Safety Assessment of Fatty Ester End-Capped Alkoxylates as Used in Cosmetics

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ABBREVIATIONS

CIR = Cosmetic Ingredient Review
Council = Personal Care Products Council
CPSC = Consumer Product Safety Commission
DART = developmental and reproductive toxicity
ET_{50} = exposure time that induces a 50% reduction in viability
FDA = Food and Drug Administration
Panel = Expert Panel for Cosmetic Ingredient Safety
PEG = polyethylene glycol
PPG = polypropylene glycol
VCRP = Voluntary Cosmetic Registration Program
wINCI *Dictionary* = web-based *International Cosmetic Ingredient Dictionary and Handbook*

ABSTRACT

The Expert Panel for Cosmetic Ingredient Safety (Panel) assessed the safety of 14 fatty ester end-capped alkoxylates as used in cosmetics. The majority of these ingredients are reported to function as surfactants – emulsifying agents in cosmetic formulations, and some are reported to function as skin-conditioning agents. The Panel reviewed the available data to determine the safety of these ingredients. The Panel concluded that the 14 fatty ester end-capped alkoxylates are safe in cosmetics in the present practices of use and concentration described in this safety assessment.

INTRODUCTION

This assessment reviews the safety of the following 14 fatty ester end-capped alkoxylates as used in cosmetic formulations:

PEG/PPG-8/3 Diisostearate
PEG-15 Butylene Glycol Diisostearate
PEG-10 Glyceryl Diisostearate
PEG-15 Glyceryl Diisostearate
PEG-20 Glyceryl Diisostearate
PEG-30 Glyceryl Diisostearate
PEG-60 Glyceryl Diisostearate
PEG-12 Glyceryl Dimyristate
PEG-12 Glyceryl Dioleate
PEG-3 Glyceryl Distearate
PEG-4 Glyceryl Distearate
PEG-12 Glyceryl Distearate
PEG-23 Glyceryl Distearate
PEG-4 Polyglyceryl-2 Distearate

Most of the fatty ester end-capped alkoxylates presented in this safety assessment are glyceryl or polyglyceryl di-fatty acid esters with ethylene glycol repeat units. According to the web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI; *Dictionary*), these ingredients function mainly as surfactants – emulsifying agents, skin-conditioning agents – emollients, and skin-conditioning agents – miscellaneous in cosmetic formulations (Table 1).[1] At the time this safety assessment was written, PEG-3 Glyceryl Distearate was not listed in the *Dictionary*, but it has reported uses in the US Food and Drug Administration (FDA) Voluntary Cosmetic Registration Program (VCRP) database.

The Expert Panel for Cosmetic Ingredient Safety (Panel) has reviewed numerous related ingredients, including glyceryl diesters, triethylene glycol and polyethylene glycols (PEGs) > 4, PEG diesters, PEGylated oils, and monoglyceryl monoesters, and concluded these ingredients are safe or safe with qualifications.[2-7] A full listing of the related report families, specific related ingredients, and the conclusions of safety determined by the Panel for these ingredients are provided in Table 2.

This safety assessment includes relevant published and unpublished data that are available for each endpoint that is evaluated. Published data are identified by conducting an exhaustive search of the world's literature. A listing of the search engines and websites that are used and the sources that are typically explored, as well as the endpoints that the Panel typically evaluates, is provided on the Cosmetic Ingredient Review (CIR) website (https://www.cir-safety.org/supplementaldoc/preliminary-search-engines-and-websites; https://www.cir-safety.org/supplementaldoc/cir-report-format-outline). Unpublished data are provided by the cosmetics industry, as well as by other interested parties.

CHEMISTRY

Definition and Structure

The definitions and idealized structures of the fatty ester end-capped alkoxylated ingredients included in this review are provided in Table 1. Most of the fatty ester end-capped alkoxylates presented in this safety assessment comprise a glycerin core, which is PEGylated (i.e., substituted with multiple ethylene glycol repeat units) and end-capped with fatty acid esters on 2 of the 3 termini (i.e., glycerin is tridentate (a triol), wherein all 3 alcohol functional groups are PEGylated ending in a terminal that may be esterified). Two of the 3 alcohols of glycerin are primary (i.e., the carbon the alcohol is attached to is only attached to 1 other carbon) and the remaining 1 is secondary (i.e., the carbon the alcohol is attached to is attached to 2 other carbons). The resulting PEG chains on those 2 primary alcohol functional groups, are the ones to be esterified. The number of units (e.g., "10" in PEG-Glyceryl Diisostearate) is representative of an average number of ethylene glycol repeat units (i.e., PEG-10 Glyceryl Diisostearate contains some PEG-9 and PEG-11 glyceryl diisostearate, in addition to PEG-10). For example, PEG-20 Glyceryl Diisostearate comprises a glycerin core that is PEGylated across those 3 alcohol functional groups and esterified on two of the resulting PEG chains with isostearic acid (Figure 1).

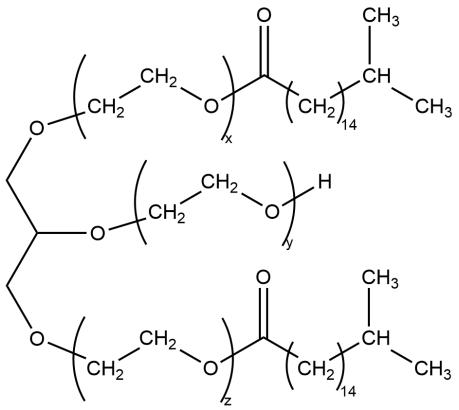


Figure 1. PEG-20 Glyceryl Diisostearate, wherein x + y + z = 20

For PEG/PPG-8/3 Diisostearate, in addition to the ethylene glycol repeat units, it also has polypropylene glycol (PPG) repeat units.

Most of the alkoxylate end-caps are stearates (i.e., 18-carbon alkyl chains). However, one ingredient is end-capped with 14-carbon alkyl chains (i.e., myristate) and one ingredient is end-capped with 18-carbon *alkenyl* chains (i.e., oleate).

Chemical Properties

A supplier reported that the molecular weight of PEG/PPG-8/3 Diisostearate is 1630 Da.[8] At room temperature, PEG-12 Glyceryl Dioleate is reported to be a liquid, while PEG-12 Glyceryl Distearate is reported to be a waxy solid.[9]

No further chemical properties data were found in the published literature, nor were additional unpublished data submitted.

Method of Manufacture

Most of the ingredients in this report comprise a glycerin core, and are manufactured rather differently. Ingredients with structures such as these are typically synthesized from the appropriate glyceryl diester (i.e. not PEGylated).[6] In such methods, the PEGylation effectually results in transesterification, or direct insertion of the PEG chain between the glycerin molecule and the fatty acid. For example, PEG-20 Glyceryl Diisostearate could be synthesized by PEGylation of Glyceryl Diisostearate. The 20 equivalents of ethylene oxide (the "20" in "PEG-20") are thus distributed across the 3 termini: some at the free alcohol functional group of the glycerin core, and the rest inserted in the 2 isostearic esters.

PEG/PPG-8/3 Diisostearate

A supplier has reported that PEG/PPG-8/3 Diisostearate is produced through the condensation of fatty acids (i.e., isostearic acid) with alcohols (i.e., polyethylene glycol/polypropylene glycol).[10] The esterification is acid-catalyzed. The by-product, water, is removed with the aid of heat and vacuum. No solvents are used in the manufacturing process.

PEG-15 Butylene Glycol Diisostearate

A supplier has reported that PEG-15 Butylene Glycol Diisostearate is produced through addition polymerization of ethylene oxide to 1,3-butylene glycol, followed by diesterification with isostearic acid.[11] No further details were provided.

PEG-10 Glyceryl Diisostearate, PEG-20 Glyceryl Diisostearate, PEG-30 Glyceryl Diisostearate, PEG-60 Glyceryl Diisostearate

A supplier has reported that PEG-10 Glyceryl Diisostearate, PEG-20 Glyceryl Diisostearate, PEG-30 Glyceryl Diisostearate, and PEG-60 Glyceryl Diisostearate are produced through addition polymerization of ethylene oxide to glycerin, followed by diesterification with isostearic acid.[11] No further details were provided.

PEG-4 Glyceryl Distearate

A supplier has reported that PEG-4 Glyceryl Distearate is produced through addition polymerization of ethylene oxide to glycerin, followed by diesterification with stearic acid.[11] No further details were provided.

Impurities

PEG/PPG-8/3 Diisostearate

A supplier has reported that the purity of PEG/PPG-8/3 Diisostearate is > 95%.[8] An expected impurity is isostearic acid (< 0.5%).

PEG-15 Butylene Glycol Diisostearate

A supplier has reported that the purity of PEG-15 Butylene Glycol Diisostearate is 100%.[11] Impurities may include isostearic acid (≤ 5%) and ethylene oxide (≤ 1 ppm).

PEG-10 Glyceryl Diisostearate, PEG-20 Glyceryl Diisostearate, PEG-30 Glyceryl Diisostearate, PEG-60 Glyceryl Diisostearate

A supplier has reported that the purity of PEG-10 Glyceryl Diisostearate, PEG-20 Glyceryl Diisostearate, PEG-30 Glyceryl Diisostearate, and PEG-60 Glyceryl Diisostearate is 100%.[11] Impurities may include isostearic acid (≤ 4%) and ethylene oxide (≤ 1 ppm).

PEG-4 Glyceryl Distearate

A supplier has reported that the purity of PEG-4 Glyceryl Distearate is 100%.[11] Impurities may include stearic acid (≤ 2%) and ethylene oxide (≤ 1 ppm).

USE

Cosmetic

The safety of the cosmetic ingredients addressed in this assessment is evaluated based on data received from the US FDA and the cosmetics industry on the expected use of these ingredients in cosmetics, and does not cover their use in airbrush delivery systems. Data are submitted by the cosmetic industry via the FDA's VCRP database (frequency of use) and in response to a survey conducted by the Personal Care Products Council (Council) (maximum use concentrations). The data are provided by cosmetic product categories, based on 21CFR Part 720. For most cosmetic product categories, 21CFR Part 720 does not indicate type of application and, therefore, airbrush application is not considered. Airbrush delivery systems are within the purview of the US Consumer Product Safety Commission (CPSC), while ingredients, as used in airbrush delivery systems, are within the jurisdiction of the FDA. Airbrush delivery system use for cosmetic application has not been evaluated by the CPSC, nor has the use of cosmetic ingredients in airbrush technology been evaluated by the FDA. Moreover, no consumer habits and practices data or particle size data are publicly available to evaluate the exposure associated with this use type, thereby preempting the ability to evaluate risk or safety.

According to 2022 VCRP survey data, PEG/PPG-8/3 Diisostearate is reported to be used in 98 formulations, with most of them being in bath soaps and detergents (Table 3).[12] The other 3 in-use ingredients in the VCRP are reported to be used in one or two formulations. The results of the concentration of use surveys conducted by the Council in 2019-2022 indicate PEG/PPG-8/3 Diisostearate has the highest concentration of use in a leave-on formulation; it is used at 5% in a leave-on hair conditioner.[13] PEG-12 Glyceryl Dimyristate has the next highest concentration of use in a leave-on formulation; it is used at up to 1.8% in body and hand products.[14] The 10 ingredients not in use according to the VCRP and industry survey are listed in Table 4.

Fatty ester end-capped alkoxylates may be used in cosmetic formulations that may be used near the eye or come into contact with mucous membranes. For example, PEG-12 Glyceryl Dimyristate is reported to be used in an eye lotion at 0.7% and PEG/PPG-8/3 Diisostearate is reported to be used in bubble baths and bath soaps and detergents (concentrations not reported).[12-14] Additionally, some of the fatty ester end-capped alkoxylates are used in cosmetic sprays and could possibly be inhaled; for example, PEG-12 Glyceryl Dimyristate is reported to be used at 1% in hair sprays.[14] In practice, as stated in the Panel's respiratory exposure resource document (https://www.cir-safety.org/cir-findings), most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and tracheobronchial regions and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.

Although products containing some of these ingredients may be marketed for use with airbrush delivery systems, this information is not available from the VCRP or the Council survey. Without information regarding the frequency and concentrations of use of these ingredients, and without consumer habits and practices data or particle size data related to this use technology, the data are insufficient to evaluate the exposure resulting from cosmetics applied via airbrush delivery systems.

All of the fatty ester end-capped alkoxylates named in the report are not restricted from use in any way under the rules governing cosmetic products in the European Union.[15]

Non-Cosmetic

PEG-12 Glyceryl Dioleate and PEG-12 Glyceryl Distearate, have been studied for use as liposomal drug carriers (encapsulation) and/or solubilizers in oral and intravenous pharmaceutical and nutraceutical products.[9,16] PEG-12 Glyceryl Distearate and PEG-23 Glyceryl Distearate have been used as part of an inactive cream formulation used to study topically applied drugs for wound healing.[17] PEG-12 Glyceryl Dimyristate was studied for use in controlled-release liposomal drug carriers for use in topical ophthalmic therapies to the back of the eye as a replacement for intravitreal injections.[18,19]

TOXICOKINETIC STUDIES

Dermal Penetration

A supplier stated that, due to its molecular weight, PPG/PPG-8/3 Diisostearate is not expected to penetrate the skin or be bioavailable.[8]

Toxicokinetics studies were not found in the published literature, and additional unpublished data were not submitted for the remaining fatty ester end-capped alkoxylates described in this safety assessment.

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

Oral

PEG/PPG-8/3 Diisostearate

A supplier reported that the LD_{50} for PEG/PPG-8/3 Diisostearate in an acute oral rat study was greater than 2000 mg/kg.[20] Data was from initial reacted materials. No further details were provided.

Short-Term Toxicity Studies

Dermal

PEG-12 Glyceryl Distearate and PEG-23 Glyceryl Distearate

PEG-12 Glyceryl Distearate and PEG-23 Glyceryl Distearate were used in a base cream that was used as a placebo and as part of a pharmaceutical test compound in a dermal efficacy study in groups of 7 female Wistar rats.[17] The placebo and test compounds were applied to damaged skin twice daily for up to 15 d. The amount of PEG-12 Glyceryl Distearate and PEG-23 Glyceryl Distearate in the base cream was not reported. No mortalities were observed during the testing period in either the placebo or treatment groups.

Oral

PEG-12 Glyceryl Dioleate and PEG-12 Glyceryl Distearate

In a 28-d oral toxicity study, groups of 5 male and 5 female Sprague- Dawley rats received 0, 250, 500, or 1000 mg/kg PEG-12 Glyceryl Dioleate or PEG-12 Glyceryl Distearate in a volume of 5 ml/kg via gavage.[9] The vehicle was corn oil. Observations for clinical signs of toxicity were made at 10, 30, 60, and 120 min and at 4 and 6 h post- dosing starting on day 1 and daily for 28 d. Animals were observed twice daily for mortality. Body weight gains were recorded on day 0 and at weekly intervals throughout the study. Feed consumption by test groups was recorded weekly, and feed consumption per rat was calculated. Urinalysis was performed after the dosing period concluded. Hematological and plasma parameters were also measured after the dosing period concluded. The rats were killed and necropsied. Histopathological examinations of the liver and kidneys were made in the control and high dose groups.

No mortalities or clinical signs of toxicity were reported during the 28-d dosing period. Body weight gains and feed consumption in the treated animals were comparable to the controls. No statistically significant changes were noted in hematological or plasma parameters. No significant findings were reported in urinalyses. There were no abnormalities reported following necropsy and histopathological examination. The authors of this study concluded that PEG-12 Glyceryl Dioleate and PEG-12 Glyceryl Distearate was non-toxic in rats.[9]

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY STUDIES

Developmental and reproductive toxicity (DART) data were not found in the published literature, and unpublished data were not submitted.

GENOTOXICITY STUDIES

Genotoxicity data were not found in the published literature, and unpublished data were not submitted.

CARCINOGENICITY STUDIES

Carcinogenicity data were not found in the published literature, and unpublished data were not submitted.

DERMAL IRRITATION AND SENSITIZATION

Human

PEG/PPG-8/3 Diisostearate

The dermal irritation and sensitization potential of a material identified as PEG/PPG-8/3 Diisostearate was studied in 114 subjects.[21] The subjects were induced with four 24-h applications of the test material (150 µl, neat) per week for 3 wk on the left upper back, followed by a week hiatus prior to four, 24-h challenge patches on naïve sites. Patches were occlusive

devices with a 2 cm^2 absorbent pad centered on the adhesive-coated surface of a 4 cm^2 water-impermeable plastic film. No clinically significant adverse effects were detected during the induction or challenge phases. The test material, when tested neat, was determined to be non-irritating and non-sensitizing.

OCULAR IRRITATION STUDIES

In Vitro

PEG/PPG-8/3 Diisostearate

A supplier has reported that PEG/PPG-8/3 Diisostearate in 10% corn oil was non-irritating in an EpiOcular™ tissue model.[20] The exposure time that induces a 50% reduction in viability (ET_{50}) was greater than 256 min, and the estimated Draize score was 0. No further details were provided.

Animal

PEG-12 Glyceryl Dimyristate

The ocular irritation potential of a topical drug formulation containing PEG-12 Glyceryl Dimyristate (100 mg; 10% w/v) was assessed in 32 male New Zealand White rabbits.[19] The rabbits received 1 drop (50 µl) of the test formulation in the right eye, every 2 h, 6 times/d (number of treatment days not reported). Control eyes received a saline balanced placebo solution. Clinical eye evaluations were then carried out under anesthesia at 10, 30, and 60 min, 6, 12, and 24 h, and 7 and 14 d post treatment. Four rabbits were killed after each clinical evaluation to obtain ocular tissue and fluids. No major findings or adverse effects were reported during the study. A Draize score of 1 was reported 30 min post-dosing, which resolved by the end of the 14-d observation period. No details regarding the scoring parameter that achieved this score at this observation point were provided. No increase in intraocular pressure was observed in any of the animals.

CLINICAL STUDIES

Ocular

PEG-12 Glyceryl Dimyristate

The tolerability, safety, and efficacy of a topical formulation containing PEG-12 Glyceryl Dimyristate (100 mg; 10% w/v) was evaluated in one eye of 12 patients with refractory pseudophakic cystoid macular edema.[18] The patients received one drop of the test material every 2 h for 90 d or until best-corrected visual acuity was achieved. No ocular surface abnormalities or adverse events were observed.

In another safety and tolerability study of the same formulation containing PEG-12 Glyceryl Dimyristate, 20 healthy male and female subjects received topical doses (one drop) in one eye 6 times/d for 2 wk, followed by 1 wk of monitoring.[19] No systemic adverse effects were reported. Mild burning and dryness of the eye (n = 6), moderate discharge (n = 2), mild tearing (n = 3), and mild blurred vision (n = 2) were reported after the end of the treatment period (day 14) and at the end of the monitoring period (day 21). No pain or discomfort were reported. No eyelid redness, conjunctival hyperemia, or edema were observed on day 21.

The same formulation containing PEG-12 Glyceryl Dimyristate was also used to assess biologic activity in 4 patients with diabetic macular edema.[19] The patients received topical doses (1 drop) in one eye 6 times/d for 6 mo. Follow-up ophthalmic clinical evaluations were performed monthly. No systemic or severe adverse effects were reported. None of the patients showed intraocular hypertension.

SUMMARY

Most of the fatty ester end-capped alkoxylates presented in this safety assessment are glyceryl fatty acid esters with ethylene glycol repeat units. According to the *Dictionary*, these ingredients function mainly as surfactants – emulsifying agents, skin-conditioning agents – emollients, and skin-conditioning agents – miscellaneous in cosmetic formulations. At the time this safety assessment was written, PEG-3 Glyceryl Distearate was not listed in the *Dictionary*, but it has reported uses in the FDA VCRP database.

A supplier has reported that PEG/PPG-8/3 Diisostearate is produced through the condensation of fatty acids (i.e., isostearic acid) with alcohols (i.e., polyethylene glycol/polypropylene glycol). The esterification is acid-catalyzed. PEG-15 Butylene Glycol Diisostearate is produced through addition polymerization of ethylene oxide to 1,3-butylene glycol, followed by diesterification with isostearic acid. PEG-10 Glyceryl Diisostearate, PEG-20 Glyceryl Diisostearate, PEG-30 Glyceryl Diisostearate, and PEG-60 Glyceryl Diisostearate are produced through addition polymerization of ethylene oxide to glycerin, followed by diesterification with isostearic acid. PEG-4 Glyceryl Distearate is produced through addition polymerization of ethylene oxide to glycerin, followed by diesterification with stearic acid.

A supplier has reported that the purity of PEG/PPG-8/3 Diisostearate is > 95%. PEG-15 Butylene Glycol Diisostearate, PEG-10 Glyceryl Diisostearate, PEG-20 Glyceryl Diisostearate, PEG-30 Glyceryl Diisostearate, and PEG-60 Glyceryl

Diisostearate, and PEG-4 Glyceryl Distearate were reported to be 100% pure. Impurities may include isostearic acid, ethylene oxide, and/or stearic acid.

According to 2022 VCRP survey data, PEG/PPG-8/3 Diisostearate is reported to be used in 98 formulations, with most of them being in bath soaps and detergents. All other in-use ingredients in the VCRP (n = 3) are reported to be used in one or two formulations. The results of the concentration of use survey conducted by the Council indicate PEG/PPG-8/3 Diisostearate has the highest concentration of use in a leave-on formulation; it is used at 5% in a leave-on hair conditioner. PEG-12 Glyceryl Dimyristate has the next highest concentration of use in a leave-on formulation; it is used at up to 1.8% in body and hand products.

A supplier reported that the LD_{50} for PEG/PPG-8/3 Diisostearate in an acute oral rat study was greater than 2000 mg/kg. In a short-term toxicity study, PEG-12 Glyceryl Distearate and PEG-23 Glyceryl Distearate, used in a base cream for pharmaceutical efficacy testing, caused no mortalities in female rats when applied twice daily for up to 15 d. PEG-12 Glyceryl Dioleate and PEG-12 Glyceryl Distearate at up to 1000 mg/kg in corn oil caused no mortalities or clinical signs of toxicity in a 28-d oral toxicity study in male and female rats. No abnormalities were observed at necropsy or in histopathological examination.

In a repeated insult patch test in 114 subjects, PEG/PPG-8/3-Diisostearate tested neat was non-irritating and non-sensitizing. PEG/PPG-8/3-Diisostearate in corn oil was determined to be non-irritating in an in vitro ocular study. In male rabbits, PEG-12 Glyceryl Dimyristate (100 mg; 10% w/v) was not an ocular irritant in a topical drug formulation where the rabbits were treated 6 times/d for several days. The same formulation was tested for tolerability, safety, and efficacy in healthy human volunteers and in patients with macular edema: no abnormalities or adverse events were observed.

Minimal data on chemical properties and impurities were made available via unpublished data submissions and no data were found in the published literature. The information on chemical and physical properties indicate that dermal penetration would be minimal. No toxicokinetic studies, DART studies, genotoxicity studies, or carcinogenicity studies were found in the published literature; and unpublished data were not submitted.

DISCUSSION

The Panel reviewed the safety of 14 fatty ester end-capped alkoxylates, which are reported to function mainly as surfactants and skin-conditioning agents in cosmetic products. Most of these ingredients are glyceryl or polyglyceryl di-fatty acid esters with ethylene glycol repeat units. The method of manufacturing and impurities data indicate these ingredients are produced similarly. The Panel concluded that the available data are sufficient for determining safety of these ingredients as reportedly used in cosmetics. The Panel noted the potential for ethylene oxide as an impurity; however, this chemical is extremely volatile and not expected to remain during formulation. The Panel also noted the lack of DART and genotoxicity studies for fatty ester end-capped alkoxylated ingredients; however, these ingredients are large molecules (>1600 Da) and are not likely to readily absorb through the skin. This finding, coupled with the favorable safety profile and lack of structural features associated with genotoxicity, obviated the need for DART and genotoxicity data.

The Panel discussed the issue of incidental inhalation exposure resulting from these ingredients. (For example, PEG-12 Glyceryl Dimyristate is reported to be used at 1% in hair sprays.) Inhalation toxicity data were not available on any of the fatty ester end-capped alkoxylated ingredients in this safety assessment. However, the Panel noted that in aerosol products, the majority of the droplets/particles would not be respirable to any appreciable amount. Furthermore, droplets/particles deposited in the nasopharyngeal or tracheobronchial 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 low concentrations at which the ingredients are used (or expected to be used) in potentially inhaled products, 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.

The Panel's respiratory exposure resource document (see link above) notes that airbrush technology presents a potential safety concern, and that no data are available for consumer habits and practices thereof. As a result of deficiencies in these critical data needs, the safety of cosmetic ingredients applied by airbrush delivery systems cannot be assessed by the Panel. Therefore, the Panel has found the data insufficient to support the safe use of cosmetic ingredients applied via an airbrush delivery system.

CONCLUSION

The Expert Panel for Cosmetic Ingredient Safety concluded that the following 14 fatty ester end-capped alkoxylates are safe in cosmetics in the present practices of use and concentration described in this safety assessment.

PEG/PPG-8/3 Diisostearate
PEG-15 Butylene Glycol Diisostearate*
PEG-10 Glyceryl Diisostearate*
PEG-15 Glyceryl Diisostearate*
PEG-20 Glyceryl Diisostearate*
PEG-30 Glyceryl Diisostearate*
PEG-60 Glyceryl Diisostearate*
PEG-12 Glyceryl Dimyristate

PEG-12 Glyceryl Dioleate*
PEG-3 Glyceryl Distearate
PEG-4 Glyceryl Distearate*
PEG-12 Glyceryl Distearate
PEG-23 Glyceryl Distearate*
PEG-4 Polyglyceryl-2 Distearate*

**Not reported to be in current use.*

TABLES

Table 1. Definitions, reported functions, and idealized structures of the ingredients in this safety assessment[1], CIR Staff

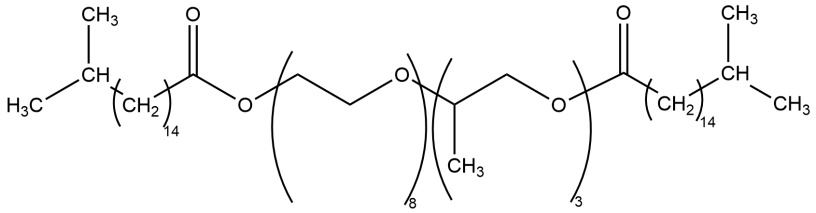
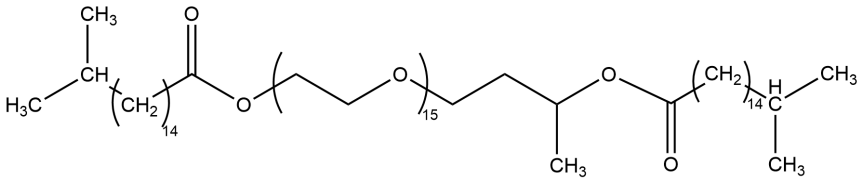
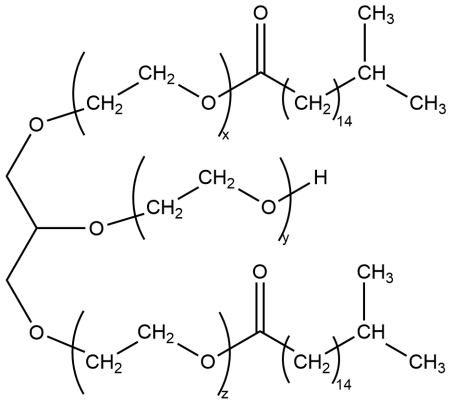
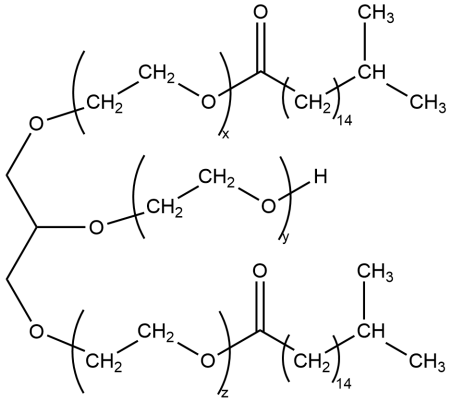
Ingredient & CAS No.	Definition	Function(s)
PEG/PPG-8/3 Diisostearate	PEG/PPG-8/3 Diisostearate is the polyethylene glycol ether of the propoxylated diester of isostearic acid containing an average ethoxylation value of 8 and propoxylation value of 3. (*Drawn block-style; connectivity may be different.*) 	Surfactant – Emulsifying Agent
PEG-15 Butylene Glycol Diisostearate	PEG-15 Butylene Glycol Diisostearate is the polyethylene glycol derivative of the diester of 1,3-butylene glycol and isostearic acid containing an average of 15 moles of ethylene oxide. (*Drawn block-style; connectivity may be different.*) 	Surfactant – Emulsifying Agent
PEG-10 Glyceryl Diisostearate	PEG-10 Glyceryl Diisostearate is the polyethylene glycol ether of glyceryl diisostearate that conforms generally to the structure:  where x+y+z has an average value of 10.	Surfactant – Emulsifying Agent
PEG-15 Glyceryl Diisostearate	PEG-15 Glyceryl Diisostearate is the polyethylene glycol ether of glyceryl diisostearate that conforms generally to the structure:  where x+y+z has an average value of 15.	Surfactant – Emulsifying Agent

Table 1. Definitions, reported functions, and idealized structures of the ingredients in this safety assessment[1],[CIR Staff]

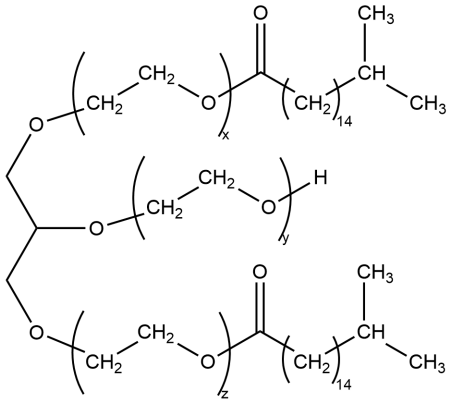
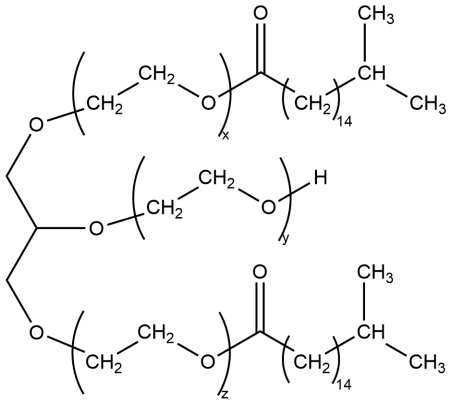
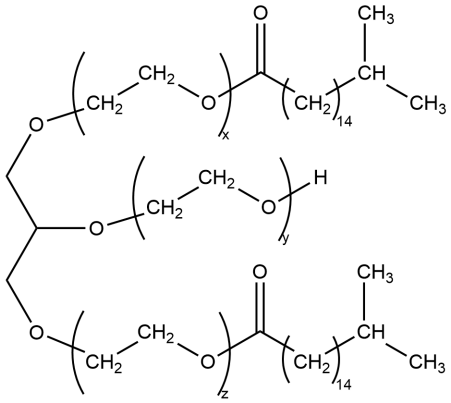
Ingredient & CAS No.	Definition	Function(s)
PEG-20 Glyceryl Diisostearate	PEG-20 Glyceryl Diisostearate is the polyethylene glycol ether of glyceryl diisostearate that conforms generally to the structure:  where x+y+z has an average value of 20.	Surfactant – Emulsifying Agent
PEG-30 Glyceryl Diisostearate	PEG-30 Glyceryl Diisostearate is the polyethylene glycol ether of glyceryl diisostearate that conforms generally to the structure:  where x+y+z has an average value of 30.	Surfactant – Emulsifying Agent
PEG-60 Glyceryl Diisostearate	PEG-60 Glyceryl Diisostearate is the polyethylene glycol ether of glyceryl diisostearate that conforms generally to the structure:  where x+y+z has an average value of 60.	Surfactant – Emulsifying Agent

Table 1. Definitions, reported functions, and idealized structures of the ingredients in this safety assessment[1],[CIR Staff]

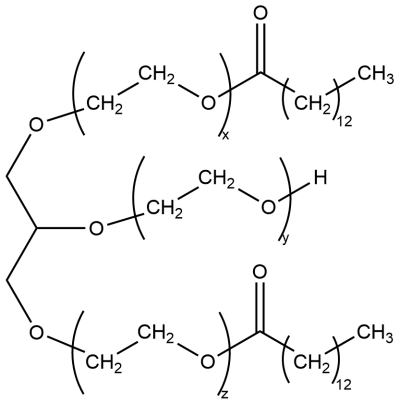
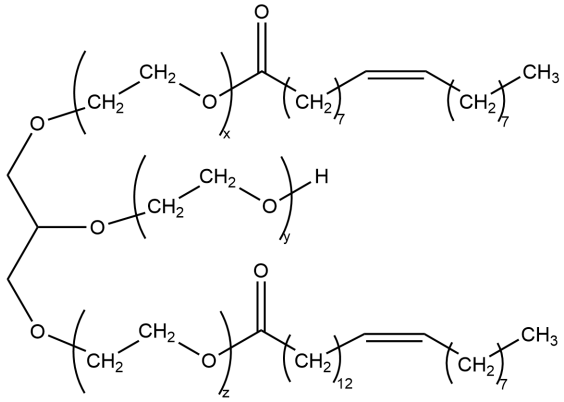
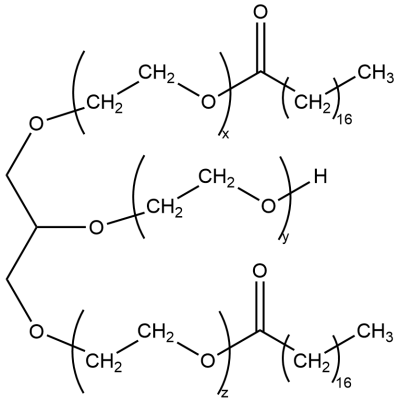
Ingredient & CAS No.	Definition	Function(s)
PEG-12 Glyceryl Dimyristate	PEG-12 Glyceryl Dimyristate is the polyethylene glycol ether of glyceryl dimyristate that conforms generally to the structure:  where x+y+z has an average value of 12.	Skin-Conditioning Agent – Misc.
PEG-12 Glyceryl Dioleate	PEG-12 Glyceryl Dioleate is the polyethylene glycol ether of glyceryl dioleate that conforms generally to the structure:  where x+y+z has an average value of 12.	Skin-Conditioning Agent – Emollient; Surfactant – Emulsifying Agent
PEG-3 Glyceryl Distearate	Not found in the *Dictionary*. (*Structure based on other PEG glyceryl diesters*)  where x+y+z has an average value or 3.	Not found in the *Dictionary*.

Table 1. Definitions, reported functions, and idealized structures of the ingredients in this safety assessment[1],[CIR Staff]

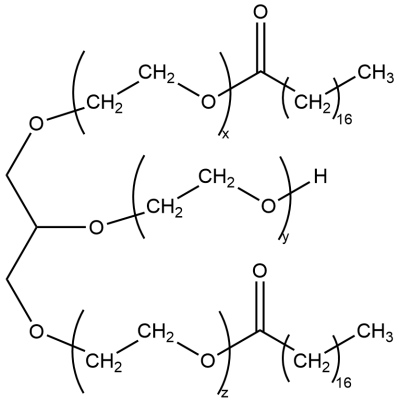
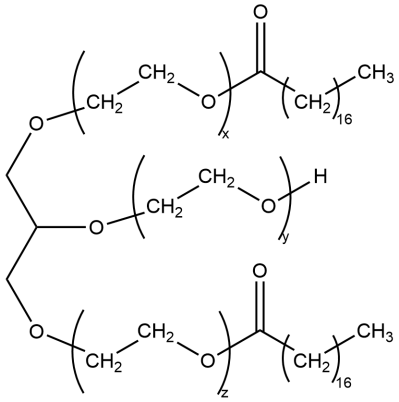
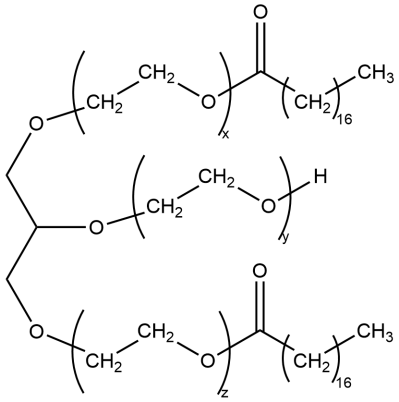
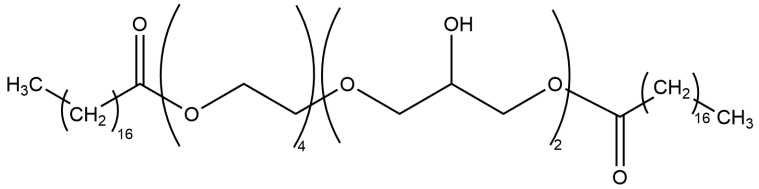
Ingredient & CAS No.	Definition	Function(s)
PEG-4 Glyceryl Distearate	PEG-4 Glyceryl Distearate is the polyethylene glycol ether of glyceryl distearate that conforms generally to the structure:  where x+y+z has an average value or 4.	Skin-Conditioning Agent – Emollient
PEG-12 Glyceryl Distearate	PEG-12 Glyceryl Distearate is the polyethylene glycol ether of glyceryl distearate that conforms generally to the structure:  where x+y+z has an average value of 12.	Skin-Conditioning Agent - Emollient
PEG-23 Glyceryl Distearate	PEG-23 Glyceryl Distearate is the polyethylene glycol ether of glyceryl distearate that conforms generally to the structure:  where x+y+z has an average value of 23.	Skin-Conditioning Agent – Misc.
PEG-4 Polyglyceryl-2 Distearate 72828-11-6	PEG-4 Polyglyceryl-2 Distearate is the polyethylene glycol ether of polyglyceryl-2 distearate with an average ethoxylation value of 4. (*Drawn block-style; connectivity may be different.*) 	Surfactant – Emulsifying Agent

Table 2. Relevant related safety assessments and Panel conclusions.

Report Family	Specific Related Ingredients	Conclusion	Reference
Glyceryl Diesters	glyceryl diisostearate, glyceryl dimyristate, glyceryl dioleate, glyceryl distearate	Safe as cosmetic ingredients provided that the content of 1,2-diesters is not high enough to induce epidermal hyperplasia	[2]
Triethylene Glycol and PEGs ≥ 4	triethylene glycol, PEG-4, PEG-8, PEG-10, PEG-12, PEG-20, PEG-60	Safe as used	[3]
PPGs	PPG-3	Safe when formulated to be nonirritating	[4]
PEG Diesters	PEG-8 diisostearate and PEG-12 dioleate	Safe when formulated to be nonirritating	[5]
PEGylated Oils	several PEG-3, PEG-4, PEG-8, PEG-10, PEG-15, PEG-20, PEG-30, PEG-60 oils and oil esters	Safe when formulated to be nonirritating	[6]
Monoglyceryl Monoesters	glyceryl isostearate, glyceryl oleate, glyceryl stearate	Safe as used	[7]

Table 3. Frequency (2022)[12] and concentration (2019-2022)[13,14] of use according to duration and exposure.

	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)
	PEG/PPG-8/3 Diisostearate		**PEG-12 Glyceryl Dimyristate**	
Totals*	**98**	**5**	**1**	**0.7-1.8**
Duration of Use				
Leave-On	*NR*	*5*	*1*	*0.7-1.8*
Rinse Off	*98*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*3*	*NR*	*NR*	*NR*
Exposure Type				
Eye Area	NR	NR	NR	0.7
Incidental Ingestion	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	NR	1[a]	1
Incidental Inhalation-Powder	NR	NR	NR	1.8[b]
Dermal Contact	97	NR	NR	0.7-1.8
Deodorant (underarm)	NR	NR	NR	NR
Hair - Non-Coloring	1	5	1	1
Hair-Coloring	NR	NR	NR	NR
Nail	NR	NR	NR	NR
Mucous Membrane	96	NR	NR	NR
Baby Products	NR	NR	NR	NR
	PEG-3 Glyceryl Distearate		**PEG-12 Glyceryl Distearate**	
Totals*	**2**	**NR**	**1**	**1**
Duration of Use				
Leave-On	*1*	*NR*	*1*	*1*
Rinse-Off	*1*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*
Exposure Type				
Eye Area	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR
Incidental Inhalation-Spray	1[a]	NR	NR	NR
Incidental Inhalation-Powder	NR	NR	NR	NR
Dermal Contact	1	NR	1	1
Deodorant (underarm)	NR	NR	NR	NR
Hair - Non-Coloring	1	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR
Nail	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR
Baby Products	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] It is possible these products are sprays, but it is not specified whether the reported uses are sprays.
[b] It is possible these products are powders, but it is not specified whether the reported uses are powders
NR – not reported

Table 4. Ingredients not reported in use.[12-14]

PEG-15 Butylene Glycol Diisostearate
PEG-10 Glyceryl Diisostearate
PEG-15 Glyceryl Diisostearate
PEG-20 Glyceryl Diisostearate
PEG-30 Glyceryl Diisostearate
PEG-60 Glyceryl Diisostearate
PEG-12 Glyceryl Dioleate
PEG-4 Glyceryl Distearate
PEG-23 Glyceryl Distearate
PEG-4 Polyglyceryl-2 Distearate

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