Safety Assessment of Glycerin Ethoxylates as Used in Cosmetics

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date to comment on this safety assessment and to identify additional published data that should be included or provide unpublished data which can be made public and included.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 All unpublished data submitted to CIR will be discussed in open meetings, will be available at the CIR office for review by any interested party and may be cited in a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

The 2019 Cosmetic Ingredient Review Expert Panel members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Ronald A. Hill, Ph.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; James G. Marks, Jr., M.D., Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Executive Director is Bart Heldreth, Ph.D. This safety assessment was prepared by Alice Akinsulie, Scientific Writer/Analyst.

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1620 L Street, NW, Suite 1200 ♢ Washington, DC 20036-4702 ♢ ph 202.331.0651 ♢ fax 202.331.0088 ♢
cirinfo@cir-safety.org

INTRODUCTION

This scientific literature review is the initial step in preparing a safety assessment of the following 8 glycerin ethoxylates as used in cosmetic formulations.

Glycereth-3	Glycereth-18
Glycereth-7	Glycereth-20
Glycereth-8	Glycereth-26
Glycereth-12	Glycereth-31

According to the web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI; *Dictionary*), all of these ingredients are reported to function in cosmetics as skin-conditioning agents, and most are reported to function as viscosity decreasing agents (Table 1).[1]

The rationale for this grouping of ingredients stems from the fact that these ingredients are structurally related as polyethylene glycol ethers of glycerin. The Panel has reviewed the safety of some of the components of these ingredients. In 2010, CIR issued a final report on the safety of polyethylene glycols (PEGs); the Panel concluded that the PEGs are safe in the present practices of use and concentration.[2] In 2015, the Panel issued a safety assessment on Glycerin, with the conclusion that glycerin was safe as a cosmetic ingredient in the practices of use and concentration described in the safety assessment.[3] These reports are available on the CIR website (https://www.cir-safety.org/ingredients).

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 CIR typically evaluates, is provided on the 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.

Much of the data included in this safety assessment was obtained from robust summaries submitted to the European Chemicals Agency (ECHA) by companies as part of the REACH chemical registration process.[4] The REACH dossier was prepared for ingredients with the generic CAS No. 31694-55-0 (identified as glycerol, ethoxylated in the dossier), but the specific identities of the ingredients were not discerned; the identification of the test article in each study was provided as a trade name, and those trade names were not found in the *Dictionary*. Therefore, it is not known how the substances being tested in these studies compare to the cosmetic ingredients being reviewed in this assessment, because the test articles are of unknown or variable composition. However, because these data were included as part of the REACH dossier on ethoxylated glycerols, they are included in this safety assessment as potential read-across. If it is known that a test substance is a cosmetic ingredient, then the INCI name will be used; otherwise, a generic term that identifies that test substance (e.g., ethoxylated glycerol) will be used.

CHEMISTRY

Definition and Structure

These ingredients are polyethylene glycol ethers of glycerin, as depicted in Figure 1.

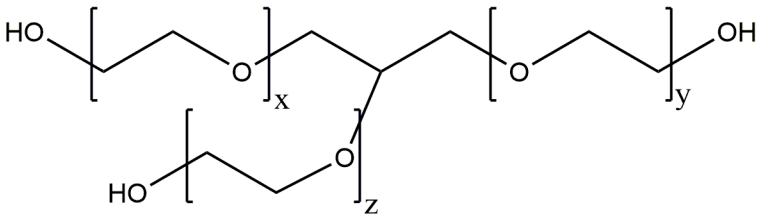

Figure 1. Glycerin ethoxylates, wherein the average ethoxylation value equals x + y + z (e.g., x + y + z = 3 in the case of Glycereth-3)

The definition of each ingredient, as given in the *Dictionary*, is provided in Table 1. For the data summarized herein as "glycerol ethoxylate," the REACH dossier describes the average ethoxylation value as between 1 and 6.5, inclusive of 1 and 6.5. Thus, the average ethoxylation value for glyceryl ethoxylate may be described as $1.0 \leq x + y + z \leq 6.5$ for the test material evaluated in those summaries. Comparing this range of average ethoxylation values to those of the ingredients in this report, Glycereth-3 (i.e. x + y + z = 3) falls in that range.

Physical and Chemical Properties

Ethoxylated glycerin is a non-volatile (vapor pressure 0.0000389 hPa at 20ºC), slightly viscous liquid at room temperature, and it is fully miscible with water.[4] Physical and chemical properties of glycerin ethoxylates are presented in Table 2.

Method of Manufacture

Method of manufacture data specific to these cosmetic ingredients were not found in the published literature, and unpublished data were not submitted. However, glycerin ethoxylates, in general, are the products resulting from the reaction of glycerin and ethylene oxide.[5]

Impurities

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

USE

Cosmetic

The safety of the cosmetic ingredient(s) addressed in this assessment is evaluated based on data received from the US Food and Drug Administration (FDA) and the cosmetics industry on the expected use of these ingredients in cosmetics. Use frequencies of individual ingredients in cosmetics are collected from manufacturers and reported by cosmetic product category in the FDA Voluntary Cosmetic Registration Program (VCRP) database. Use concentration data are submitted by the cosmetic industry in response to a survey, conducted by the Personal Care Products Council (Council), of maximum reported use concentrations by product category.

The glycerin ethoxylates are used widely in a variety of rinse-off and leave-on cosmetics products. According to 2019 VCRP survey data, Glycereth-26 is reported to be used in 379 formulations, and Glycereth-7 is reported to be used in 80 formulations (Table 3).[6] The three other in-use ingredients are reported to be used in 21 formulations or less. The results of the concentration of use survey conducted by the Council in 2018 indicates Glycereth-26 has the highest concentration of use, at 39.5% in skin cleansing products.[7] The highest concentration of use reported for products resulting in leave-on dermal exposure is Glycereth-26. It is reported at 6% in eye lotion.

Uses were reported in the VCRP for Glycereth-20, but no concentration of use was reported for this ingredient in response to the industry survey. The ingredients not in use, according to the VCRP and industry survey, are Glycereth-3, 8, and 31.

A few of the glycerin ethoxylates have uses that may be incidentally ingested or come into contact with mucous membranes; for example, Glycereth-7 is reported to be in 67 lipstick formulation (concentration of use data was not reported for this category) and Glycereth-18 is reported to be used in bath soaps and detergents at a maximum concentration of 0.3%. Additionally, these ingredients have been reported to be used in products that may come into contact with the eyes; for example, Glycereth-26 is reported to be used at up to 6% in eye lotions. Moreover, these ingredients are reported to be used in spray products that could possibly be inhaled. Glycereth-26 was reported to be used at up to 1% in body and hand products. In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters > 10 µm, with propellant sprays yielding a greater fraction of droplets/particles < 10 µm compared with pump sprays.[8,9] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and thoracic regions of the respiratory tract and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.[10,11]

The ethoxylated glycerin ingredients named in the report are not restricted from use in any way under the rules governing cosmetic products in the European Union.[12]

Non-Cosmetic

Non-cosmetic uses of the glycerin ethoxylate ingredients were not discovered in the published literature.

TOXICOKINETICS STUDIES

Toxicokinetics data (such as dermal penetration and absorption, distribution, metabolism, and excretion data) were not discovered in the published literature, and unpublished data were not submitted.

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

Acute dermal, oral, and inhalation data are summarized in Table 4.

Glycereth-3

No toxicity was observed when Glycereth-3, at concentrations of 1 - 50%, was given to rats orally at doses of 0.025 -10 mL/kg body weight.[4] The oral LD_{50} of Glycereth-3 tested at concentrations of 1-50% was >10 mL/kg in male and female rats. No mortality occurred in an inhalation study when 3 male and 3 female rats (species not specified) were exposed (whole body) to an aerosol of 3.575 mg/L of Glycereth-3 for 8 hours.

Ethoxylated glycerol (a read-across source for Glycereth-3)

The dermal LD_{50} of an ethoxylated glycerol in male and female Wistar rats was > 5000 mg/kg.[4]

In female Wistar rats, the oral LD_{50} of an ethoxylated glycerol was > 2000 mg/kg.[4] In another oral toxicity study, the LD_{50} of an ethoxylated glycerol in Sprague-Dawley rats was > 10,000 mg/kg; 5 male rats were dosed with 11,550 mg/kg and 5 female rats dosed with 10,000 mg/kg of the test article, and no mortality occurred.

In an inhalation study of an ethoxylated glycerol, 6 rats (strain not specified) were exposed to 0.178 mg/l of the test article for 7 hours, and another group of 6 rats was exposed (whole body) to 0.143 mg/l of the test article for 7 h as a vapor.[4]

Short-Term Toxicity Studies

Oral

Propoxylated nitrilotriethanol (a read-across source for ethoxylated glycerol, according to the ECHA dossier)

A pilot study was performed using 2 male and 2 female Wistar rats.[4] Animals were administered a propoxylated nitrilotriethanol at doses of 0, 65, 160, 400, 1000 mg/kg for two weeks. No clinical findings or relevant effects on body weight development were observed. In a short-term oral exposure study, a propoxylated nitrilotriethanol (MW ~ 340 g/mol) in water was administered once daily by gavage to Wistar rats (5 per sex) at doses of 0, 100, 300, and 1000 mg/kg bw for 31 days in accord with Organization for Economic Co-operation and Development test guideline (OECD TG) 407.[4] No mortality was observed in either sex. There was no effect observed upon hematological, clinical biochemistry or macroscopic examination at any dose. The histopathological evaluation revealed slightly more pronounced hypertrophy of the follicular cell epithelium in the thyroid gland of females of the high dose. Biochemical analysis revealed significantly low plasma creatinine concentrations in males dosed with 1000 mg/kg and higher levels in all groups of treated females. Based on these results, the no-observable-adverse-effect-level (NOAEL) was considered to be 1000 mg/kg bw/day.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY STUDIES

Oral

Propoxylated nitrilotriethanol (a read-across source for ethoxylated glycerol, according to the ECHA dossier)

A reproductive/developmental toxicity screen test was performed in accord with OECD TG 421.[4] Groups of 12 male and 12 female Wistar rats were administered a propoxylated nitrilotriethanol (average MW 280 g/mol) in water at doses of 0, 100, 300, and 1000 mg/kg bw by gavage. Concentration of test article and days of dosing were not specified. Typically, in a study following this TG females are dosed throughout the study; however, that was not stated in the summary. The rats in each dose group were allowed to deliver. Body weights were determined daily during pregnancy, and dams were examined shortly after birth and on day 4 postpartum. Transient salivation was noted in both sexes of the parental rats dosed with 1000 mg/kg. Slight body weight loss occurred in females of the 1000 mg/kg dose group during lactation, and marginal body weight gains were noted during the premating period at all doses. No significant embryotoxic or teratogenic effects nor abnormalities were noted, and no effects on reproductive performance were observed. Four pups from the F_1 generations developed filiformed tip at 1000 mg/kg compared to 3 pups in the control group. No adverse effect levels (NOELs) were determined to be 100 mg/kg in females and 300 mg/kg in males, based increased incidence of salivation. Under the test conditions the NOAEL was derived as 1000 mg/kg because the mild body weight loss observed with females at the highest dose group (1000 mg/kg bw/day) was considered to be a non-adverse treatment-related effect, as it follows a statistically significant increased body weight gain compared to the control group in the premating phase.

GENOTOXICITY

In Vitro

Ethoxylated glycerol

The mutagenicity of an ethoxylated glycerol was evaluated in an Ames test, performed in accordance with OECD TG 471.[4] *Salmonella typhimurium* strains TA 1535, TA 1537, TA 98, and TA 100 and *Escherichia coli* WP2 were studied in the presence and absence of metabolic activation. The test article dissolved in water was administered at concentrations of 0, 33,

100, 333, 1000, 2500, and 5000 µg/plate. Appropriate positive and negative controls were used. The test article did not produce any mutagenic effects.

Propoxylated glycerol (a read-across source for ethoxylated glycerol, according to the ECHA dossier)

In a mammalian chromosomal aberration study performed in accord with OECD TG 473, a propoxylated glycerol was considered to be non-clastogenic to human lymphocytes with or without metabolic activation.[4] (No other details were provided.)

Propoxylated nitrilotriethanol (a read-across for ethoxylated glycerol, according to the ECHA dossier)

Chinese hamster lung fibroblasts (CHL) V79 cells were used in a mammalian cell gene mutation assay (hypoxanthine-guanine phosphoribosyl transferase (HGPRT) test) to evaluate the mutagenicity of a propoxylated nitrilotriethanol (average MW 265 g/mol) in ethanol.[4] Cells were treated with the test article at doses of 400, 800, 1200, 1600, 2000, 2400, and 2800 µg/ml without metabolic activation and 42, 84, 168, 336, 672, 1344, and 2688 µg/ml with metabolic activation. Appropriate positive and negative controls were used. The test article did not induce mutagenic effects in the presence or absence of a metabolic activation system.

CARCINOGENICITY STUDIES

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

DERMAL IRRITATION AND SENSITIZATION

Irritation

In Vitro

In an in vitro study performed in accord with OECD TG 439, dermal irritation potential was assessed by a single topical application of 30 µL of an ethoxylated glycerol applied undiluted to a reconstructed three-dimensional human epidermis model (EpiDerm™).[4] Thirty microliters (µL) of sterile phosphate buffered saline (PBS) was used as negative control and applied for 1 hour followed by a 42-hours post-incubation period. The tissues were washed with sterile PBS 1 hour after the application. The test substance is not expected to be irritating.

Animal

Glycereth-3

Skin irritation potential was evaluated using 2 Vienna white rabbits using a test method comparable to OECD TG 404.[4] Glycereth-3 (1 mL) was applied neat to shaved skin area of 2.5 cm x 2.5 cm by an occlusive dressing for 20 hours, and the test sites were observed at 24 hours, 48 hours, and 8 days. No edema and erythema findings were observed. The test article was considered to be non-irritant to rabbit skin.

Ethoxylated glycerol

Patch tests were performed over an area of 2.5 cm x 2.5 cm on the back of 2 male Vienna white rabbits in a study comparable to OECD TG 404.[4] Animals were administered an ethoxylated glycerol to the skin for 20 hours under occlusive patches, and observations were made at 24 hours, 48 hours, and 8 days. After patch removal, the skin was washed with water. Irritation reactions were scored according to the following scales: 0 (no erythema) to 4 (severe erythema) and 0 (no edema) to 4 (severe edema). The mean erythema scores was 1.25 (with a score of 1.0 in one rabbit, which was fully reversible within 48 h, and a score of 1.5 in the other rabbit, which was fully reversible within 8 days). The test article was considered to be non-irritating

SENSITIZATION

Animal

Propoxylated glycerol (a read-across source for ethoxylated glycerol, according to the ECHA dossier)

The sensitization potential of a propoxylated glycerol (MW 300 g/mol) was evaluated with a Buehler test according to OECD TG 406.[4] Dunkin Hartley guinea pigs (10 males and 10 females) received 0.5 mL of the undiluted test article for the topical induction with an occlusive dressing for 6 hours on day 1, 7 and 14. Challenge consisted of a topical application of 0.5 mL undiluted test article held in place by an occlusive dressing for an exposure period 6 hours on day 28. Five males and 5 females served as the control group. The test article was not a sensitizer.

OCULAR IRRITATION STUDIES

In Vitro

Ethoxylated glycerol

The potential irritation of an ethoxylated glycerol was studied in a Bovine Corneal Opacity and Permeability (BCOP) test conducted according to OECD TG 437.[4] Ethoxylated glycerol (750 µL) was applied directly to the epithelial surface of the cornea using a syringe (open chamber method) for 10 minutes. Highly deionized water was used as the negative control, and a 1% (w/v) solution of sodium hydroxide in highly de-ionized water served as the positive control (treatment group consisted of 3 corneas). The opacity and permeability assessments of the cornea were derived by an In Vitro Irritancy Score (IVIS), which is used to classify the irritancy level of the test article. The calculated mean IVIS was 3.0 ± 1.2, 2.6 ± 3.3, and 184.0 ± 20.9, respectively in the test group, the negative control group and the positive control group. It was concluded the test substance does not cause serious eye damage in the BCOP test.

The potential of the same ethoxylated glycerol to cause eye irritation was further evaluated in a second study, in accord with OECD TG 405 and using a three-dimensional human cornea model.[4] Fifty µL of the undiluted test article was applied to a reconstructed three-dimensional human cornea model EpiOcular™ (2 tissue sample per treatment). The treated tissue was incubated for 30 minutes, washed out, and post-incubated under normal medium and culture conditions for 2 hours. The negative control tissues received applications of 50 µL of highly de-ionized water. The test article was considered to be non-irritating.

Animal

Glycereth-3

Ocular irritation was evaluated in 2 Vienna white rabbits using test methods that are similar to OECD TG 405.[4] The animals received a single application of 50 µL of undiluted Glycereth-3 instilled into the conjunctival sac of the right eye without washing and were observed for 8 days. The left eye of the animals remained untreated and served as a control. Slight conjunctivae redness was observed in both animals after 10 min, 1 hour, and 3 hours. These effects were fully reversible within 24 hours. The test article was found to be non-irritating.

Ethoxylated glycerol

Vienna white rabbits were used to test for ocular irritation using test methods that are similar to OECD TG 405.[4] Fifty microliters of an undiluted ethoxylated glycerol were instilled into the conjunctival sac of one eye of 2 animals. The saline-treated contralateral eye served as a control. The eyes were not washed out and were observed for a total of 8 days. Hyperemia was noted in the blood vessels of both animals. In one animal, this effect was not fully reversible within 8 days; however, a similar observation was noted in the control eye of this animal. The test article was considered non-irritating.

SUMMARY

This is a safety assessment of 8 glycerin ethoxylates as used in cosmetics. These ingredients are all polyethylene glycol ethers of glycerin. All of the ingredients in this report are reported to function as skin-conditioning agents, and most are reported to function as viscosity decreasing agents.

The glycerin ethoxylates are primarily are used widely in a variety of rinse-off and leave-on cosmetics products, and most of these reported uses are in some type of hair or skin cleansing formulations. Glycereth-26 has the highest reported frequency of use (379 formulations), and Glycereth-7 has the second greatest reported number of uses (80). Glycereth-26 has the highest concentration of use, at 39.5% in skin cleansing products. The highest concentrations of use reported for products resulting in leave-on dermal exposure is 6% Glycereth-26 in eye lotions. In Europe, the ethoxylated glycerin ingredients named in the report are not restricted from use in any way under the rules governing cosmetic products.

Glycereth-3, at concentrations ranging from 1 - 50%, was administered orally to 6 groups of Fischer 344 rats. Dosing was followed by a 7-day observation period. The oral LD_{50} was > 10 mL/kg. In another study, 3 male and 3 female rats were used to determine acute inhalation toxicity. Glycereth-3 at a concentration of 3.575 mg/L, was tested in rats as an aerosol/mist for 8 hours. No mortality occurred.

Studies involving acute dermal and oral toxicity of ethoxylated glycerol reported no signs of toxicity. The acute dermal LD_{50} of an ethoxylated glycerol was calculated to be > 5000 mg/kg in rats. No evidence of toxicity was observed in an acute oral toxicity study using two groups of three female Sprague-Dawley rats, and the oral LD_{50} of the ethoxylated glycerol was greater than 2000 mg/kg. No evidence of toxicity was reported when an ethoxylated glycerol was administered orally to 2 groups of 5 Sprague-Dawley rats. The LD_{50} was > 10,000 mg/kg. The acute inhalation toxicity of an ethoxylated glycerol was evaluated in a study involving 12 rats (strains not specified). Animals were exposed whole-body to 0.178 mg/L in experiment 1 and 0.143 mg/L in experiment 2, for 7 hours. No mortality occurred.

In a pilot study, 2 male and 2 female Wister rats received a propoxylated nitrilotriethanol at doses of 0, 65, 160, 400, and 1000 mg/kg for two weeks; no clinical findings or relevant effects on body weight development were observed. In a repeated dose toxicity study, rats (5 per sex) were administered a propoxylated nitrilotriethanol (MW ~ 340 g/mol) in water at doses of 0, 100, 300, and 1000 mg/kg. No mortality was observed in either sex. No clinical effects were observed in either sex of all dose groups. The histopathological evaluation revealed slightly more pronounced hypertrophy of the follicular cell epithelium in the thyroid gland of females of the high dose. Based on these results, the NOAEL was considered to be 1000 mg/kg bw/day.

A reproductive/developmental toxicity screening test was performed with 12 male and 12 female Wistar rats. Animals were administered a propoxylated nitrilotriethanol (average MW 280 g/mol) in water at doses up to 1000 mg/kg. The rats in each dose group were allowed to deliver. Transient salivation was noted in both sexes of the parental rats dosed with 1000 mg/kg. Slight body weight loss occurred in females of the 1000 mg/kg dose group during lactation and marginal body weight gains were noted during the premating period at all doses. There were no effects on total body weights, or viability of offspring, and no embryotoxic or teratogenic effects were reported. The NOAEL was > 1000 mg/kg bw/day.

An ethoxylated glycerol was not mutagenic in Ames tests at concentrations up to 5000 µg/plate, with or without metabolic activation in S. *typhimurium* strains TA 1535, TA 1537, TA 98, and TA 100, and *E. coli* WP2. In a mammalian chromosomal aberration study, a propoxylated glycerol was not clastogenic to human lymphocytes (concentrations not reported) with or without metabolic activation.

A propoxylated nitrilotriethanol was evaluated for genotoxicity in a mammalian cell gene mutation assay CHL fibroblasts at doses of 400, 800, 1200, 1600, 2000, 2400, and 2800 µg/ml (-S9), and 42, 84, 168, 336, 672, 1344, and 2688 µg/ml (+S9) in ethanol. The test article did not induce mutagenic effects in the presence or absence of a metabolic activation system.

Based on observations made following a single topical application of 30 µL of an ethoxylated glycerol to a reconstructed three-dimensional human epidermis model, the test substance is not expected to be irritating. In a dermal irritation study, Glycereth-3 was applied for 20 hours to a shaved skin area of 2.5 cm x 2.5 cm of 2 Vienna white rabbits using an occlusive dressing. The test article was considered to be non-irritant to the skin. Topical application of an ethoxylated glycerol was considered to be non-irritating when applied to the skin of 2 male rabbits and following an observation period of 24 hours, 48 hours, and 8 days. The mean erythema score was 1.25, with all effects fully reversed within 8 days.

The sensitization potential of a propoxylated glycerol (MW 300 g/mol) was evaluated in a Buehler test using 10 male and 10 female Dunkin Hartley guinea pigs. Six-h occlusive patches of undiluted test article were used for both induction (days 1, 7 and 14) and at challenge. The test article was not a sensitizer.

The potential of an ethoxylated glycerol to cause damage to the eyes was evaluated in vitro in a BCOP test. The test article did not show ocular irritation potential under the test conditions. The potential of the test article to cause eye irritation was further evaluated using a three-dimensional human cornea model. The test article did not show an eye irritation potential under the test conditions.

Ocular irritation potential of Glycereth-3 was studied using 2 Vienna rabbits. The test article (50 µL) was instilled into 1 eye of each of the rabbits and the left eye served as a control. Slight conjunctivae redness was observed in both animals after 10 min, 1 hour, and 3 hours. The test article was found to be non-irritating. In another study, 50 µL of an undiluted ethoxylated glycerol was applied to the conjunctival sac of one eye of 2 white Vienna rabbits. Hyperemia was noted in blood vessels of both animals. In one animal, this effect was not fully reversible within 8 days. The test article was found to be non-irritating.

INFORMATION SOUGHT

The CIR is seeking the following information on all ingredients that comprise the glycerin ethoxylate family for use in the resulting safety assessment:

1. Method of manufacture
2. Impurities data
3. Dermal absorption; if absorbed, systemic toxicity data may be needed
4. Dermal irritation and sensitization data at concentrations of use
5. Any other data relevant to the determination of the safety of these ingredients as used in cosmetics

TABLES

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

Ingredient CAS No.	Definition & Structure*	Function(s)
Glycereth-3 31694-55-0 (generic)	Glycereth-3 is the polyethylene glycol ether of glycerin with an average ethoxylation value of 3. [The chemical structure of this ingredient conforms to that of Figure 1, wherein x + y + z = 3.]	Skin-Conditioning Agents - Emollient; Surfactants - Cleansing Agents; Surfactants - Emulsifying Agents
Glycereth-7 31694-55-0 (generic)	Glycereth-7 is the polyethylene glycol ether of glycerin with an average ethoxylation value of 7. [The chemical structure of this ingredient conforms to that of Figure 1, wherein x + y + z = 7.]	Skin-Conditioning Agents - Humectant; Viscosity Decreasing Agents
Glycereth-8 31694-55-0 (generic)	Glycereth-8 is the polyethylene glycol ether of glycerin with an average ethoxylation value of 8. [The chemical structure of this ingredient conforms to that of Figure 1, wherein x + y + z = 8.]	Skin-Conditioning Agents - Emollient; Skin-Conditioning Agents - Humectant; Viscosity Decreasing Agents
Glycereth-12 31694-55-0 (generic)	Glycereth-12 is the polyethylene glycol ether of glycerin with an average ethoxylation value of 12. [The chemical structure of this ingredient conforms to that of Figure 1, wherein x + y + z = 12.]	Skin-Conditioning Agents - Humectant; Viscosity Decreasing Agents
Glycereth-18 31694-55-0 (generic)	Glycereth-18 is a polyethylene glycol ether of glycerin containing an average of 18 moles of ethylene oxide. [The chemical structure of this ingredient conforms to that of Figure 1, wherein x + y + z = 18.]	Skin-Conditioning Agents - Humectant
Glycereth-20 31694-55-0 (generic)	Glycereth-20 is the polyethylene glycol ether of glycerin with an average ethoxylation value of 20. [The chemical structure of this ingredient conforms to that of Figure 1, wherein x + y + z = 20.]	Skin-Conditioning Agents - Humectant; Viscosity Decreasing Agents
Glycereth-26 31694-55-0 (generic)	Glycereth-26 is the polyethylene glycol ether of glycerin with an average ethoxylation value of 26. [The chemical structure of this ingredient conforms to that of Figure 1, wherein x + y + z = 26.]	Skin-Conditioning Agents - Humectant; Viscosity Decreasing Agents
Glycereth-31 31694-55-0 (generic)	Glycereth-31 is the polyethylene glycol ether of glycerin with an average ethoxylation value of 31. [The chemical structure of this ingredient conforms to that of Figure 1, wherein x + y + z = 31.]	Skin-Conditioning Agents - Humectant; Viscosity Decreasing Agents

Table 2. Physical and Chemical Properties

Property	Value	Reference
Glycereth-3		
Molecular Weight (g/mol)	224.25	[13]
log P	-1.79 (estimated)	[13]
Glycereth-7		
Molecular Weight (g/mol)	400.47	[13]
log P	-2.42 (estimated)	[13]
Glycereth-8		
Molecular Weight (g/mol)	444.52	[13]
log P	-2.57 (estimated)	[13]
Glycereth-12		
Molecular Weight (g/mol)	620.73	[13]
log P	-3.19 (estimated)	[13]
Glycereth-18		
Molecular Weight (g/mol)	885.05	[13]
log K_{ow}	-7.19 (estimated)	[14]
Glycereth-20		
Molecular Weight (g/mol)	972.57	[13]
log K_{ow}	-7.73 (estimated)	[14]
Glycereth-26		
Molecular Weight (g/mol)	1237.47	[13]
log K_{ow}	-9.38 (estimated)	[14]
Glycereth-31		
Molecular Weight (g/mol)	1457.74	[13]
log K_{ow}	-10.75 (estimated)	[14]

Table 3. Frequency (2019)[6] and concentration (2018)[7] of use data for glycerin ethoxylates

	# of Uses[6]	Max Conc of Use (%)[7]	# of Uses[6]	Max Conc of Use (%)[7]	# of Uses[6]	Max Conc of Use (%)[7]
	Glycereth-7		**Glycereth-12**		**Glycereth-18**	
Totals*	**80**	**1 - 2**	**6**	**0.09 - 0.35**	**21**	**0.019 - 0.32**
Duration of Use						
Leave-On	*76*	*1*	*6*	*0.21 - 0.35*	8	*0.019 - 0.3*
Rinse-Off	*4*	*2*	*NR*	*0.09*	13	*0.3 - 0.32*
Diluted for (Bath) Use	*0*	*NR*	*NR*	*NR*	NR	*NR*
Exposure Type						
Eye Area	NR	NR	3	0.09-0.35	NR	0.019-0.036
Incidental Ingestion	67	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	2[a]; 6[b]	NR	2[a]	NR	1[a]; 5[b]	NR
Incidental Inhalation-Powder	2[a]	NR	2[a]	NR	1[a]	0.3[c]
Dermal Contact	13	1- 2	4	0.09- 0.21	21	0.036-0.32
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous Membrane	68	NR	NR	NR	9	0.3
Baby Products	NR	NR	NR	NR	NR	NR

	Glycereth-20		**Glycereth-26**		
Totals*	**2**	**NR**	**379**	**0.3 - 39.5**	
Duration of Use					
Leave-On	*2*	*NR*	286	*0.3 - 6*	
Rinse Off	*NR*	*NR*	93	*0.9 - 39.5*	
Diluted for (Bath) Use	*NR*	*NR*	NR	*NR*	
Exposure Type					
Eye Area	NR	NR	18	2-6	
Incidental Ingestion	NR	NR	NR	NR	
Incidental Inhalation-Spray	1[a]; 1[b]	NR	5; 104[a]; 116[b]	1; 2[b]	
Incidental Inhalation-Powder	1[a]	NR	104[a];	1 - 4[c]	
Dermal Contact	2	NR	328	1-39.5	
Deodorant (underarm)	NR	NR	NR	NR	
Hair - Non-Coloring	NR	NR	49	0.3-1	
Hair-Coloring	NR	NR	1	NR	
Nail	NR	NR	NR	NR	
Mucous Membrane	NR	NR	35	NR	
Baby Products	NR	NR	NR	NR	

NR = Not reported.

* 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.] Not specified whether a powder or a spray, so this information is captured for both categories of incidental inhalation.

[b.] It is possible these products may be sprays, but it is not specified whether the reported uses are sprays.

[c.] It is possible these products may be powders, but it is not specified whether the reported uses are powders.

Table 4. Acute toxicity studies

Test Article/ Concentration/ Vehicle	Animals	No./Group	Dose/Protocol	LD_{50}/Results	Reference
			Dermal		
Ethoxylated glycerol; 5000 mg/kg without a vehicle	Wistar rats	5/sex	According to OECD TG 402. Rats were dermally administered test article; applied to a 40 cm^2 skin area and covered by a semi-occlusive dressing for 24 hours.	No mortality occurred. No systemic clinical signs were observed during clinical examination. No local effects were observed. LD_{50} is > 5000 mg/kg	[4]
			Oral		
Glycereth-3; 1 – 50% (v/v) solution at doses of 0.025 - 10 mL/kg bw in Water	Fischer 344 rats	13 male and 11 females	Similar to OECD TG 401. Three females were administered 0.025 mL/kg of a 1% (v/v) solution another 3 female rats were administered 0.2 mL/kg of a 10% solution. Three male rats were administered 1.6 mL/kg of a 10% solution. Another 5 male rats were administered 3.2 mL/kg of a 50% solution. Five females were administered 6.4 mL/kg of a 50% solution and 5 males were administered 10 mL/kg of a 50% solution. Ten untreated animals were used as a negative control.	No mortality occurred and no abnormalities observed. The LD_{50} in male and female rats is > 10 mL/kg.	[4]
Ethoxylated glycerol; 2000 mg/kg without vehicle	Wistar rats	2 groups of 3 females	According to OECD TG 423. Both groups of rats were administered test article at a maximum dosage-volume of 1.73 mL/kg.	No mortality occurred. No clinical signs were observed during the observation period. The mean body weight of the test groups increased throughout the study period within the normal range. LD_{50} is > 2000 mg/kg	[4]
Ethoxylated glycerol, undiluted	Sprague-Dawley rats	5/sex	Similar to OECD TG 401. Five male rats were administered with 11,550 mg/kg bw and 5 female rats were exposed at a dose 10,000 mg/kg bw. Animals were observed for 14 days after administration.	No mortality occurred. Diarrhea was noted for a few hours after application; aggressiveness, convulsion and dirty fur were observed at days 3 and 4; animals fully recovered within 5 days. LD_{50} in male and female rat is > 10,000 mg/kg	[4]
			Inhalation		
Glycereth-3; 3.575 mg/L	"White, normal rats"	3/sex	Similar to OECD TG 403. Rats were exposed to test article in an aerosol/mist form for 8 hours and observed for 14 days.	No mortality or clinical signs of toxicity noted	[4]
Ethoxylated glycerol; 0.178 mg/L and 0.143 mg/L without vehicle	Rats	6 animals (males and females)/ experiment	Similar to OECD TG 403. Rats were exposed (whole body) to 0.178 mg/L in experiment 1 and 0.143 mg/L in experiment 2 as a vapor for 7 hours and observed for 14 days.	No mortality or clinical signs of toxicity noted.	[4]

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