with 5% in pet	47
Glyceryl Hydrogenated Rosinate	Female with severe bullous eruption on the wrist and hand following repeated application of a medicated patch	- Patch testing with a standard series, the patch, and constituents of the patch, including 20% Glyceryl Hydrogenated Rosinate in pet resulted in a strong positive reaction (+++) to the patch and to Glyceryl Hydrogenated Rosinate on days 2 and 4 - No reactions were observed in 5 control subjects	48
Glyceryl Isostearate	Female with a history of persistent itchy and scaly erythema on the lips that appeared after using 5 different lipsticks	- Patient had positive patch test reactions to all 5 lipsticks and 4 ingredients from 2 of the formulations, including 1% Glyceryl Isostearate in pet. - No reactions were observed in 3 control subjects patched tested with the same ingredients	49
Glyceryl Rosinate	Female with history of venous eczematous ulcerations on both legs, with recurrent eczematous dermatitis presented with an ulcer after application of medicated wound dressings; patient had sensitivities to multiple compounds	- Positive patch test (+) to a medicated patch and 20% Glyceryl Rosinate in pet	50
Glyceryl Stearate	Female with dermatitis of the arms due to a body lotion that was originally used for months without an effect	- Patch testing with the lotion had positive (+) results - Subsequent testing with ingredients of the lotion resulted in positive reaction to 20% Glyceryl Stearate in pet (?+ at 48 hours; + at 72 hours) - No reactions were observed in 20 control subjects	51

Abbreviations: Pet, petrolatum; ROAT, repeated open application test.

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