Safety Assessment of Glycerin Ethoxylates as Used in Cosmetics

Status:	Draft Report for Panel Review
Release Date:	May 10, 2019
Panel Meeting Date:	June 6-7, 2019

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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Cosmetic Ingredient Review

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Memorandum

To: CIR Expert Panel Members and Liaisons

From: Alice Akinsulie
Scientific Writer/Analyst

Date: May 10, 2019

Subject: Draft Report on Glycerin Ethoxylates

Enclosed is the Draft Report on the Safety Assessment of 8 Glycerin Ethoxylates ingredients (identified as *glyeth062019rep* in the report package). This is the first time the Panel is reviewing this document. According to the *Dictionary*, all of these ingredients, which are structurally related as polyethylene glycol ethers of glycerin, are reported to function in cosmetics as skin-conditioning agents, and most are reported to function as viscosity decreasing agents

According to 2019 VCRP survey data, Glycereth-26 has the highest frequency of use, with a total of 379 formulations. The Council provided concentration of use survey data (identified as *glyeth062019data1* and *glyeth062019data2*). The results of the concentration of use survey conducted in 2018 by the Council indicate that Glycereth-26 has the highest maximum concentration of use, and is used at up to 39.5% in skin cleansing products. The concentration reported for this rinse-off use product category is much higher than that reported for other product categories; the highest maximum leave-on use concentration reported is 6% Glycereth-26 in eye lotions.

Comments on the SLR (*glyeth062019pcpc*) were received from the Council and have been addressed.

The following unpublished data were received and have been incorporated into the document: (*glyeth062019data3*)

- EpiOcular™ irritation study on product containing 0.35% Glycereth-12
- HRIPT on product containing 0.35% Glycereth-12
- HRIPT on product containing 5% Glycereth-26

The following are also included in this package for your review:

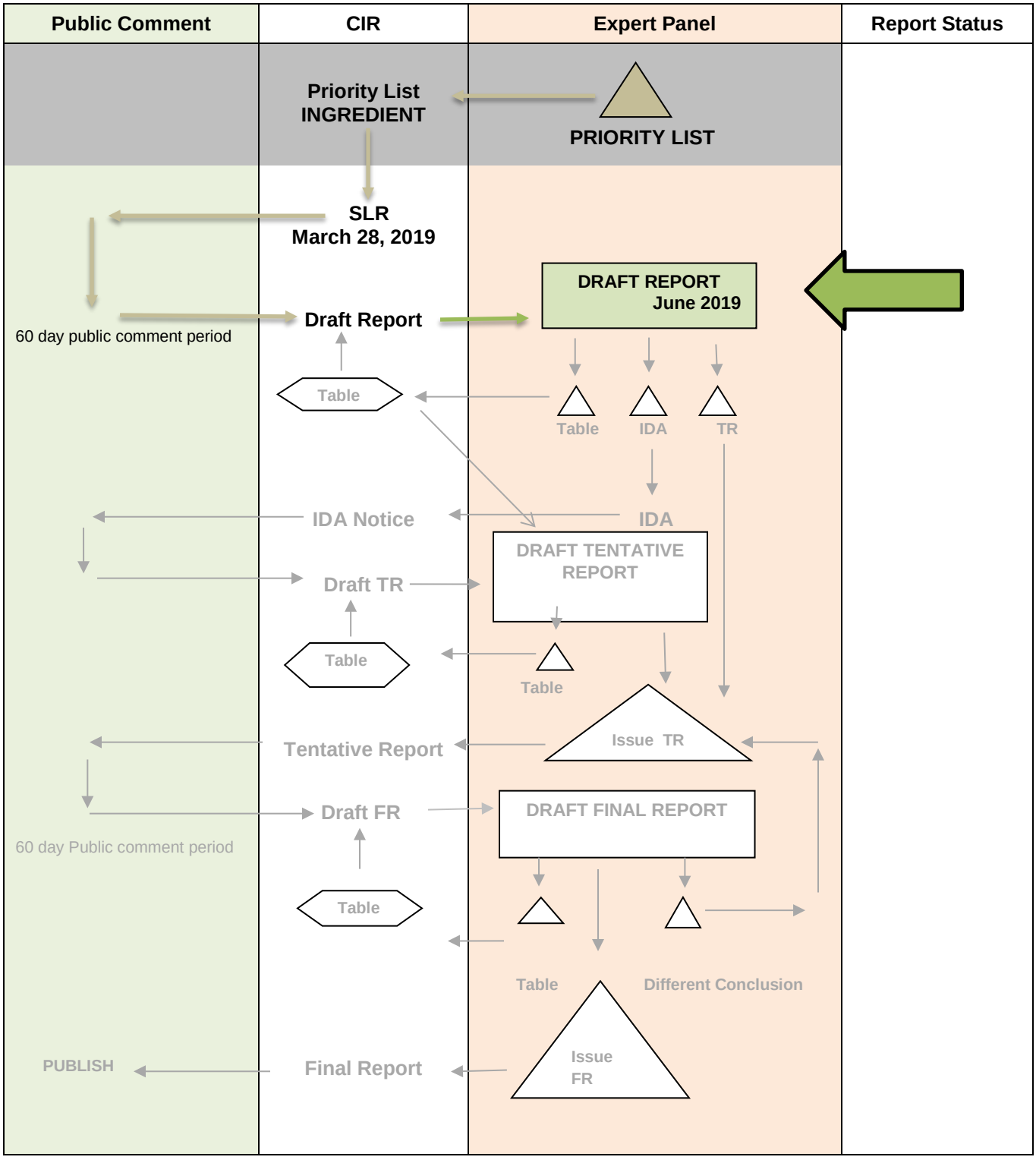
- *glyeth062019flow*: flow chart
- *glyeth062019hist*: history
- *glyeth062019prof*: data profile
- *glyeth062019strat*: search strategy
- *glyeth062019fda*: 2019 VCRP data (US FDA)

After reviewing these documents, if the available data are deemed sufficient to make a determination of safety, the Panel should identify matters to be addressed in the Discussion, and then issue a Tentative Report with a safe as used, safe with qualifications, or unsafe conclusion. If, however, the available data are insufficient, the Panel should issue an Insufficient Data Announcement (IDA), specifying the data needs therein.

SAFETY ASSESSMENT FLOW CHART

INGREDIENT/FAMILY Glycerin Ethoxylates

MEETING June 2019



CIR History of:

Glycerin Ethoxylates

A Scientific Literature Review (SLR) on Glycerin Ethoxylates was issued on March 28, 2019.

Draft Report, Teams/Panel: June 6-7, 2019

Glycerin Ethoxylates Data Profile* – June 06-07, 2019 – Alice Akinsulie

				Toxicokinetics			Acute Tox			Repeated Dose Tox			DART		Genotox		Carci		Dermal Irritation			Dermal Sensitization				Ocular Irritation		Clinical Studies	
	Reported Use	Method of Mfg	Impurities	log P	Dermal Penetration	ADME	Dermal	Oral	Inhalation	Dermal	Oral	Inhalation	Dermal	Oral	In Vitro	In Vivo	Dermal	Oral	In Vitro	Animal	Human	In Vitro	Animal	Human	Phototoxicity	In Vitro	Animal	Retrospective/ Multicenter	Case Reports
Glycereth-3				X			X	X	X						X					X						X	X		
Glycereth-7	X			X																									
Glycereth-8				X																									
Glycereth-12	X			X																				X		X			
Glycereth-18	X			X																									
Glycereth-20	X			X																									
Glycereth-26	X			X																				X					
Glycereth-31				X																									

* "X" indicates that data were available in a category for the ingredient

[Glycerin Ethoxylates]

Ingredient	CAS #(generic)	InfoB	SciFin	PubMed	TOXNET	FDA	EU	ECHA	IUCLID	SIDS	ECETOC	HPVIS	NICNAS	NTIS	NTP	WHO	FAO	NIOSH	FEMA	Web
Glycereth 3	31694-55-0	✓	0/9	0/674	✓	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	✓
Glycereth 7	31694-55-0	✓	0/7	0/205	NR	NR	✓	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	✓
Gycereth 8	31694-55-0	✓	0/1	0/173	NR	NR	✓	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	✓
Glycereth 12	31694-55-0	✓	NR	0/79	NR	NR	✓	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	✓
Glycereth 18	31694-55-0	✓	0/1	0/41	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	✓
Glycereth 20	31694-55-0	✓	1/3	0/93	NR	NR	✓	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	✓
Glycereth 26	31694-55-0	✓	1/129	0/18	✓	NR	✓	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	✓
Glycereth 31	31694-55-0	✓	NR	0/26	NR	NR	✓	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	✓
Glycerin Ethoxylate	31694-55-0	NR	1/225	0/7	NR	NR	NR	✓	NR	NR	NR	✓	NR	NR	NR	NR	NR	NR	NR	✓

***NR – No results were found; Check mark - Data available; 0/0 – relevant/hits**

Web Search

1,2,3-Propanetriol, ethoxylated
Ethoxylated glycerine
Ethoxylated glycerol
Glycereth
Glycereth 12
Glycereth 26
Glycerol poly(oxyethylene) ether
Glycerol polyoxyethylene ether
Glycerol, ethoxylated
Lupranol VP 9209
Acute toxicity; Repeated dose toxicity; Subacute toxicity; Short-term toxicity; Subchronic toxicity; Chronic toxicity; Adverse health effects; Hypersensitivity; Sensitization; Carcinogenicity; Genotoxicity; Mutagenicity; Dermal absorption; Dermal penetration; Dermal irritation; Developmental toxicity; Reproductive toxicity; In vitro toxicity; Ocular effects; Oral exposure; Phototoxicity; Photosensitivity

Typical Search Terms

- INCI names
- CAS numbers
- chemical/technical names
- additional terms will be used as appropriate

LINKS

Search Engines

- Pubmed (- http://www.ncbi.nlm.nih.gov/pubmed)
- Toxnet (https://toxnet.nlm.nih.gov/); (includes Toxline; HSDB; ChemIDPlus; DART; IRIS; CCRIS; CPDB; GENE-TOX)
- Scifinder (https://scifinder.cas.org/scifinder)

appropriate qualifiers are used as necessary
search results are reviewed to identify relevant documents

Pertinent Websites

- wINCI - http://webdictionary.personalcarecouncil.org

- FDA databases http://www.ecfr.gov/cgi-bin/ECFR?page=browse
- FDA search databases: http://www.fda.gov/ForIndustry/FDABasicsforIndustry/ucm234631.htm;,
- EAFUS: http://www.accessdata.fda.gov/scripts/fcn/fcnnavigation.cfm?rpt=eafuslisting&displayall=true
- GRAS listing: http://www.fda.gov/food/ingredientspackaginglabeling/gras/default.htm
- SCOGS database: http://www.fda.gov/food/ingredientspackaginglabeling/gras/scogs/ucm2006852.htm
- Indirect Food Additives: http://www.accessdata.fda.gov/scripts/fdcc/?set=IndirectAdditives
- Drug Approvals and Database: http://www.fda.gov/Drugs/InformationOnDrugs/default.htm
- http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/UCM135688.pdf
- FDA Orange Book: https://www.fda.gov/Drugs/InformationOnDrugs/ucm129662.htm
- OTC ingredient list: https://www.fda.gov/downloads/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cder/ucm135688.pdf
- (inactive ingredients approved for drugs: http://www.accessdata.fda.gov/scripts/cder/iig/

- HPVIS (EPA High-Production Volume Info Systems) - https://ofmext.epa.gov/hpvis/HPVISlogon
- NIOSH (National Institute for Occupational Safety and Health) - http://www.cdc.gov/niosh/
- NTIS (National Technical Information Service) - http://www.ntis.gov/
- NTP (National Toxicology Program) - http://ntp.niehs.nih.gov/
- Office of Dietary Supplements https://ods.od.nih.gov/
- FEMA (Flavor & Extract Manufacturers Association) - http://www.femaflavor.org/search/apachesolr_search/

- EU CosIng database: http://ec.europa.eu/growth/tools-databases/cosing/
- ECHA (European Chemicals Agency – REACH dossiers) – http://echa.europa.eu/information-on-chemicals;jsessionid=A978100B4E4CC39C78C93A851EB3E3C7.live1
- ECETOC (European Centre for Ecotoxicology and Toxicology of Chemicals) - http://www.ecetoc.org
- European Medicines Agency (EMA) - http://www.ema.europa.eu/ema/
- IUCLID (International Uniform Chemical Information Database) - https://iuclid6.echa.europa.eu/search
- OECD SIDS (Organisation for Economic Co-operation and Development Screening Info Data Sets)- http://webnet.oecd.org/hpv/ui/Search.aspx
- SCCS (Scientific Committee for Consumer Safety) opinions: http://ec.europa.eu/health/scientific_committees/consumer_safety/opinions/index_en.htm
- NICNAS (Australian National Industrial Chemical Notification and Assessment Scheme)- https://www.nicnas.gov.au/

- International Programme on Chemical Safety http://www.inchem.org/
- FAO (Food and Agriculture Organization of the United Nations) - http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/jecfa-additives/en/
- WHO (World Health Organization) technical reports - http://www.who.int/biologicals/technical_report_series/en/

- www.google.com - a general Google search should be performed for additional background information, to identify references that are available, and for other general information

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INTRODUCTION

This is 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 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 is used; otherwise, a generic term that identifies that test substance (e.g., "ethoxylated glycerol") is used.

CHEMISTRY

Definition and Structure

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

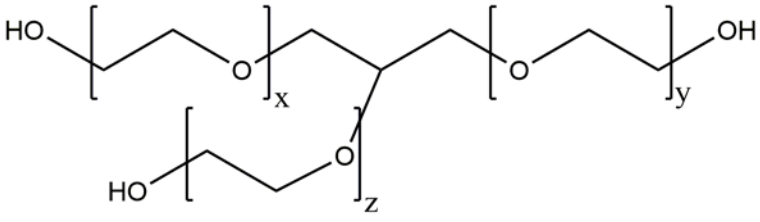

Figure 1. Glycerin ethoxylates, wherein the average ethoxylation value equals x + y + z (e.g., x + y + z = 3 in the case of Glycereth-3)

The definition of each ingredient, as given in the *Dictionary*, is provided in Table 1. For the data summarized herein as "ethoxylated glycerol," 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 "ethoxylated glycerol" 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, these ingredients, 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 ingredients 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.

These ingredients are used 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 indicate Glycereth-26 has the highest maximum 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 6% Glycereth-26 in eye lotion formulations.

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 formulations (concentration of use data were 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 spray formulations. 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 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

“Ethoxylated glycerol” is used in a number of non-cosmetic applications such as modelling clay adhesives, sealants, polymer preparations and compounds, coatings, and paints.[4]

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 "ethoxylated glycerol" in male and female Wistar rats was > 5000 mg/kg.[4]

In female Wistar rats, the oral LD_{50} of "ethoxylated glycerol" was > 2000 mg/kg.[4] In another oral toxicity study, the LD_{50} of "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 "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 hours as a vapor.[4] The average weight at the initiation of the study was 196 g in male and 178 g in female rats. Seven hours after exposure, no mortalities were observed. A marked gain in body weight was observed in females at 266 g and in males at 200 g.

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 (with molar equivalents of 3.2 propoxyl) 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 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 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. Neither significant embryotoxic or teratogenic effects, nor abnormalities, were noted, and no effects on reproductive performance were observed. Four pups from the F_1 generation 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 on increased incidence of salivation. Under the test conditions, the NOAEL was derived as 1000 mg/kg because reduction of body weight was observed with females at the highest dose group (1000 mg/kg bw/day). The mild weight loss 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" (a read-across source for Glycereth-3)

The mutagenicity of "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 with and without 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 concentrations 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 metabolic activation.

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 accordance with OECD TG 439, dermal irritation potential was assessed by a single topical application of 30 µL of "ethoxylated glycerol" applied undiluted to a reconstructed three-dimensional human epidermis model (EpiDerm™).[4] Sterile phosphate buffered saline (PBS; 30 µl) was used as negative control. The tissues were washed with sterile PBS 1 hour after the application. The results predicted that 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 h, 48 h, and 8 days. No edema and erythema findings were observed. The test article was considered to be non-irritant to rabbit skin.

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) were patched with 0.5 mL of the undiluted test article for the topical induction, using 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 a 6-h exposure period on day 28. Five males and 5 females served as the control group. The test article was not a sensitizer.

Human

Glycereth-12

A human repeat insult patch test (HRIPT) of a product containing 0.35% Glycereth-12 was performed in 100 subjects.[13] The test material (0.2) was applied with an occlusive, hypoallergenic patch to the infrascapular regions of the back for nine applications. After a 14-day rest period, the same concentration and amount of the test substance was used in the challenge phase; patches were applied to a previously untested site, and reactions were scored 24 and 48 hours after application. There were no signs of irritation or sensitization.

Glycereth-26

A product containing 5% Glycerth-26 tested in an HRIPT on 55 subjects.[13] The test material was applied to a 1 in^2 absorbent pad portion of an adhesive dressing and applied to the skin under semi-occlusion for 24 hours. Nine induction applications were made. After a 2-week rest period, a 24-hour challenge application was made to a previously untreated site in the same manner as the induction applications, and reactions were scored 24 and 72 h after application. The test material did not demonstrate a potential for eliciting dermal irritation or allergic contact sensitization.

OCULAR IRRITATION STUDIES

In Vitro

Glycerth-12

In an EpiOcular™ assay, a 20% aqueous dilution of a product containing 0.35% Glycereth-12 was tested at 100 µL; the effective test concentration was 0.07% Glycereth-12.[13] Appropriate negative and positive controls were used. The estimated Draize ocular irritation score of the test material at 100% was predicted to be 0, and it was classified to be non-irritant.

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

The potential irritation of "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 in the test group, the negative control group, and the positive control group, respectively. 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 an EpiOcular™ three-dimensional human cornea model.[4] Fifty µL of the undiluted test article was applied (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 a test method that is similar to OECD TG 405.[4] Undiluted Glycereth-3 (50 µL) was instilled into the conjunctival sac of the right eye of each animal without washing, and the eyes 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" (a read-across source for Glycereth-3)

Two Vienna white rabbits were used to test for ocular irritation following a protocol similar to OECD TG 405.[4] Fifty microliters of undiluted "ethoxylated glycerol" were instilled into the conjunctival sac of one eye of each animal. 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. Data on "ethoxylated glycerols," propoxylated nitrilotriethanol and propoxylated glycerol are included in this safety assessment as potential read-across, according to the ECHA dossier. These ingredients are polyethylene glycol ethers of glycerin.

These ingredients are mostly in leave-on 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.

Glycereth-3, at concentrations ranging from 1 - 50%, was administered orally to 6 groups of Fischer 344 rats. 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 "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 "ethoxylated glycerol" was greater than 2000 mg/kg. No evidence of toxicity was reported when "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 "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.

"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 with 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 "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.

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-hour occlusive patches of undiluted test article were used for both induction (days 1, 7, and 14) and challenge. The test article was not a sensitizer.

A product containing 0.35% Glycereth-12 was evaluated for skin sensitization potential in an HRIPT using 100 subjects. Neither irritation nor sensitization were observed. The skin sensitization potential of a product containing 5% Glycereth-26 was evaluated in a maximization test involving 55 subjects. No adverse reactions were observed and there were no instances of dermal irritation or allergic contact sensitization.

In an EpiOcular™ assay, a 20% aqueous dilution of a product containing Glycereth-12 (0.35%) was predicted to not be an ocular irritant. The potential of "ethoxylated glycerol" to cause damage to the eyes was evaluated in vitro in a BCOP test and in an EpiOcular™ assay. The test article did not show ocular irritation potential under either the test condition.

Ocular irritation potential of Glycereth-3 was studied using 2 Vienna rabbits. The test article (50 µL) was instilled into the right eye of each rabbit and the left eyes served as controls. Slight conjunctivae redness was observed in both tested animals after 10 min, 1 hour, and 3 hours. The test article was found to be non-irritating. In another study, 50 µL of 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.

DISCUSSION

To be formulated.

CONCLUSION

To be determined.

TABLES

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

Ingredient CAS No.	Definition	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
	"ethoxylated glycerol"	
Physical Form	Liquid	[4]
Color	clear	[4]
Density/Specific Gravity (@ 20ºC)	1.163	[4]
Viscosity (@ 20 ºC)	399	[4]
Vapor pressure (@ 20ºC)	0.0000389	[4]
Melting Point (ºC)	-49.1	[4]
Boiling Point (ºC)	260	[4]
Water Solubility (g/L @ 20ºC)	1000	[4]
	Glycereth-3	
Molecular Weight (g/mol)	224.25	[14]
log P	-1.79 (estimated)	[14]
	Glycereth-7	
Molecular Weight (g/mol)	400.47	[14]
log P	-2.42 (estimated)	[14]
	Glycereth-8	
Molecular Weight (g/mol)	444.52	[14]
log P	-2.57 (estimated)	[14]
	Glycereth-12	
Molecular Weight (g/mol)	620.73	[14]
log P	-3.19 (estimated)	[14]
	Glycereth-18	
Molecular Weight (g/mol)	885.05	[14]
log K_{ow}	-7.19 (estimated)	[15]
	Glycereth-20	
Molecular Weight (g/mol)	972.57	[14]
log K_{ow}	-7.73 (estimated)	[15]
	Glycereth-26	
Molecular Weight (g/mol)	1237.47	[14]
log K_{ow}	-9.38 (estimated)	[15]

Table 2. Physical and Chemical Properties

Property	Value	Reference
	Glycereth-31	
Molecular Weight (g/mol)	1457.74	[14]
log K_{ow}	-10.75 (estimated)	[15]

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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2019 VCRP Data

CATEGORY	MAINTERM	COUNT
07E - Lipstick	GLYCERETH-7	67
10E - Other Personal Cleanliness Products	GLYCERETH-7	1
12A - Cleansing	GLYCERETH-7	3
12D - Body and Hand (exc shave)	GLYCERETH-7	2
12F - Moisturizing	GLYCERETH-7	2
12I - Skin Fresheners	GLYCERETH-7	1
12J - Other Skin Care Preps	GLYCERETH-7	1
13B - Indoor Tanning Preparations	GLYCERETH-7	3
03F - Mascara	GLYCERETH-12	2
03G - Other Eye Makeup Preparations	GLYCERETH-12	1
07C - Foundations	GLYCERETH-12	1
12C - Face and Neck (exc shave)	GLYCERETH-12	2
07I - Other Makeup Preparations	GLYCERETH-18	1
10A - Bath Soaps and Detergents	GLYCERETH-18	9
12A - Cleansing	GLYCERETH-18	4
12C - Face and Neck (exc shave)	GLYCERETH-18	1
12F - Moisturizing	GLYCERETH-18	4
12G - Night	GLYCERETH-18	1
12J - Other Skin Care Preps	GLYCERETH-18	1
12C - Face and Neck (exc shave)	GLYCERETH-20	1
12F - Moisturizing	GLYCERETH-20	1
03A - Eyebrow Pencil	GLYCERETH-26	1
03D - Eye Lotion	GLYCERETH-26	12
03F - Mascara	GLYCERETH-26	1
03G - Other Eye Makeup Preparations	GLYCERETH-26	4
04A - Cologne and Toilet waters	GLYCERETH-26	3
04E - Other Fragrance Preparation	GLYCERETH-26	1
05A - Hair Conditioner	GLYCERETH-26	9
05B - Hair Spray (aerosol fixatives)	GLYCERETH-26	1
05E - Rinses (non-coloring)	GLYCERETH-26	1
05F - Shampoos (non-coloring)	GLYCERETH-26	26
05G - Tonics, Dressings, and Other Hair Grooming Aids	GLYCERETH-26	4
05I - Other Hair Preparations	GLYCERETH-26	8
06D - Hair Shampoos (coloring)	GLYCERETH-26	1
07C - Foundations	GLYCERETH-26	2
07F - Makeup Bases	GLYCERETH-26	1
07H - Makeup Fixatives	GLYCERETH-26	1
07I - Other Makeup Preparations	GLYCERETH-26	2
10A - Bath Soaps and Detergents	GLYCERETH-26	30

10E - Other Personal Cleanliness Products	GLYCERETH-26	5
11D - Preshave Lotions (all types)	GLYCERETH-26	1
11E - Shaving Cream	GLYCERETH-26	1
11G - Other Shaving Preparation Products	GLYCERETH-26	2
12A - Cleansing	GLYCERETH-26	12
12B - Depilatories	GLYCERETH-26	1
12C - Face and Neck (exc shave)	GLYCERETH-26	92
12D - Body and Hand (exc shave)	GLYCERETH-26	12
12F - Moisturizing	GLYCERETH-26	87
12G - Night	GLYCERETH-26	8
12H - Paste Masks (mud packs)	GLYCERETH-26	4
12I - Skin Fresheners	GLYCERETH-26	8
12J - Other Skin Care Preps	GLYCERETH-26	29
13B - Indoor Tanning Preparations	GLYCERETH-26	7
13C - Other Suntan Preparations	GLYCERETH-26	2

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review

FROM: Carol Eisenmann, Ph.D.
Personal Care Products Council

DATE: May 31, 2018

SUBJECT: Concentration of Use by FDA Product Category: Glycerin Ethoxylates

Concentration of Use by FDA Product Category – Glycerin Ethoxylates*

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

Ingredient	Product Category	Maximum Concentration of Use
Glycereth-26	Eye shadows	2%
Glycereth-26	Eye lotions	4-6%
Glycereth-26	Shampoos (noncoloring)	0.9-1%
Glycereth-26	Tonics, dressings and other hair grooming aids	0.3%
Glycereth-26	Foundations	3%
Glycereth-26	Shaving cream	9%
Glycereth-26	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	3-39.5%
Glycereth-26	Face and neck products Not spray	 3-3.5%
Glycereth-26	Body and hand products Not spray Spray	 1-4% 1%
Glycereth-26	Moisturizing products Not spray	 1%
Glycereth-26	Skin fresheners	2%
Glycereth-26	Other skin care preparations	3-5%
Glycereth-26	Other suntan products Not spray	 4%
Glycereth-7	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	2%
Glycereth-7	Moisturizing products Not spray	 1%
Glycereth-12	Eye makeup removers	0.09%
Glycereth-12	Mascaras	0.35%
Glycereth-12	Other eye makeup preparations	0.21%
Glycereth-18	Eyeliners	0.036%
Glycereth-18	Mascaras	0.019%
Glycereth-18	Bath soaps and detergents	0.3%
Glycereth-18	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.32%
Glycereth-18	Body and hand products Not spray	 0.3%

*Ingredients included in the title of the table but not found in the table were included in the concentration of use survey, but no uses were reported.

Information collected in 2018
Table prepared: June 26, 2018

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review (CIR)

FROM: Carol Eisenmann, Ph.D.
Personal Care Products Council

DATE: April 23, 2019

SUBJECT: Glycereth-12 and Glycereth-26

Anonymous. 2019. Summary information: Safety studies on Glycerin Ethoxylates (Glycereth-12 and Glycereth-26).

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April 2019

Summaries of Studies on Products Containing Glycerin Ethoxylates

1. Products containing Glycereth-12 at 0.35%

a. HRIPT

- Completed in 2014
- 100 subjects completed the study
- 0.2 gram of neat test article was dispensed onto occlusive hypoallergenic patch (Parke Davis Hypoallergenic Readi bandages); patch applied directly to skin of infrascapular regions on back;
- Induction phase covered 9 consecutive 24-hour exposures made every Monday, Wednesday and Friday; 14 days rest period; challenge dose of 0.2 gram (neat) at naïve site and reactions scored at 24 and 48 hours post exposure.
- No adverse reactions noted during the course of study.
- When tested under occlusive conditions, the product containing Glycereth-12 at 0.35% may be considered as a non-primary irritant or non-primary sensitizer.

b. EpiOcular

- Completed in 2014
- Test article (containing Glycereth-12 at 0.35%) was diluted to 20% in distilled water and tested at 100µL
- Distilled water served as negative control and 0.3% triton X-100 was used as positive control.
- Results: At 100%, test article's estimated Draize ocular irritation score is approximately '0' and has a 'non-irritating' irritancy classification.

2. Products containing Glycereth-26 at 5%

a. HRIPT

- Study completed in 2016
- 55 subjects completed the study
- Test material was cut into 1" x 1" pieces and test sample was placed over absorbent pad portion of an adhesive dressing to form a semi-occlusive patch; applied to the skin on upper back between the scapulae region

- Induction phase covered 9 consecutive 24-hour exposures made every Monday, Wednesday and Friday; two weeks rest period; Challenge patch was applied to virgin test site and reactions scored at 24 and 72 hours post application.
- No reactions were noted during the course of the study.
- Under the conditions of this study, test material containing 5% of Glycereth-26 indicated no potential for dermal irritation or allergic contact sensitization.

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review (CIR)

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: April 23, 2019

SUBJECT: Scientific Literature Review: Safety Assessment of Glycerin Ethoxylates as Used in Cosmetics (release date March 28, 2019)

The Personal Care Products Council has no suppliers listed for Glycereth-31.

The Personal Care Products Council respectfully submits the following comments on the scientific literature review, Safety Assessment of Glycerin Ethoxylates as Used in Cosmetics.

Key Issue

As noted in the Chemistry section, the dossier submitted to ECHA associated with CAS No. 31694-55-0 indicated an ethoxylation value between 1 and 6.5; therefore, the Introduction should not say that the "specific identities of the ingredients were not discerned". The Introduction should also indicate that the dossier was on a material with ethoxylate values between 1 and 6.5. This should also be made clear in subheadings in which the information is from the dossier and did not pertain specifically to Glycereth-3 or propoxylated nitrilotriethanol.

Additional Considerations

Introduction - In addition to PEGs and Glycerin, are there other components of these ingredients? Perhaps "some of" should be deleted in the second paragraph.

Cosmetic Use; Summary - There were a total of 59,788 products reported to the VCRP (from 2019). Therefore, the most used ingredient in the report on Glycerin Ethoxylates, Glycereth-26, reported to be used in 379 products, was reported to be used in less than 1% of the products reported to the VCRP. When discussing the use of Glycereth-26, the word "widely" should be deleted from the Cosmetic Use section and the Summary.

Non-Cosmetic Use - The ECHA dossier provides some consumer product uses (adhesives and sealants, coatings and rigid foam) that should be stated in the Non-Cosmetic Use section.

Acute, Ethoxylated glycerol - Please state the results of the inhalation exposure study.

Short-term - The molar equivalents (3.2) of the tested propoxylated nitrilotriethanol should also be stated.

Genotoxicity, In Vitro - Units of µg/mL should be called "concentration" rather than "dose".

Table 2 - The Physical and Chemical properties included in the dossier submitted to ECHA should be added to Table 2.