
Safety Assessment of PEG Diesters as Used in Cosmetics

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ABSTRACT

This is a safety assessment of 55 polyethylene glycol (PEG) diesters as used in cosmetics. These ingredients mostly function in cosmetics as surfactants. The Cosmetic Ingredient Review (CIR) Expert Panel (Panel) reviewed relevant data related to these ingredients. The similar structure, properties, functions and uses of these ingredients enabled grouping them and using the available toxicological data to assess the safety of the entire group. Much of the information for these ingredients consists of data on the PEG component and the various fatty acids that make up these ingredients. The Panel concluded that these PEG diesters are safe in cosmetics when formulated to be non-irritating. This conclusion supersedes the conclusion reached in the 3 former safety assessments.

INTRODUCTION

This is a safety assessment of 55 PEG diesters as used in cosmetics. These ingredients are diesters of various fatty acids with the common core of the PEG moiety. These ingredients mostly function in cosmetics as surfactants (Table 1).¹

In 1999, the Panel published a safety assessment of PEG distearates with the conclusion of safe as used (Table 2).² Because they are similarly structured fatty acid diesters with a PEG core, PEG dilaurates and other similar ingredients are included in this safety assessment. In 2000, a safety assessment of PEG dilaurates (which also included PEG laurates) was published with the conclusion of safe for use in cosmetics at concentrations up to 25%.³ In 2011, a safety assessment of pelargonic acid-related ingredients, which included PEG-2 diisononanoate, was published with a conclusion of safe in the present practices of use and concentration.⁴ Because there were little data available on the individual ingredients in these safety assessments, the Panel relied on read across and information on the moieties of these ingredients. Summaries of the reports on PEG distearate and PEG dilaurates are provided below; only new data are reported in the body of this safety assessment.

PEG-50 distearate, which was included in the original (1999) safety assessment, was not listed in the *International Cosmetic Ingredient Dictionary and Handbook*⁵ (INCI) and is not currently listed as a cosmetic ingredient in the current edition.¹ Since this compound has a reported use in the Food and Drug Administration's (FDA) Voluntary Cosmetic Registration Program (VCRP), it is included in this safety assessment.

The following previously unreviewed PEG diesters have been added to this safety assessment because of similarities in chemical structure and cosmetic function to the previously reviewed PEG diesters:

| | |
|---------------------------|-----------------------|
| PEG-40 distearate | PEG-175 diisostearate |
| PEG-190 distearate | PEG-2 dioleate |
| PEG-250 distearate | PEG-3 dioleate |
| PEG-150 dibehenate | PEG-4 dioleate |
| PEG-3 dicaprylate/caprate | PEG-6 dioleate |
| PEG-4 dicocoate | PEG-8 dioleate |
| PEG-8 dicocoate | PEG-10 dioleate |
| PEG-4 diheptanoate | PEG-12 dioleate |
| PEG-2 diisostearate | PEG-20 dioleate |
| PEG-3 diisostearate | PEG-32 dioleate |
| PEG-4 diisostearate | PEG-75 dioleate |
| PEG-6 diisostearate | PEG-150 dioleate |
| PEG-8 diisostearate | PEG-3 dipalmitate |
| PEG-12 diisostearate | PEG-8 ditallate |
| PEG-90 diisostearate | PEG-12 ditallate |

CIR has conducted safety assessments of the acids and related moieties of these PEG diester ingredients (Table 2). The Panel concluded that coconut acid, isostearic acid, oleic acid, lauric acid, stearic acid, PEG stearates (PEG monoesters), stearates, and tall oil acid were safe as used.⁶⁻¹⁸ The Panel concluded that steareths (PEG ethers) were safe as used when formulated to be nonirritating.¹⁹⁻²¹

SUMMARIES OF ORIGINAL REPORTS

PEG Distearates

PEG-2,-3,-4,-6,-8,-9,-12,-20,-32,-50,-75,-120,-150, and -175 Distearate are the polyethylene glycol diesters of Stearic Acid.² These ingredients are surfactants that function as emulsifying, cleansing, and solubilizing agents in cosmetics. Product formulation data submitted to the Food and Drug Administration (FDA) indicate that PEG-2, -3, -4, -6,-8, -12, -50, and -150 Distearate were in use, and that they were used in 283 cosmetic formulations.

Because few data on the PEGs Distearate regarding metabolism, toxicity, mutagenicity, carcinogenicity, and clinical safety were available, this review presented data on the PEGs, Stearic Acid, Steareths, and the PEGs Stearate separately, as these data were considered applicable to the safety evaluation of the PEGs Distearate.

PEG Distearate absorption and metabolism data were not available. PEG absorption is related to molecular weight. Lower molecular weight PEGs are readily absorbed through damaged skin. Oral and intravenous studies on PEGs indicate that these substances are excreted, unchanged, in the urine and feces. In general, fatty acids (such as Stearic Acid) are readily absorbed and distributed to the tissues in humans. Fatty acids can traverse the placental barrier.

Toxicity data for the PEGs Distearate were not available. The PEGs Stearate, and Steareths had low oral toxicity in acute, short-term, subchronic and chronic studies. PEGs in general have a low oral and dermal toxicity; the larger molecular weight PEGs appear to be less toxic than the smaller PEGs in oral studies. The acute toxicity of cosmetic formulations containing up to 13% Stearic Acid was low. In subchronic and chronic feeding studies using rats the effects were more severe.

PEG Stearates were slightly irritating at undiluted concentrations in test animals. PEGs were nonirritating to the skin of rabbits and guinea pigs, and PEG-75 was not a sensitizer. Stearic Acid irritation ranged from moderate to no reaction. Cosmetic product formulations containing 1.0% Stearic Acid were weak, grade I sensitizers. Primary irritation and sensitization studies involving Stearic Acid and the PEGs Stearate were negative. Minimal ocular irritation occurred in tests with the PEGs, Stearic Acid, Steareths, and PEGs Stearate.

Although monoalkyl ethers of ethylene glycol are reproductive toxins and teratogenic agents, it was considered unlikely that the PEGs Distearate would cause reproductive or developmental effects based on their structural characteristics. In subchronic and chronic feed studies, PEG-6 [through]32 and PEG-75 did not induce adverse reproductive effects in rats. In a multigenerational study lasting 2 years, feed containing 10-20% PEG-8 Stearate or PEG-40 Stearate was fed to rats; the rats fed the diet had decreased offspring survival time, reproductive performance, and lactation efficiency, as well as increased offspring mortality. Neither PEG-8 Stearate nor PEG-40 Stearate at a dietary concentration of 5% affected reproductive success.

In mutagenicity studies, PEG-8 was negative in the Chinese hamster ovary cell mutation test and the sister chromatid exchange test. At concentrations up to 150 g/l, PEG-150 was not mutagenic in the mouse lymphoma forward mutation assay. Stearic Acid was not mutagenic in the Ames test. PEG-8 was not carcinogenic when administered orally, intraperitoneally, or subcutaneously to rodents. A low incidence of carcinomas, sarcomas, and lymphomas was evident in mice receiving multiple subcutaneous injections of Stearic Acid.

In clinical studies, PEG-8 was a mild sensitizer and irritant. Contact dermatitis and systemic toxicity in burn patients were attributed to a PEG-based topical ointment. The Steareths, PEGs Stearate, and Stearic Acid were not irritants, sensitizers, or phototoxins. Formulations containing Stearic Acid were not photosensitizing.

PEG Dilaurates

The PEGs Dilaurate, PEGs Laurate, and PEG-2 Laurate SE are PEG diesters or esters of lauric acid that function as surfactants in cosmetic formulations.³ In 1997, PEG-8 Dilaurate and PEG-12 Dilaurate were used in 40 cosmetic formulations, and PEG-2, -4, -8, -10, -15, and -200 Laurate were used in 20 formulations. The remaining ingredients from this family had no reports of use. In 1984, data submitted to the FDA indicated that the PEGs Dilaurate and PEGs Laurate were used at concentrations up to 25%.

The CIR Expert Panel has previously reviewed the safety in cosmetics of the PEGs Stearate, PEGs Distearate, PEGs, Laureths, and Lauric Acid. Based on the similarity in chemical structures, data from those evaluations have been used as a further basis for the safety assessment of the PEGs Dilaurate and PEGs Laurate in cosmetics.

These polyoxyethylene ester surfactants and emulsifiers are produced by the ethoxylation of fatty acids during uncatalyzed or alkali-catalyzed reactions. PEG-2 Laurate has been produced by the interesterification of coconut oil with diethylene glycol. PEG-n Laurate could contain unspecified amounts of the lauric acid diester of PEG and unreacted PEG. PEG-6 may contain small, unquantified amounts of monomer and dimers, and samples PEG-32 and PEG-75 contained peroxides as a result of autoxidation. In general, ethoxylated surfactants can contain 1,4-dioxane, a by-product of ethoxylation, which is then removed during purification of the finished products. Traces of the reactants, stearic acid, ethylene oxide, and the catalysts used could remain in the finished product.

Data on the absorption, metabolism, distribution, and excretion of the PEGs Dilaurate and PEGs Laurate were not available. PEG-40 Stearate was hydrolyzed *in vitro* by pancreatic lipase. In metabolism studies with rats, rabbits, dogs, and humans, the lower-molecular-weight PEGs were absorbed by the digestive tract and excreted in the urine and feces. The PEGs were readily absorbed through damaged skin.

Fatty acids such as Lauric Acid are absorbed, digested, and transported in animals and humans. During labeling studies, radioactivity was found in various tissues, blood, and lymph after oral, IV, IP, and intraduodenal administration of labelled fatty acids. The fatty acids can undergo β -oxidation to yield acetyl-CoA. Placental transfer of the fatty acids has been observed. Lauric Acid is transported via the lymph and portal systems; fatty acids are typically transported esterified to glycerol in chylomicrons and very-low-density lipoproteins.

The acute oral LD₅₀ of PEG-12 Laurate was >25 g/kg in Harlan mice. In the same study, the IV LD₅₀ was 500 mg/kg. During short-term feeding studies using chicks, concentrations of up to 2% PEG-4 or -8 Laurate did not cause adverse effects. Rats fed a diet containing 15.9 g/kg/day of 25% PEG-20 Laurate had diarrhea, inflammation of the anal

region, and blood clots in the anorectal region after 59 days of treatment. In a 70-day study, rats given 5% to 25% PEG-20 Laurate had diarrhea and inflammation of the anal region. The ingredient was irritating to the gastrointestinal tract, but not necrotizing, and monocyte/macrophage hyperplasia and splenic giant cells were noted more frequently in rats of the treated group than rats of the control group. In a chronic oral toxicity study, nine rats were fed 6% PEG-8 Dilaurate for 505 days. Four of the rats in each of the treatment and control groups died. Of the rats given PEG-8 Dilaurate, one had cystic spots on the liver, one had hemorrhagic lungs, and one had a large fibrosarcoma. In microscopic examinations, three rats had focal parenchymal hepatitis. Of the rats of the control group, four had hemorrhagic and congested lungs, one had hypertrophied testes, one had a concretion in the urinary bladder, two had cystic kidneys, and two had hepatic parasites. In microscopic examinations, one control rat had adrenal cortical hyperplasia, two had chronic interstitial nephritis of the kidneys, two had splenic lymphoid hyperplasia, one had focal parenchymal hepatitis, and one had hepatic vacuolization. During another feeding study, rats fed up to 25% PEG-20 Laurate for 2 years had hepatic cysts, cecal enlargement, slight gastric mucosal hyperplasia, and slight squamous epithelial hyperplasia. PEG-12 Laurate at a concentration of 1% did not cause ocular irritation in rabbits.

The IV LD₅₀ values in Harlan mice for PEG-8 and -20 Distearate were 365 mg/kg and 220 mg/kg, respectively. The oral LD₅₀ values of PEG-2-150 Stearate ranged from >10 g/kg to 32 g/kg in rats. The IP LD₅₀ of PEG-8 Stearate in rats was >9 ml/kg. No signs of toxicity were observed when rats were given IP injections of 2.5 g/kg PEG-50 or -100 Stearate. A hair cream containing 1.5% PEG-6 Stearate had an oral LD₅₀ of >34.6 g/kg. The acute dermal LD₅₀ of 15% PEG-8 Stearate in rabbits was >10 ml/kg; the only effect noted was erythema at the application site at 24 hours. The PEGs Stearate caused only slight skin irritation and minimal ocular irritation when tested at concentrations of 100% in animals. PEG-8, -40, and -100 Stearate did not cause significant changes in growth mortality rates, microscopic observations, or hematological values during long-term feeding studies. In clinical studies, the PEGs Stearate were not irritating or sensitizing when tested at concentrations of 25%. In addition, they did not cause photosensitization. PEG-8 and -40 Stearate did not cause reproductive or developmental effects, and were noncarcinogenic.

In acute toxicity studies, the PEGs had low oral and dermal toxicity. The PEGs were not irritating to the skin of rabbits or guinea pigs, and minimally irritating to the skin of humans. They did not cause sensitization in animal or human studies using intact skin, but sensitization and nephrotoxicity were observed in bum patients that were treated with a PEG-based cream. PEG was determined to be the causative agent in both animal and human studies. In ocular irritation studies, the PEGs caused mild, transient ocular irritation in rabbits. Cosmetic product formulations containing up to 13% Lauric Acid did not cause primary or cumulative irritation and did not cause sensitization.

The available data indicated that the PEGs were not mutagenic or carcinogenic.

A product formulation containing 5% Lauric Acid was nontoxic to rats during an oral toxicity study. Transient signs of toxicity (mucoid diarrhea, depression, unkempt fur, etc.) were observed when male rats were fed 0.46 to 10 g/kg Lauric Acid. In this study, one rat died; it had congested lungs and kidneys, and advanced autolytic changes. In a subchronic oral toxicity study, rats fed 10% Lauric Acid had no signs of toxicity. Lauric Acid was also noncarcinogenic in animal tests. It is generally recognized that the PEG monomer, ethylene glycol, and certain of its monoalkyl ethers are reproductive and developmental toxins. The PEGs Dilaurate and PEGs Laurate are diesters and esters of PEG and, as such, are chemically different from PEG alkyl ethers. Hence, they are not expected to cause adverse reproductive or developmental effects.

CHEMISTRY

Definition and Structure

The ingredients in this report are the PEG diesters of various acids (eg, stearic acid, lauric acid, oleic acid). The different chain lengths of the PEGs are formed by condensing ethylene oxide and water. The average number of ethylene oxide repeat units per polyethylene glycol chain correspond to the number in the name (eg, PEG-4 diheptanoate is prepared from a polyethylene glycol chain, that is 4 ethylene oxide repeated units long on average, esterified on both ends of the chain with heptanoic acid).¹⁷

PEG-8 ditallate and PEG-12 ditallate are the diesters of the corresponding PEGs and tall oil acid. The composition of tall oil acid varied with the source pine tree species, climate, and other growing conditions.²² For example, one source reported the composition to consist of oleic acid (48%), linoleic acid (35%), conjugated linoleic acid (7%), stearic acid (2%), palmitic acid (1%), other acids (4%), and unsaponifiable matter (2%).

Physical and Chemical Properties

The PEG distearates have a broad range of properties depending on the degree of polymerization of the PEG segment.²³ The physical forms of these ingredients range from liquids to solids. Solubility is also dependent on the length of the PEG component. Typically, these ingredients are soluble in oil and hydrocarbon solvents when less than 8 ethylene oxide units are present. Ingredients with short polyethylene glycol components in this group are insoluble in water. Solubility in water begins with compounds containing 12-15 ethylene oxide units and increases proportionally the longer the PEG chain gets. For example, PEG-2 dilaurate and PEG-4 dilaurate are dispersible in water while PEG-150 dilaurate is soluble in water.²⁴ Specific gravity and viscosity increase with increasing ethylene oxide repeat units.²³ As a representative example, though, PEG-4 diheptanoate was reported to be a clear liquid with a boiling point of >300°C, a specific gravity of 0.996, and

a vapor pressure of <0.1 mmHg at 37°C.²⁵ It is soluble in alcohol, acetone, and most organic solvents. PEG-150 dilaurate is a tan, waxy solid with a slight fatty odor.²⁴ The melting range is 53-60°C and it is soluble in isopropanol, toluene, and water (Table 3).

Method of Manufacture

In general, the PEGs diesters are manufactured by the esterification of an acid with ethylene oxide or with a polyethylene glycol.²⁶

Impurities

Traces of the reactants, stearic acid, ethylene oxide, and the catalytic agents used, may remain in the finished product.¹⁷

PEG-150 distearate was reported to contain peroxide concentrations of 1.97 and 1.92 µEq thiosulfate/g glycol.²⁷ PEGs may contain small amounts of monomer and dimers, as well as peroxides.²⁸ Peroxide in PEGs is dependent upon the molecular weight of the PEG and its age.²⁷

Because PEGs may contain trace amounts of 1,4-dioxane, a by-product of ethoxylation, this impurity may be present in PEG diesters.²⁹ 1,4-Dioxane is a known animal carcinogen.³⁰ Commercial grade triethylene glycol has been found to contain <1 ppm dioxane.³¹ The cosmetic industry reported that it is aware that 1,4-dioxane may be an impurity in PEGs and, thus, uses additional purification steps to limit it in these ingredients before blending into cosmetic formulations.¹⁷

PEG-4 diheptanoate was reported to be 88% pure; the remaining substance consisted of triethylene glycol di-*n*-heptanoate (6%), mixed ester of tetraethylene glycol with *n*-heptanoic and 2-methylhexanoic acids (4%), and other mixed esters (2%).²⁵

It was reported that PEGs may contain small amounts of ethylene oxide monomer and dimers.³² The amounts were not quantified.

USE

Cosmetic

The Panel assesses the safety of cosmetic ingredients based on the expected use of these ingredients in cosmetics. The Panel reviews data received from the FDA and the cosmetics industry to determine the expected cosmetic use. The data received from the FDA are collected from manufacturers on the use of individual ingredients in cosmetics, by cosmetic product category, through the FDA VCRP, and the data from the cosmetic industry are submitted in response to a survey of the maximum reported use concentrations, by category, conducted by the Personal Care Products Council (Council).

Of the ingredients in this safety assessment, PEG-150 distearate was reported to have the highest number of uses at 690 in 2015 (an increase from 187 in 1996).^{2,33,34} Most of these uses are in bath and personal cleansing products and shampoos. The rest of the ingredients are reported to have 48 or fewer uses (Tables 4, 5).

PEG-50 distearate, which was included in the original safety assessment, was not then and is not currently listed in the INCI Dictionary.¹ However, the VCRP has 1 reported use in a cleansing product.³³ In 1996, it was used in 1 cleansing preparation.²

A survey was conducted by the Personal Care Products Council (Council) of the maximum use concentrations for each ingredient in this group.³⁵ PEG-150 distearate was reported to have the highest concentration of use at up to 33.2% (an increase from 5% in 1995).^{2,35} PEG-150 distearate is reported to be used in a rinse-off baby product up to 9.4%, bath products up to 4.5%, and in skin cleansing products up to 33.2%. PEG-4 dilaurate and PEG-8 dilaurate were reported to be used up to 25% in 1984, and are currently used up to 12% and 15%, respectively.³ The rest of the ingredients were reported to be used at 15% or less (Tables 4, 5). Table 6 lists the 32 ingredients that have no reported uses according to the VCRP and the Council survey.

In some cases, the VCRP reported uses but no concentration-of-use data were available. For example, PEG-120 distearate is reported to be used in 7 formulations, but no use concentration data were available. In other cases, no reported uses were received in the VCRP, but a use concentration was provided in the industry survey. For example, PEG-175 distearate was not reported in the VCRP to be in use, but the industry survey indicated that it is used in shaving cream formulations at up to 0.089%. It should be presumed that PEG-175 distearate is used in at least one cosmetic formulation.

PEG-12 dioleate was reported to be used in pump hair sprays up to 0.024% and PEG-4 dilaurate was reported to be used in pump spray suntan products at 0.072%; these products could possibly be inhaled. In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters >10 µm, with propellant sprays yielding a greater fraction of droplets/particles below 10 µm compared with pump sprays.³⁶⁻³⁹ Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and bronchial regions and would not be respirable (ie, they would not enter the lungs) to any appreciable amount.^{36,38}

All of the PEG diesters named in the report, with the exception of PEG-3 dicaprylate/caprate, PEG-4 diheptanoate, and PEG-50 distearate, are not restricted from use under the rules governing cosmetic products in the European Union.⁴⁰ PEG-3 dicaprylate/caprate, PEG-4 diheptanoate, and PEG-50 distearate are not listed in the European Union CosIng database.

Non-Cosmetic

Several of the PEG diesters may be used as defoaming agents in foods, as indirect food additives in paperboard products, in food contact surfaces, and as additives in animal feed and drinking water (Table 7).

TOXICOKINETICS

Dermal Penetration Enhancement

Neither PEG-8 dioleate (5% w/w) nor PEG-8 dilaurate (5% w/w) enhanced the dermal penetration of ketoprofen through full-thickness CD-1 nude mouse skin when added to a drug delivery plaster preparation.⁴¹ PEG-12 dioleate (5%) did enhance the dermal penetration of ketoprofen with an enhancement ratio (ER) of 1.54 ± 0.22 . The study was conducted using Franz cells; the receptor cell was filled with freshly prepared degassed pH 7.4 phosphate-buffered saline. The samples were taken from the receptor cell and analyzed by high-performance liquid chromatography (HPLC) at 1, 2, 4, 8, and 24 h.

TOXICOLOGICAL STUDIES

Acute Toxicity

Oral – Non-Human

PEG-4 DIHEPTANOATE

The oral LD₅₀ values reported for PEG-4 diheptanoate in rats ranged from >2->25 g/kg (Table 8).^{25, 42} Clinical signs included labored breathing, belly-to-cage posture, lacrimation, staining of the face, stained and wet perineal area, and weight loss.

Inhalation – Non-Human

PEG-4 DIHEPTANOATE

All the CrI:CD rats (n=6) exposed to vaporized (by applying heat, not aerosolized) PEG-4 diheptanoate (14.2 mg/L) for 4 h died during the exposures; all rats (n=6) exposed to 13.7 mg/L or less survived.²⁵ At all concentrations (2.1-14.2 mg/L), the clinical signs included salivation, red nasal discharge, and irregular respiration during the exposure period. The rats recovered quickly during the recovery period. Lethargy was observed starting at a concentration of 12.7 mg/L or greater. Rats exposed to 13.7 mg/L showed moderate weight loss (approximately 10% of initial body weight) the first 3-4 days post-exposure. The rats with weight loss also presented an unthrifty appearance with staining of the perineal area prominent during the first week of the 14-day recovery period.

Repeated Dose Toxicity

Oral – Non-Human

PEG-4 DIHEPTANOATE

There were no adverse effects observed when PEG-4 diheptanoate (1 g/kg in corn oil) was administered by gavage to CrI:CD rats (10/sex) for 28 consecutive days.²⁵ Pathologic examinations at the end of the test period and after the 14-day recovery period were unremarkable.

Inhalation – Non-Human

PEG-4 DIHEPTANOATE

Following the repeated inhalation exposure of vaporized (by applying heat, not aerosolized) PEG-4 diheptanoate (1.0 mg/L) for 6 h/day, 5 days/week for 4 weeks, clinical signs for CrI:CD rats (n=10) were mild salivation, reduced response to auditory stimulation, and shallow and rapid respiration sporadically during the exposure periods.²⁵ The clinical signs were absent when the rats were not being exposed and during the 14-day recovery period. A trace of lung noise and brown staining of the nose were observed in 1 of the treated rats during recovery. Body weight changes were similar to the controls. Gross pathologic evaluation was unremarkable. Histopathologic examination of tissues found no lesions attributable to the test substance.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

New data on the reproductive and developmental toxicity of PEG diesters were not found in the published literature, nor were unpublished data provided.

GENOTOXICITY

PEG-4 DIHEPTANOATE

PEG-4 diheptanoate was not mutagenic at up to 10 000 µg/plate in a reverse mutation assay using *Salmonella typhimurium* (strains TA98, TA100, TA1535, TA1537) or at up to 23.9 mM in a mammalian cell gene mutation assay using Chinese hamster ovary cells (Table 9).⁴²

CARCINOGENICITY

New data on the carcinogenicity of PEG diesters were not found in the published literature, nor were unpublished data provided.

IRRITATION AND SENSITIZATION

Irritation

Dermal – Non-Human

PEG-4 DIHEPTANOATE

PEG-4 diheptanoate (100%; 0.5 mL) caused slight (1), mild (3), or no (2) erythema to the skin of New Zealand White rabbits (n=6) when administered to the skin for 24 h.²⁵ At the removal of the test material, there was no edema observed on any of the rabbits. At 24 h after removal, there was little change in the erythema responses and edema (moderate in 1 rabbit; mild in 2 rabbits, and absent in 3 rabbits).

There was no skin irritation observed in a preliminary study using male BC/DHA guinea pigs (n=3) treated with PEG-4 diheptanoate (5% or 25%; 0.05 mL in dimethyl phthalate).²⁵ At a concentration of 50%, mild irritation in 1 guinea pig was observed, and at 100% there was mild irritation on all 3 guinea pigs.

Ocular

PEG-4 DIHEPTANOATE

There were no lasting reactions observed when PEG-4 diheptanoate (100%; 0.1 mL) was instilled in the conjunctival sac of New Zealand White rabbits (n=2).²⁵ The cornea, iris, and conjunctiva of 1 rabbit (the treated eye of this rabbit remained unwashed following administration) showed no adverse effects. The eye of the other rabbit (the treated eye of this rabbit was washed with copious amounts of water 20 seconds after administration) showed slight conjunctival swelling which lasted for 4 h. The swelling was resolved at 24 h. No changes in the corneal or iritic tissues were observed.

Sensitization

Dermal – Non-Human

PEG-4 DIHEPTANOATE

In a dermal sensitization study using male BC/DHA guinea pigs (n=10), PEG-4 diheptanoate (5% or 25%; 0.05 mL in dimethyl phthalate) was not sensitizing when challenged at 5% or 50%.²⁵ The test substance was administered to the shaved skin of the shoulder of the guinea pigs followed 2 days later by an injection of dimethyl phthalate (1%; 0.1 mL). Three more injections, 1 week apart, were administered to complete the induction phase. After a 13-day rest period, the challenge was administered as a topical administration of PEG-4 diheptanoate (5% or 50% in dimethyl phthalate; 0.05 mL) to the same shaven shoulder. The control consisted of a group of naïve guinea pigs (n=10) that were administered the challenge. Test sites were evaluated for reactions at 24 and 48 h after administration of the challenge.

SUMMARY

This is a safety assessment of PEG diesters as used in cosmetics. These ingredients are diesters of various fatty acids with the common core of the PEG moiety and mostly function in cosmetics as surfactants. Several of these ingredients have been reviewed by the Panel previously and the data in those safety assessments were considered along with the new data presented here.

In previous safety assessments, it was concluded that several PEG distearates were safe as used in cosmetics and several PEG dilaurates were safe up to 25%. PEG-2 diisononanoate was also found to be safe as used. Because there were little data available on the individual ingredients in these safety assessments, the Panel relied on read across and information on the moieties of these ingredients.

Of the ingredients in this safety assessment, PEG-150 distearate was reported to have the highest number of uses at 690 (an increase from 187 in 1996). Most of these uses are in bath and personal cleansing products and shampoos. The rest of the ingredients are reported to have 48 or fewer uses. PEG-150 distearate was reported to have the highest concentration of use at up to 33.2% (an increase from 5% in 1995). PEG-150 distearate is reported to be used in a rinse-off baby product at up to 9.4%, bath products at up to 4.5%, and in skin cleansing products up to 33.2%. PEG-4 dilaurate and PEG-8 dilaurate were reported to be used at up to 25% in 1984, and are currently used at up to 12% and 15%, respectively. The rest of the ingredients were reported to be used at 15% or less.

Neither PEG-8 dioleate nor PEG-8 dilaurate at 5% enhanced the dermal penetration of ketoprofen through mouse skin when added to a drug delivery plaster preparation. PEG-12 dioleate at 5% did enhance the dermal penetration of ketoprofen with an ER of 1.54±0.22.

The oral LD₅₀ values reported for PEG-4 diheptanoate in rats ranged from >2->25 g/kg.

Vaporized PEG-4 diheptanoate was lethal within 4 h to rats at 14.2 mg/L but not at 13.7 mg/L. Clinical signs included salivation, red nasal discharge, and irregular respiration during the exposure period. The rats recovered quickly during the recovery period.

There were no adverse effects observed when 1 g/kg PEG-4 diheptanoate was administered by gavage to rats for 28 consecutive days.

In the repeated inhalation exposure of vaporized PEG-4 diheptanoate at 1.0 mg/L for 6 h/day, 5 days/week for 4 weeks, clinical signs for rats were mild salivation, reduced response to auditory stimulation, and shallow, rapid respiration sporadically during the exposure periods.

PEG-4 diheptanoate was not mutagenic in a reverse mutation assay up to 10 000 µg/plate using *S. typhimurium* or in a mammalian cell gene mutation assay using Chinese hamster ovary cells up to 23.9 mM.

At 100%, PEG-4 diheptanoate caused slight to moderate erythema and edema when administered to rabbit skin for 24 h. There was no skin irritation observed in guinea pigs treated with PEG-4 diheptanoate at 5% or 25% but mild irritation was observed in 1 of 3 guinea pigs at 50% and in 3 of 3 at 100%.

There were no lasting reactions observed when PEG-4 diheptanoate at 100% was instilled in the conjunctival sac of rabbits.

In a dermal sensitization study using guinea pigs, PEG-4 diheptanoate at 5% or 25% was not sensitizing when challenged at 5% or 50%.

DISCUSSION

Because these ingredients are similarly structured fatty acid diesters with a PEG core and have similar functions in cosmetics, the Panel agreed with combining the PEG distearates, PEG dilaurates, and other similar PEG-diester ingredients into a single report.

Although there are data gaps for individual PEG diesters, the similar chemical structures, physicochemical properties, and functions and concentrations used in cosmetics allow grouping these ingredients together and interpolating the available toxicological data to support the safety of the entire group. Data from previous reports, on chemically analogous ingredients, and on the components of these ingredients were also used to evaluate the safety of these ingredients. It should be noted that although the conclusion in the 2000 report of PEG dilaurates limited their use in cosmetics to concentrations up to 25%, the data presented in this report alleviated the need for that limitation.

Because some of the components of the PEG diesters are obtained from plant sources (eg, PEG-8 ditallate, PEG-12 ditallate, and PEG-8 dicocoate), the Panel expressed concern about pesticide residues and heavy metals that may be present in botanical ingredients. The Panel was also concerned about the possible presence of 1,4-dioxane and ethylene oxide impurities. They stressed that the cosmetics industry should continue to use current good manufacturing practices (cGMPs) to limit impurities in the ingredient before blending into cosmetic formulations.

The Panel recognized that these ingredients, particularly PEG-12 dioleate, can enhance the penetration of other compounds through the skin (eg, ketoprofen). 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.

AMENDED CONCLUSION

The CIR Expert Panel concluded that the following ingredients are safe in cosmetics when formulated to be non-irritating. This conclusion supersedes the earlier conclusions issued by the Expert Panel in 1999, 2000, and 2011.

| | | |
|----------------------------|--------------------|---------------------|
| PEG-150 dibehenate* | PEG-16 dilaurate* | PEG-4 distearate |
| PEG-3 dicaprylate/caprate* | PEG-20 dilaurate* | PEG-6 distearate |
| PEG-4 dicocoate* | PEG-32 dilaurate* | PEG-8 distearate |
| PEG-8 dicocoate | PEG-75 dilaurate* | PEG-9 distearate* |
| PEG-4 diheptanoate | PEG-150 dilaurate* | PEG-12 distearate |
| PEG-2 diisononanoate | PEG-2 dioleate* | PEG-20 distearate* |
| PEG-2 diisostearate* | PEG-3 dioleate* | PEG-32 distearate* |
| PEG-3 diisostearate* | PEG-4 dioleate* | PEG-40 distearate* |
| PEG-4 diisostearate* | PEG-6 dioleate* | PEG-50 distearate |
| PEG-6 diisostearate | PEG-8 dioleate | PEG-75 distearate* |
| PEG-8 diisostearate | PEG-10 dioleate* | PEG-120 distearate |
| PEG-12 diisostearate | PEG-12 dioleate | PEG-150 distearate |
| PEG-90 diisostearate | PEG-20 dioleate* | PEG-175 distearate |
| PEG-175 diisostearate | PEG-32 dioleate* | PEG-190 distearate* |
| PEG-2 dilaurate* | PEG-75 dioleate* | PEG-250 distearate |
| PEG-4 dilaurate | PEG-150 dioleate* | PEG-8 ditallate* |
| PEG-6 dilaurate* | PEG-3 dipalmitate* | PEG-12 ditallate* |
| PEG-8 dilaurate | PEG-2 distearate | |
| PEG-12 dilaurate* | PEG-3 distearate | |

*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 they would be used in product categories and at concentrations comparable to others in this group.

TABLES

Table 1. The definitions and functions of the PEG diesters in this safety assessment.¹

| Ingredient and CAS No. | Definition/structure | Function |
|---|---|--------------------------------|
| PEG-2 distearate 109-30-8 52668-97-0 9005-08-7 (generic) | PEG-2 distearate is the polyethylene glycol diester of stearic acid that conforms to the formula: $\text{CH}_3(\text{CH}_2)_{16}\overset{\text{O}}{\parallel}\text{C}-(\text{OCH}_2\text{CH}_2)_n\text{O}-\overset{\text{O}}{\parallel}\text{C}(\text{CH}_2)_{16}\text{CH}_3$ where n has an average value of 2. | Surfactant – emulsifying agent |
| PEG-3 distearate 9005-08-7 (generic) | PEG-3 distearate is the polyethylene glycol diester of stearic acid that conforms to the formula: $\text{CH}_3(\text{CH}_2)_{16}\overset{\text{O}}{\parallel}\text{C}-(\text{OCH}_2\text{CH}_2)_n\text{O}-\overset{\text{O}}{\parallel}\text{C}(\text{CH}_2)_{16}\text{CH}_3$ where n has an average value of 3. | Surfactant – emulsifying agent |
| PEG-4 distearate 142-20-1 9005-08-7 (generic) | PEG-4 distearate is the polyethylene glycol diester of stearic acid that conforms to the formula: $\text{CH}_3(\text{CH}_2)_{16}\overset{\text{O}}{\parallel}\text{C}-(\text{OCH}_2\text{CH}_2)_n\text{O}-\overset{\text{O}}{\parallel}\text{C}(\text{CH}_2)_{16}\text{CH}_3$ where n has an average value of 4. | Surfactant – emulsifying agent |
| PEG-6 distearate 9005-08-7 (generic) | PEG-6 distearate is the polyethylene glycol diester of stearic acid that conforms to the formula: $\text{CH}_3(\text{CH}_2)_{16}\overset{\text{O}}{\parallel}\text{C}-(\text{OCH}_2\text{CH}_2)_n\text{O}-\overset{\text{O}}{\parallel}\text{C}(\text{CH}_2)_{16}\text{CH}_3$ where n has an average value of 6. | Surfactant – emulsifying agent |
| PEG-8 distearate 9005-08-7 (generic) | PEG-8 distearate is the polyethylene glycol diester of stearic acid that conforms to the formula: $\text{CH}_3(\text{CH}_2)_{16}\overset{\text{O}}{\parallel}\text{C}-(\text{OCH}_2\text{CH}_2)_n\text{O}-\overset{\text{O}}{\parallel}\text{C}(\text{CH}_2)_{16}\text{CH}_3$ where n has an average value of 8. | Surfactant – emulsifying agent |
| PEG-9 distearate 109-34-2 9005-08-7 (generic) | PEG-9 distearate is the polyethylene glycol diester of stearic acid that conforms to the formula: $\text{CH}_3(\text{CH}_2)_{16}\overset{\text{O}}{\parallel}\text{C}-(\text{OCH}_2\text{CH}_2)_n\text{O}-\overset{\text{O}}{\parallel}\text{C}(\text{CH}_2)_{16}\text{CH}_3$ where n has an average value of 9. | Surfactant – emulsifying agent |
| PEG-12 distearate 9005-08-7 (generic) | PEG-12 distearate is the polyethylene glycol diester of stearic acid that conforms to the formula: $\text{CH}_3(\text{CH}_2)_{16}\overset{\text{O}}{\parallel}\text{C}-(\text{OCH}_2\text{CH}_2)_n\text{O}-\overset{\text{O}}{\parallel}\text{C}(\text{CH}_2)_{16}\text{CH}_3$ where n has an average value of 12. | Surfactant – emulsifying agent |
| PEG-20 distearate 9005-08-7 (generic) | PEG-20 distearate is the polyethylene glycol diester of stearic acid that conforms to the formula: $\text{CH}_3(\text{CH}_2)_{16}\overset{\text{O}}{\parallel}\text{C}-(\text{OCH}_2\text{CH}_2)_n\text{O}-\overset{\text{O}}{\parallel}\text{C}(\text{CH}_2)_{16}\text{CH}_3$ where n has an average value of 20. | Surfactant – emulsifying agent |
| PEG-32 distearate 9005-08-7 (generic) | PEG-32 distearate is the polyethylene glycol diester of stearic acid that conforms to the formula: $\text{CH}_3(\text{CH}_2)_{16}\overset{\text{O}}{\parallel}\text{C}-(\text{OCH}_2\text{CH}_2)_n\text{O}-\overset{\text{O}}{\parallel}\text{C}(\text{CH}_2)_{16}\text{CH}_3$ where n has an average value of 32. | Surfactant – emulsifying agent |
| PEG-40 distearate 9005-08-7 (generic) | PEG-40 distearate is the polyethylene glycol diester of stearic acid that conforms to the formula: $\text{CH}_3(\text{CH}_2)_{16}\overset{\text{O}}{\parallel}\text{C}-(\text{OCH}_2\text{CH}_2)_n\text{O}-\overset{\text{O}}{\parallel}\text{C}(\text{CH}_2)_{16}\text{CH}_3$ where n has an average value of 40. | Surfactant – emulsifying agent |

Table 1. The definitions and functions of the PEG diesters in this safety assessment.¹

| Ingredient and CAS No. | Definition/structure | Function |
|---|--|---|
| PEG-75 distearate 9005-08-7 (generic) | PEG-75 distearate is the polyethylene glycol diester of stearic acid that conforms to the formula: $\text{CH}_3(\text{CH}_2)_{16}\overset{\text{O}}{\parallel}\text{C}-(\text{OCH}_2\text{CH}_2)_n\text{O}-\overset{\text{O}}{\parallel}\text{C}(\text{CH}_2)_{16}\text{CH}_3$ where n has an average value of 75. | Surfactant – emulsifying agent; surfactant – solubilizing agent |
| PEG-120 distearate 9005-08-7 (generic) | PEG-120 distearate is the polyethylene glycol diester of stearic acid that conforms to the formula: $\text{CH}_3(\text{CH}_2)_{16}\overset{\text{O}}{\parallel}\text{C}-(\text{OCH}_2\text{CH}_2)_n\text{O}-\overset{\text{O}}{\parallel}\text{C}(\text{CH}_2)_{16}\text{CH}_3$ where n has an average value of 120. | Surfactant – emulsifying agent; surfactant – solubilizing agent |
| PEG-150 distearate 9005-08-7 (generic) | PEG-150 distearate is the polyethylene glycol diester of stearic acid that conforms to the formula: $\text{CH}_3(\text{CH}_2)_{16}\overset{\text{O}}{\parallel}\text{C}-(\text{OCH}_2\text{CH}_2)_n\text{O}-\overset{\text{O}}{\parallel}\text{C}(\text{CH}_2)_{16}\text{CH}_3$ where n has an average value of 150. | Surfactant – cleansing agent; surfactant – solubilizing agent |
| PEG-175 distearate 9005-08-7 (generic) | PEG-175 distearate is the polyethylene glycol diester of stearic acid that conforms to the formula: $\text{CH}_3(\text{CH}_2)_{16}\overset{\text{O}}{\parallel}\text{C}-(\text{OCH}_2\text{CH}_2)_n\text{O}-\overset{\text{O}}{\parallel}\text{C}(\text{CH}_2)_{16}\text{CH}_3$ where n has an average value of 175. | Surfactant – cleansing agent; surfactant – solubilizing agent |
| PEG-190 distearate 9005-08-7 (generic) | PEG-190 distearate is the polyethylene glycol diester of stearic acid that conforms generally to the formula: $\text{C}_{17}\text{H}_{35}\overset{\text{O}}{\parallel}\text{C}-(\text{OCH}_2\text{CH}_2)_n\text{O}-\overset{\text{O}}{\parallel}\text{C}\text{C}_{17}\text{H}_{35}$ where n has an average value of 190. | Surfactant – cleansing agent; surfactant – emulsifying agent; surfactant – solubilizing agent; viscosity increasing agent – aqueous |
| PEG-250 distearate 9005-08-7 (generic) | PEG-250 distearate is the polyethylene glycol diester of stearic acid that conforms generally to the formula: $\text{CH}_3(\text{CH}_2)_{16}\overset{\text{O}}{\parallel}\text{C}-(\text{OCH}_2\text{CH}_2)_n\text{O}-\overset{\text{O}}{\parallel}\text{C}(\text{CH}_2)_{16}\text{CH}_3$ where n has an average value of 250. | Surfactant – cleansing agent; surfactant – solubilizing agent |
| PEG-150 dibehenate No CAS No. | PEG-150 dibehenate is the polyethylene glycol diester of behenic acid that conforms generally to the formula: $\text{CH}_3(\text{CH}_2)_{20}\overset{\text{O}}{\parallel}\text{C}-(\text{OCH}_2\text{CH}_2)_n\text{O}-\overset{\text{O}}{\parallel}\text{C}(\text{CH}_2)_{20}\text{CH}_3$ where n has an average value of 150. | Surfactant – cleansing agent; surfactant – solubilizing agent |
| PEG-3 dicaprylate/caprate 68583-52-8 | PEG-3 dicaprylate/caprate is the polyethylene glycol diester of a mixture of caprylic and capric acids containing an average of 3 moles of ethylene oxide $\text{RC}-(\text{OCH}_2\text{CH}_2)_n\text{O}-\text{CR}$ where n has an average value of 3 and RCO- represents the residue of either caprylic or capric acid [R is a 7 or 9 carbon alkyl chain]. | Surfactant – emulsifying agent |
| PEG-4 dicocoate 69278-77-9 | PEG-4 dicocoate is the polyethylene glycol diester of coconut acid that conforms generally to the formula: $\text{RC}-(\text{OCH}_2\text{CH}_2)_n\text{O}-\text{CR}$ where n has an average value of 4 and RCO- represents the fatty acids derived from coconut oil. | Skin-conditioning agent – emollient; surfactant – emulsifying agent |
| PEG-8 dicocoate No CAS No. | PEG-8 dicocoate is the polyethylene glycol diester of coconut acid that conforms generally to the formula: $\text{RC}-(\text{OCH}_2\text{CH}_2)_n\text{O}-\text{CR}$ where n has an average value of 8 and RCO- represents the fatty acids derived from coconut oil. | Surfactant – emulsifying agent |
| PEG-4 diheptanoate 70729-68-9 | PEG-4 diheptanoate is the polyethylene glycol diester of heptanoic acid that conforms to the formula: $\text{CH}_3(\text{CH}_2)_5\overset{\text{O}}{\parallel}\text{C}-(\text{OCH}_2\text{CH}_2\text{O})_4-\overset{\text{O}}{\parallel}\text{C}(\text{CH}_2)_5\text{CH}_3$ | Skin-conditioning agent – emollient; surfactant – emulsifying agent |

Table 1. The definitions and functions of the PEG diesters in this safety assessment.¹

| Ingredient and CAS No. | Definition/structure | Function |
|---|---|--|
| PEG-2 diisononanoate No CAS No. | PEG-2 diisononanoate is the polyethylene glycol diester of isononanoic acid that conforms to the formula: $\text{C}_8\text{H}_{17}\text{C}(=\text{O})-(\text{OCH}_2\text{CH}_2)_n\text{O}-\text{C}(=\text{O})\text{C}_8\text{H}_{17}$ where n has an average value of 2. | Surfactant – emulsifying agent |
| PEG-2 diisostearate No CAS No. | PEG-2 diisostearate is the polyethylene glycol diester of isostearic acid that conforms generally to the formula: $\text{C}_{17}\text{H}_{35}\text{C}(=\text{O})-(\text{OCH}_2\text{CH}_2)_n\text{O}-\text{C}(=\text{O})\text{C}_{17}\text{H}_{35}$ where n has an average value of 2. | Surfactant – emulsifying agent |
| PEG-3 diisostearate No CAS No. | PEG-3 diisostearate is the polyethylene glycol diester of isostearic acid that conforms generally to the formula: $\text{C}_{17}\text{H}_{35}\text{C}(=\text{O})-(\text{OCH}_2\text{CH}_2)_n\text{O}-\text{C}(=\text{O})\text{C}_{17}\text{H}_{35}$ where n has an average value of 3. | Surfactant – emulsifying agent |
| PEG-4 diisostearate No CAS No. | PEG-4 diisostearate is the polyethylene glycol diester of isostearic acid that conforms generally to the formula: $\text{C}_{17}\text{H}_{35}\text{C}(=\text{O})-(\text{OCH}_2\text{CH}_2)_n\text{O}-\text{C}(=\text{O})\text{C}_{17}\text{H}_{35}$ where n has an average value of 4. | Surfactant – emulsifying agent |
| PEG-6 diisostearate No CAS No. | PEG-6 diisostearate is the polyethylene glycol diester of isostearic acid that conforms generally to the formula: $\text{C}_{17}\text{H}_{35}\text{C}(=\text{O})-(\text{OCH}_2\text{CH}_2)_n\text{O}-\text{C}(=\text{O})\text{C}_{17}\text{H}_{35}$ where n has an average value of 6. | Surfactant – emulsifying agent |
| PEG-8 diisostearate No CAS No. | PEG-8 diisostearate is the polyethylene glycol diester of isostearic acid that conforms to the formula: $\text{C}_{17}\text{H}_{35}\text{C}(=\text{O})-(\text{OCH}_2\text{CH}_2)_n\text{O}-\text{C}(=\text{O})\text{C}_{17}\text{H}_{35}$ where n has an average value of 8. | Surfactant – emulsifying agent |
| PEG-12 diisostearate No CAS No. | PEG-12 diisostearate is the polyethylene glycol diester of isostearic acid that conforms generally to the formula: $\text{C}_{17}\text{H}_{35}\text{C}(=\text{O})-(\text{OCH}_2\text{CH}_2)_n\text{O}-\text{C}(=\text{O})\text{C}_{17}\text{H}_{35}$ where n has an average value of 12. | Surfactant – emulsifying agent |
| PEG-90 diisostearate No CAS No. | PEG-90 diisostearate is the polyethylene glycol diester of isostearic acid that conforms generally to the formula: $\text{C}_{17}\text{H}_{35}\text{C}(=\text{O})-(\text{OCH}_2\text{CH}_2)_n\text{O}-\text{C}(=\text{O})\text{C}_{17}\text{H}_{35}$ where n has an average value of 90. | Surfactant – cleansing agent |
| PEG-175 diisostearate No CAS No. | PEG-175 diisostearate is the polyethylene glycol diester of isostearic acid that conforms generally to the formula: $\text{C}_{17}\text{H}_{35}\text{C}(=\text{O})-(\text{OCH}_2\text{CH}_2)_n\text{O}-\text{C}(=\text{O})\text{C}_{17}\text{H}_{35}$ where n has an average value of 175. | Surfactant – emulsifying agent; viscosity increasing agent – aqueous |
| PEG-2 dilaurate 6281-04-5 9005-02-1 (generic) | PEG-2 dilaurate is the polyethylene glycol diester of lauric acid that conforms to the formula: $\text{CH}_3(\text{CH}_2)_{10}\text{C}(=\text{O})-(\text{OCH}_2\text{CH}_2)_n\text{O}-\text{C}(=\text{O})(\text{CH}_2)_{10}\text{CH}_3$ where n has an average value of 2. | Surfactant – emulsifying agent |
| PEG-4 dilaurate 9005-02-1 (generic) | PEG-4 dilaurate is the polyethylene glycol diester of lauric acid that conforms to the formula: $\text{CH}_3(\text{CH}_2)_{10}\text{C}(=\text{O})-(\text{OCH}_2\text{CH}_2)_n\text{O}-\text{C}(=\text{O})(\text{CH}_2)_{10}\text{CH}_3$ where n has an average value of 4. | Surfactant – emulsifying agent |
| PEG-6 dilaurate 9005-02-1 (generic) | PEG-6 dilaurate is the polyethylene glycol diester of lauric acid that conforms to the formula: $\text{CH}_3(\text{CH}_2)_{10}\text{C}(=\text{O})-(\text{OCH}_2\text{CH}_2)_n\text{O}-\text{C}(=\text{O})(\text{CH}_2)_{10}\text{CH}_3$ where n has an average value of 6. | Surfactant – emulsifying agent |

Table 1. The definitions and functions of the PEG diesters in this safety assessment.¹

| Ingredient and CAS No. | Definition/structure | Function |
|--|--|---|
| PEG-8 dilaurate 9005-02-1 (generic) | PEG-8 Dilaurate is the polyethylene glycol diester of lauric acid that conforms to the formula: $\text{CH}_3(\text{CH}_2)_{10}\overset{\text{O}}{\parallel}\text{C}-(\text{OCH}_2\text{CH}_2)_n\text{O}-\overset{\text{O}}{\parallel}\text{C}(\text{CH}_2)_{10}\text{CH}_3$ where n has an average value of 8. | Surfactant – emulsifying agent |
| PEG-12 dilaurate 9005-02-1 (generic) | PEG-12 Dilaurate is the polyethylene glycol diester of lauric acid that conforms to the formula: $\text{CH}_3(\text{CH}_2)_{10}\overset{\text{O}}{\parallel}\text{C}-(\text{OCH}_2\text{CH}_2)_n\text{O}-\overset{\text{O}}{\parallel}\text{C}(\text{CH}_2)_{10}\text{CH}_3$ where n has an average value of 12. | Surfactant – emulsifying agent |
| PEG-16 dilaurate 9005-02-1 (generic) | PEG-16 Dilaurate is the polyethylene glycol diester of lauric acid that conforms generally to the formula: $\text{CH}_3(\text{CH}_2)_{10}\overset{\text{O}}{\parallel}\text{C}-(\text{OCH}_2\text{CH}_2)_n\text{O}-\overset{\text{O}}{\parallel}\text{C}(\text{CH}_2)_{10}\text{CH}_3$ where n has an average value of 16. | Surfactant – emulsifying agent |
| PEG-20 dilaurate 9005-02-1 (generic) | PEG-20 dilaurate is the polyethylene glycol diester of lauric acid that conforms to the formula: $\text{CH}_3(\text{CH}_2)_{10}\overset{\text{O}}{\parallel}\text{C}-(\text{OCH}_2\text{CH}_2)_n\text{O}-\overset{\text{O}}{\parallel}\text{C}(\text{CH}_2)_{10}\text{CH}_3$ where n has an average value of 20. | Surfactant – emulsifying agent |
| PEG-32 dilaurate 9005-02-1 (generic) | PEG-32 dilaurate is the polyethylene glycol diester of lauric acid that conforms to the formula: $\text{CH}_3(\text{CH}_2)_{10}\overset{\text{O}}{\parallel}\text{C}-(\text{OCH}_2\text{CH}_2)_n\text{O}-\overset{\text{O}}{\parallel}\text{C}(\text{CH}_2)_{10}\text{CH}_3$ where n has an average value of 32. | Surfactant – emulsifying agent |
| PEG-75 dilaurate 9005-02-1 (generic) | PEG-75 dilaurate is the polyethylene glycol diester of lauric acid that conforms to the formula: $\text{CH}_3(\text{CH}_2)_{10}\overset{\text{O}}{\parallel}\text{C}-(\text{OCH}_2\text{CH}_2)_n\text{O}-\overset{\text{O}}{\parallel}\text{C}(\text{CH}_2)_{10}\text{CH}_3$ where n has an average value of 75. | Surfactant – cleansing agent; surfactant – solubilizing agent |
| PEG-150 dilaurate 9005-02-1 (generic) | PEG-150 dilaurate is the polyethylene glycol diester of lauric acid that conforms to the formula: $\text{CH}_3(\text{CH}_2)_{10}\overset{\text{O}}{\parallel}\text{C}-(\text{OCH}_2\text{CH}_2)_n\text{O}-\overset{\text{O}}{\parallel}\text{C}(\text{CH}_2)_{10}\text{CH}_3$ where n has an average value of 150. | Surfactant – cleansing agent; surfactant – solubilizing agent |
| PEG-2 dioleate No CAS No. | PEG-2 dioleate is the polyethylene glycol diester of oleic acid that conforms generally to the formula: $\text{CH}(\text{CH}_2)_7\overset{\text{O}}{\parallel}\text{C}-(\text{OCH}_2\text{CH}_2)_n\text{O}-\overset{\text{O}}{\parallel}\text{C}(\text{CH}_2)_7\text{CH}$ $\begin{array}{c} \parallel \\ \text{CH}(\text{CH}_2)_7\text{CH}_3 \end{array} \qquad \begin{array}{c} \parallel \\ \text{CH}_3(\text{CH}_2)_7\text{CH} \end{array}$ where n has an average value of 2. | Surfactant – emulsifying agent |
| PEG-3 dioleate No CAS No. | PEG-3 dioleate is the polyethylene glycol diester of oleic acid that conforms generally to the formula: $\text{CH}(\text{CH}_2)_7\overset{\text{O}}{\parallel}\text{C}-(\text{OCH}_2\text{CH}_2)_n\text{O}-\overset{\text{O}}{\parallel}\text{C}(\text{CH}_2)_7\text{CH}$ $\begin{array}{c} \parallel \\ \text{CH}(\text{CH}_2)_7\text{CH}_3 \end{array} \qquad \begin{array}{c} \parallel \\ \text{CH}_3(\text{CH}_2)_7\text{CH} \end{array}$ where n has an average value of 3. | Surfactant – emulsifying agent |
| PEG-4 dioleate 134141-38-1 52668-97-0 (generic) 9005-07-6 (generic) | PEG-4 dioleate is the polyethylene glycol diester of oleic acid that conforms to the formula: $\text{CH}(\text{CH}_2)_7\overset{\text{O}}{\parallel}\text{C}-(\text{OCH}_2\text{CH}_2)_n\text{O}-\overset{\text{O}}{\parallel}\text{C}(\text{CH}_2)_7\text{CH}$ $\begin{array}{c} \parallel \\ \text{CH}(\text{CH}_2)_7\text{CH}_3 \end{array} \qquad \begin{array}{c} \parallel \\ \text{CH}_3(\text{CH}_2)_7\text{CH} \end{array}$ where n has an average value of 4. | Surfactant – emulsifying agent |
| PEG-6 dioleate 52668-97-0 (generic) 9005-07-6 (generic) | PEG-6 dioleate is the polyethylene glycol diester of oleic acid that conforms to the formula: $\text{CH}(\text{CH}_2)_7\overset{\text{O}}{\parallel}\text{C}-(\text{OCH}_2\text{CH}_2)_n\text{O}-\overset{\text{O}}{\parallel}\text{C}(\text{CH}_2)_7\text{CH}$ $\begin{array}{c} \parallel \\ \text{CH}(\text{CH}_2)_7\text{CH}_3 \end{array} \qquad \begin{array}{c} \parallel \\ \text{CH}_3(\text{CH}_2)_7\text{CH} \end{array}$ where n has an average value of 6. | Surfactant – emulsifying agent |

Table 1. The definitions and functions of the PEG diesters in this safety assessment.¹

| Ingredient and CAS No. | Definition/structure | Function |
|---|--|---|
| PEG-8 dioleate 52668-97-0 (generic) 9005-07-6 (generic) | PEG-8 dioleate is the polyethylene glycol diester of oleic acid that conforms to the formula: $\begin{array}{c} \text{O} \\ \parallel \\ \text{CH}(\text{CH}_2)_7\text{C} - (\text{OCH}_2\text{CH}_2)_n\text{O} - \text{C}(\text{CH}_2)_7\text{CH} \\ \parallel \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \parallel \\ \text{CH}(\text{CH}_2)_7\text{CH}_3 \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \text{CH}_3(\text{CH}_2)_7\text{CH} \end{array}$ <p>where n has an average value of 8.</p> | Surfactant – emulsifying agent |
| PEG-10 dioleate 52668-97-0 (generic) 9005-07-6 (generic) | PEG-10 dioleate is the polyethylene glycol diester of oleic acid that conforms to the formula: $\begin{array}{c} \text{O} \\ \parallel \\ \text{CH}(\text{CH}_2)_7\text{C} - (\text{OCH}_2\text{CH}_2)_n\text{O} - \text{C}(\text{CH}_2)_7\text{CH} \\ \parallel \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \parallel \\ \text{CH}(\text{CH}_2)_7\text{CH}_3 \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \text{CH}_3(\text{CH}_2)_7\text{CH} \end{array}$ <p>where n has an average value of 10.</p> | Surfactant – emulsifying agent |
| PEG-12 dioleate 52668-97-0 (generic) 9005-07-6 (generic) | PEG-12 dioleate is the polyethylene glycol diester of oleic acid that conforms to the formula: $\begin{array}{c} \text{O} \\ \parallel \\ \text{CH}(\text{CH}_2)_7\text{C} - (\text{OCH}_2\text{CH}_2)_n\text{O} - \text{C}(\text{CH}_2)_7\text{CH} \\ \parallel \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \parallel \\ \text{CH}(\text{CH}_2)_7\text{CH}_3 \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \text{CH}_3(\text{CH}_2)_7\text{CH} \end{array}$ <p>where n has an average value of 12.</p> | Surfactant – emulsifying agent |
| PEG-20 dioleate 52668-97-0 (generic) 9005-07-6 (generic) | PEG-20 dioleate is the polyethylene glycol diester of oleic acid that conforms to the formula: $\begin{array}{c} \text{O} \\ \parallel \\ \text{CH}(\text{CH}_2)_7\text{C} - (\text{OCH}_2\text{CH}_2)_n\text{O} - \text{C}(\text{CH}_2)_7\text{CH} \\ \parallel \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \parallel \\ \text{CH}(\text{CH}_2)_7\text{CH}_3 \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \text{CH}_3(\text{CH}_2)_7\text{CH} \end{array}$ <p>where n has an average value of 20.</p> | Surfactant – emulsifying agent |
| PEG-32 dioleate 52668-97-0 (generic) 9005-07-6 (generic) | PEG-32 dioleate is the polyethylene glycol diester of oleic acid that conforms to the formula: $\begin{array}{c} \text{O} \\ \parallel \\ \text{CH}(\text{CH}_2)_7\text{C} - (\text{OCH}_2\text{CH}_2)_n\text{O} - \text{C}(\text{CH}_2)_7\text{CH} \\ \parallel \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \parallel \\ \text{CH}(\text{CH}_2)_7\text{CH}_3 \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \text{CH}_3(\text{CH}_2)_7\text{CH} \end{array}$ <p>where n has an average value of 32.</p> | Surfactant – emulsifying agent |
| PEG-75 dioleate 52668-97-0 (generic) 9005-07-6 (generic) | PEG-75 dioleate is the polyethylene glycol diester of oleic acid that conforms to the formula: $\begin{array}{c} \text{O} \\ \parallel \\ \text{CH}(\text{CH}_2)_7\text{C} - (\text{OCH}_2\text{CH}_2)_n\text{O} - \text{C}(\text{CH}_2)_7\text{CH} \\ \parallel \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \parallel \\ \text{CH}(\text{CH}_2)_7\text{CH}_3 \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \text{CH}_3(\text{CH}_2)_7\text{CH} \end{array}$ <p>where n has an average value of 75.</p> | Surfactant – cleansing agent; surfactant – solubilizing agent |
| PEG-150 dioleate 52668-97-0 (generic) 9005-07-6 (generic) | PEG-150 dioleate is the polyethylene glycol diester of oleic acid that conforms to the formula: $\begin{array}{c} \text{O} \\ \parallel \\ \text{CH}(\text{CH}_2)_7\text{C} - (\text{OCH}_2\text{CH}_2)_n\text{O} - \text{C}(\text{CH}_2)_7\text{CH} \\ \parallel \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \parallel \\ \text{CH}(\text{CH}_2)_7\text{CH}_3 \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \text{CH}_3(\text{CH}_2)_7\text{CH} \end{array}$ <p>where n has an average value of 150.</p> | Surfactant – cleansing agent |
| PEG-3 dipalmitate 32628-06-1 (generic) | PEG-3 dipalmitate is the polyethylene glycol diester of palmitic acid that conforms generally to the formula: $\begin{array}{c} \text{O} \\ \parallel \\ \text{CH}_3(\text{CH}_2)_{14}\text{C} - (\text{OCH}_2\text{CH}_2)_n\text{O} - \text{C}(\text{CH}_2)_{14}\text{CH}_3 \\ \parallel \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \parallel \end{array}$ <p>where n has an average value of 3.</p> | Surfactant – emulsifying agent |
| PEG-8 ditallate 61791-01-3 (generic) | PEG-8 ditallate is the polyethylene glycol diester of tall oil acid that conforms generally to the formula: $\begin{array}{c} \text{O} \\ \parallel \\ \text{RC} - (\text{OCH}_2\text{CH}_2)_n\text{O} - \text{CR} \\ \parallel \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \parallel \end{array}$ <p>where RCO- represents the tall oil fatty radicals and n has an average value of 8.</p> | Surfactant – emulsifying agent |
| PEG-12 ditallate 61791-01-3 (generic) | PEG-12 ditallate is the polyethylene glycol diester of tall oil acid that conforms generally to the formula: $\begin{array}{c} \text{O} \\ \parallel \\ \text{RC} - (\text{OCH}_2\text{CH}_2)_n\text{O} - \text{CR} \\ \parallel \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \parallel \end{array}$ <p>where RCO- represents the tall oil fatty radicals and n has an average value of 12.</p> | Surfactant – emulsifying agent |

Table 2. Previous safety assessment of PEG diesters and component moieties of the ingredients in this safety assessment.

| Ingredients | Conclusion | Maximum concentration in safety assessment | Reference |
|---|--|--|-------------------|
| Previous safety assessment of PEG diesters | | | |
| PEG diesters - PEG-2 distearate, PEG-3 distearate, PEG-4 distearate, PEG-6 distearate, PEG-8 distearate, PEG-9 distearate, PEG-12 distearate PEG-20 distearate, PEG-32 distearate, PEG-50 distearate, PEG-75 distearate, PEG-120 distearate, PEG-150 distearate, PEG-175 distearate | Safe for use in cosmetic formulations under the present practices of use. | 5% | ² |
| PEG Dilaurates – PEG-2 dilaurate, PEG-4 dilaurate, PEG-6 dilaurate, PEG-8 dilaurate, PEG-12 dilaurate, PEG-16 dilaurate, PEG-20 dilaurate, PEG-32 dilaurate, PEG-75 dilaurate, PEG-150 dilaurate (also included PEG-2, -4, -6, -8, -9, -10, -12, -14, -20, -32, -75, -150, and -200 Laurate; and PEG-2 Laurate SE) | Safe for use in cosmetics at concentrations up to 25%. | 25% | ³ |
| PEG-2 diisononanoate (included with nonanoic acid and its nonanoate esters) | Safe as cosmetic ingredients in the present practices of use and concentration described in this safety assessment | 74% | ⁴ |
| Safety assessments on related moieties | | | |
| Coconut oil, acid and related ingredients | Safe as used | 100% | ^{6-8,15} |
| Isostearic acid | Safe as used. | 26% | ^{8,10} |
| Oleic acid, lauric acid, stearic acid | Safe as used. | > 50%; 43% | ^{9,11} |
| PEGs | Safe as used. | 85% | ¹²⁻¹⁴ |
| PEG stearates | Safe as used. | 25% | ^{8,17} |
| Stearates | Safe as used | 87% | ^{8,16} |
| Steareths | Safe when formulated to be nonirritating | 25%; 32% in products diluted for the bath | ¹⁹⁻²¹ |
| Tall oil acid, sodium tallate, potassium tallate, ammonium tallate | Safe as used. | 8% | ¹⁸ |

Table 3. Chemical and physical properties of PEG diesters.

| Property | Value | Reference |
|---------------------------------|-----------------------|---------------|
| PGE-4 diheptanoate | | |
| Physical Form | Liquid | ²⁵ |
| Color | Clear | ²⁵ |
| Density/Specific Gravity | 0.996 | ²⁵ |
| Vapor pressure mmHg@ 37°C | <0.1 | ²⁵ |
| Boiling Point °C | >300 | ²⁵ |
| Other Solubility g/L | | |
| Alcohol | Soluble | ²⁵ |
| Acetone | Soluble | ²⁵ |
| PEG-4 dilaurate | | |
| Physical Form | Viscous (oily) liquid | ²⁴ |
| Color | Pale yellow | ²⁴ |
| Density/Specific Gravity @ 25°C | 0.96 | ⁴³ |
| Melting Point °C | <14 | ⁴⁴ |
| Water Solubility | Dispersible | ²⁴ |
| Other Solubility | | |
| Mineral oil | Soluble | ²⁴ |
| Acetone | Soluble | ²⁴ |
| Isopropyl alcohol | Soluble | ²⁴ |
| PEG-8 dilaurate | | |
| Physical Form | Liquid | ²⁴ |
| Color | Clear, pale yellow | ²⁴ |
| Odor | Slightly fatty | ²⁴ |
| Density/Specific Gravity @ 25°C | 0.985-0.995 | ²⁴ |
| Water Solubility | Dispersible | |
| Other Solubility | | |
| Isopropyl alcohol | Soluble | ⁴⁵ |
| Acetone | Soluble | ⁴⁶ |
| Mineral oil | Soluble | ⁴⁷ |

Table 4. Current and historical frequency and concentration of use of PEG diesters according to duration and exposure.^{2-4,33,35}

| | <i># of Uses</i> | | <i>Max Conc of Use (%)</i> | | <i># of Uses</i> | | <i>Max Conc of Use (%)</i> | |
|-------------------------------|-----------------------------------|----------------------------------|----------------------------|---------------|---|---------------------------------|----------------------------|-------------|
| | 2015 | 1996 | 2014 | 1995 | 2015 | 1996 | 2014 | 1995 |
| | PEG-150 distearate | | | | PEG-175 distearate | | | |
| Totals* | 690 | 187 | 0.003-33.2 | 1-5 | NR | NR | 0.089 | NR |
| Duration of Use | | | | | | | | |
| <i>Leave-On</i> | 54 | 59 | 0.006-9 | 1-5 | NR | NR | NR | NR |
| <i>Rinse-Off</i> | 602 | 101 | 0.0003-33.2 | 1-5 | NR | NR | 0.089 | NR |
| <i>Diluted for (Bath) Use</i> | 34 | 27 | 1-1.5 | 1.75 | NR | NR | NR | NR |
| Exposure Type | | | | | | | | |
| Eye Area | 5 | 2 | 0.07-1.8 | 0.5 | NR | NR | NR | NR |
| Incidental Ingestion | NR | NR | 0.05 | NR | NR | NR | NR | NR |
| Incidental Inhalation-Spray | 16 ^a ; 12 ^c | 10 ^a ; 2 ^c | 0.006-2.4 ^a | NR | NR | NR | NR | NR |
| Incidental Inhalation-Powder | 1; 12 ^c | 4; 2 ^c | 0.024-9 ^b | NR | NR | NR | NR | NR |
| Dermal Contact | 487 | 117 | 0.0003-33.2 | 1-5 | NR | NR | 0.089 | NR |
| Deodorant (underarm) | 1 ^a | NR | NR | NR | NR | NR | NR | NR |
| Hair - Non-Coloring | 202 | 69 | 0.006-4.5 | 1-5 | NR | NR | NR | NR |
| Hair-Coloring | NR | NR | 0.0075-0.15 | NR | NR | NR | NR | NR |
| Nail | NR | 1 | NR | NR | NR | NR | NR | NR |
| Mucous Membrane | 399 | 42 | 0.0003-4.5 | 1.75 | NR | NR | NR | NR |
| Baby Products | 26 | 14 | 0.75-9.4 | NR | NR | NR | NR | NR |
| | PEG-2 diisosnoate | | | | PEG-4 dilaurate | | | |
| Totals* | NR | NR | 1.7 | 2 | 38 | 15 | 0.028-12 | 1-25 |
| Duration of Use | | | | | | | | |
| <i>Leave-On</i> | NR | NR | 1.7 | 2 | 18 | 5 | 0.032-12 | NR |
| <i>Rinse-Off</i> | NR | NR | NR | NR | 15 | 1 | 0.028-0.72 | NR |
| <i>Diluted for (Bath) Use</i> | NR | NR | NR | NR | 5 | 9 | NR | NR |
| Exposure Type | | | | | | | | |
| Eye Area | NR | NR | NR | NR | 9 | NR | 0.04-2 | NR |
| Incidental Ingestion | NR | NR | NR | NR | NR | NR | NR | NR |
| Incidental Inhalation-Spray | NR | NR | NR | NR | 6 ^a ; 3 ^c | 2 ^a ; 1 ^c | 0.072; 0.036 ^a | NR |
| Incidental Inhalation-Powder | NR | NR | NR | NR | 3 ^c | 1 ^c | 0.036-0.25 ^b | NR |
| Dermal Contact | NR | NR | NR | NR | 32 | 15 | 0.028-12 | NR |
| Deodorant (underarm) | NR | NR | NR | NR | NR | NR | NR | NR |
| Hair - Non-Coloring | NR | NR | NR | NR | 6 | NR | 0.036-0.72 | NR |
| Hair-Coloring | NR | NR | NR | NR | NR | NR | NR | NR |
| Nail | NR | NR | 1.7 | 2 | NR | NR | NR | NR |
| Mucous Membrane | NR | NR | NR | NR | 7 | 9 | NR | NR |
| Baby Products | NR | NR | NR | NR | NR | NR | NR | NR |
| | PEG-8 dilaurate | | | | *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. NR – no reported use ^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. ^c Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories. ^d Not spray ^e Pump spray ^f No breakdown of use was provided in the original report. | | | |
| Totals* | 10 down | 25 | 0.18-15 | 0.1-25 | | | | |
| Duration of Use | | | | | | | | |
| <i>Leave-On</i> | 1 | 9 | 6 | NR | | | | |
| <i>Rinse-Off</i> | 3 | 9 | 0.18-6 | NR | | | | |
| <i>Diluted for (Bath) Use</i> | 6 | 7 | 15 | NR | | | | |
| Exposure Type | | | | | | | | |
| Eye Area | 2 | NR | 0.18 | NR | | | | |
| Incidental Ingestion | NR | NR | NR | NR | | | | |
| Incidental Inhalation-Spray | 1 ^a | NR | 6 ^a | NR | | | | |
| Incidental Inhalation-Powder | NR | NR | NR | NR | | | | |
| Dermal Contact | 9 | 11 | 0.018-15 | NR | | | | |
| Deodorant (underarm) | NR | NR | NR | NR | | | | |
| Hair - Non-Coloring | 1 | 13 | 6 | NR | | | | |
| Hair-Coloring | NR | NR | NR | NR | | | | |
| Nail | NR | 1 | NR | NR | | | | |
| Mucous Membrane | 6 | 7 | 15 | NR | | | | |
| Baby Products | NR | NR | NR | NR | | | | |

Table 5. Frequency and concentration of use of PEG diesters, that have no historical use data, according to duration and exposure.^{33,35}

| Use type | Maximum Concentration | | Maximum Concentration | | Uses | Maximum Concentration (%) | Uses | Maximum Concentration (%) |
|-------------------------------|-----------------------|------------|-----------------------|--|---|---------------------------|------|---------------------------|
| | Uses | (%) | Uses | (%) | | | | |
| Total/range | 4 | 1-5 | 2 | 0.024-4.5 | NR = Not Reported; Totals = Rinse-off + Leave-on Product Uses. | | | |
| <i>Duration of use</i> | | | | | Note: Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure type uses may not equal the sum total uses. | | | |
| Leave-on | 2 | 1 | NR | 0.024-4.5 | ^a It is possible these products are sprays, but it is not specified whether the reported uses are sprays. | | | |
| Rinse-off | NR | 5 | 2 | 0.12-1 | ^b It is possible these products are powders, but it is not specified whether the reported uses are powders. | | | |
| Diluted for (bath) use | 2 | NR | NR | NR | ^c Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories. | | | |
| <i>Exposure type</i> | | | | | ^d Not spray | | | |
| Eye area | 2 | 1 | NR | NR | ^e Pump hair spray | | | |
| Incidental ingestion | NR | NR | NR | NR | | | | |
| Incidental Inhalation-sprays | NR | NR | NR | 0.24 ^e ; 0.024 ^a | | | | |
| Incidental inhalation-powders | NR | NR | NR | 0.12-0.15 ^b | | | | |
| Dermal contact | 2 | 5 | 2 | 0.1-4.5 | | | | |
| Deodorant (underarm) | NR | NR | NR | NR | | | | |
| Hair-noncoloring | NR | NR | NR | 0.024-0.24 | | | | |
| Hair-coloring | NR | NR | NR | NR | | | | |
| Nail | NR | NR | NR | NR | | | | |
| Mucous Membrane | 2 | NR | 1 | NR | | | | |
| Baby | NR | NR | NR | NR | | | | |

Table 6. Ingredients not reported to be in current use.^{33,35}

| | | |
|---------------------|----------------------------|---------------------|
| PEG-9 distearate | PEG-20 distearate | PEG-32 distearate |
| PEG-40 distearate | PEG-75 distearate | PEG-190 distearate |
| PEG-150 dibehenate | PEG-3 dicaprylate/caprates | PEG-4 dicocoate |
| PEG-2 diisostearate | PEG-3 diisostearate | PEG-4 diisostearate |
| PEG-2 dilaurate | PEG-6 dilaurate | PEG-12 dilaurate |
| PEG-16 dilaurate | PEG-20 dilaurate | PEG-32 dilaurate |
| PEG-75 dilaurate | PEG-150 dilaurate | PEG-2 dioleate |
| PEG-3 dioleate | PEG-4 dioleate | PEG-6 dioleate |
| PEG-10 dioleate | PEG-20 dioleate | PEG-32 dioleate |
| PEG-75 dioleate | PEG-150 dioleate | PEG-3 dipalmitate |
| PEG-8 ditallate | PEG-12 ditallate | |

Table 7. FDA Code of Federal Regulations that apply to the PEG diesters in this safety assessment.

| Use related to food | Ingredients | Code |
|--|---|---------------|
| Can be used for coloring shell eggs if there is no penetration of the shell. | PEG-2 distearate | 21CFR73.1 |
| May be used as defoaming agents in food as an emulsifier not to exceed 10% by weight of defoamer formulation. | PEG-8 dioleate; PEG-12 dioleate | 21CFR173.340 |
| May be used as indirect food additives: adhesives. | PEG-4 distearate; PEG-6 distearate; PEG-8 distearate; PEG-9 distearate; PEG-12 distearate; PEG-20 distearate; PEG-8 dicocoate; PEG-4 dilaurate; PEG-6 dilaurate; PEG-8 dilaurate; PEG-12 dilaurate; PEG-4 dioleate PEG-6 dioleate; PEG-8 dioleate; PEG-10 dioleate; PEG-12 dioleate; PEG-8 ditallate; PEG-12 ditallate | 21CFR175.105 |
| May be used as paper and paperboard components of paper and paperboard in contact with aqueous and fatty foods. | PEG-8 dioleate; PEG-4 dilaurate | 21CFR176.170 |
| May be used as paper and paperboard substances for use only as components of paper and paperboard; components of paper and paperboard in contact with dry food. | PEG-4 dilaurate | 21CFR176.180 |
| May be used as paper and paperboard substances for use only as components of paper and paperboard; defoaming agents used in coatings. | PEG-8 dioleate; PEG-4 dilaurate; PEG-12 dioleate | 21CFR176.200 |
| May be used as paper and paperboard substances for use only as components of paper and paperboard; defoaming agents used in the manufacture of paper and paperboard. | PEG-4 distearate; PEG-6 distearate; PEG-8 distearate; PEG-12 distearate; PEG-20 distearate; PEG-32 distearate; PEG-8 dicocoate; PEG-2 dilaurate; PEG-4 dilaurate; PEG-6 dilaurate; PEG-8 dilaurate; PEG-12 dilaurate; PEG-20 dilaurate; PEG-4 dioleate; PEG-6dioleate; PEG-8 dioleate; PEG-12 dioleate; PEG-20 dioleate; PEG-32 dioleate; PEG-8 ditallate; PEG-12 ditallate | 21CFR176.210 |
| May be used as indirect food additives: polymers. Substances for use as basic components of single and repeated use food contact surfaces; closures with sealing gaskets for food containers. | PEG-8 distearate; PEG-8 dioleate; PEG-12 dicocoate; PEG-8 dilaurate; PEG-8 ditallate | 21CFR177.1210 |
| May be used as indirect food additives: polymers. Substances for use as basic components of single and repeated use food contact surfaces; filters, resin-bonded. | PEG-8 distearate; PEG-9 distearate; PEG-12 distearate; PEG-20 distearate; PEG-32 distearate; PEG-8 dicocoate; PEG-8 dilaurate; PEG-12 dilaurate; PEG-20 dilaurate; PEG-32 dilaurate; PEG-8 dioleate; PEG-10 dioleate; PEG-12 dioleate; PEG-20 dioleate; PEG-32 dioleate | 21CFR177.2260 |
| May be used as indirect food additives: polymers. Substances for use as basic components of single and repeated use; rubber articles intended for repeated use. | PEG-3 dicaprylate/caprates | 21CFR177.2600 |
| May be used as indirect food additives: polymers. Substances for use as basic components of single and repeated use; textiles and textile fibers. | PEG-8 distearate; PEG-9 distearate; PEG-12 distearate; PEG-20 distearate; PEG-32 distearate; PEG-8 dicocoate; PEG-2 dilaurate; PEG-8 dilaurate; PEG-12 dilaurate; PEG-20 dilaurate; PEG-32 dilaurate; PEG-8 dioleate; PEG-12 dioleate; PEG-20 dioleate; PEG-32 dioleate; PEG-8 ditallate; PEG-12 ditallate | 21CFR177.2800 |
| Food additives permitted in feed and drinking water of animals. | PEG-8 dioleate | 21CFR573.800 |
| Food additives permitted in feed and drinking water of animals: The food additive polyoxyethylene glycol (400) mono- and dioleates may be safely used as an emulsifier in calf-milk replacer formulations. | PEG-8 dioleate | 21CFR573.820 |

Table 8. Acute oral toxicity studies of PEG-4 diheptanoate.

| Animal (n) | Results | Comments | Reference |
|-------------------------|--|---|---------------|
| CrI:CD rats (10/sex) | Oral LD ₅₀ was 25 g/kg for female rats and >25 g/kg for male rats | Clinical signs included labored breathing, belly-to-cage posture, lacrimation, staining of the face, stained and wet perineal area, and weight loss. All deaths occurred within 2 days of dosing. | ²⁵ |
| Wistar rats (5/sex) | Oral LD ₅₀ >2 g/kg | There was no mortality reported. Weight gains were normal in all rats. Gross pathological examination at necropsy revealed no treatment-related findings. There were no abnormal clinical signs observed except slight piloerection and sporadic findings (eg, ventral or limb position, reduced activity, reduced turgor) up to 6 h after oral administration. | ⁴² |
| Male Chr:CD rats (10) | Oral LD ₅₀ >25 g/kg | One mortality occurred on the day after dosing. Clinical signs were hyperemia, lethargy, and prostration. No systemic toxicity or adverse effects were reported. No gross abnormalities or lesions were observed. Slight initial weight loss was observed. No necropsies were performed. | ⁴² |
| Female CrI:CD rats (10) | Oral LD ₅₀ estimated to be 24-25 g/kg | Test doses: 14, 19, 22, 23, 24, 24.5, 24.75, 24.9 and 25 g/kg in corn oil. Mortalities at each dose level: 0, 0, 0, 0, 4, 1, 2, and 10, respectively. All deaths occurred within 2 days. Clinical signs, observed at all dose levels, included flat body posture, moribund condition, labored breathing, stained/wet perineal area, lacrimation, stained face, weakness, ataxia, lethargy, prostration, salivation and chromodacryorrhea. Body weight decrease was observed at all dose levels. No necropsies were performed. | ⁴² |

Table 9. Genotoxicity assays of PEG-4 diheptanoate.⁴²

| Assay | Concentration | Results |
|--|---|--|
| Bacterial reverse mutation assay using <i>S. typhimurium</i> strains TA98, TA100, TA1535, TA1537 | 500-10 000 µg/plate, 100-2500 µg/plate (based on toxicity with TA1535). OECD 471 with independent repeat. Positive Control: <i>N</i> -methyl- <i>N'</i> -nitro- <i>N</i> -nitroguanidine (TA100 and TA1535 without S9), 9-aminoacridine (TA1537 without S9), 2-nitrofluorene (TA98 without S9) and 2-aminoanthracene (all strains with S9). | Negative with and without metabolic activation |
| Mammalian cell gene mutation assay using Chinese hamster ovary cells | Without metabolic activation: 0.27-23.9 mM, metabolic activation: 0.25-23.9 mM. 3 independent tests; duplicate cultures/treatment. | Negative with and without metabolic activation |

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