TECHNICAL REPORT – CPSR REPORT

Report No. （6625）097-1177 **Date 2025-04-15**

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Client:	Mid Ocean Brands B.V.		
Address:	7/F, Kings Tower,111 King Lam Street, Cheung Sha Wan, Kowloon, Hong Kong.		
Sample name:	Wet Wipes (1 formulation)		
Net weight:	42g (10 wipes) per consumer product		
Style/ Item No.:	MO3863	Country of Origin:	China
Manufacturer:	vendor code:113285	Expiry Date:	/
Production Date :	/	Date of Receipt:	2025-04-07
Sample Source:	/	Assessment Period:	2025-04-07 to 2025-04-11
Status of Sample:	/	Appropriate Age Grade:	/
Client Specified Age Grade:	/	Tested Age Grade:	/

Test specification:

Cosmetic Product Safety Assessment

Test result*:

Please refer to the assessment based on the EU Cosmetic Regulation (EC) No 1223/2009 issued by Toxicological & Regulatory Assessor.

Note: *: The results were performed at external authorized lab.

Bureau Veritas Testing Technical Service (Zhejiang) Co., Ltd Shanghai Branch

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PART A – Cosmetic product safety information

A.1 Quantitative and Qualitative Composition of Products

A.1.1 Nominal Composition

The table below shows the aggregated break-down components of all raw materials from the product. Substances may have more than one function in the product. If so, the main function is given.

INCI Name	CAS No.	Conc. (%), w/w	Function
AQUA	7732-18-5	93.90	Solvent
GLYCERIN	56-81-5	2.00	Humectant
PROPYLENE GLYCOL	57-55-6	2.00	Humectant
ALOE BARBADENSIS LEAF EXTRACT	85507-69-3	1.00	Skin conditioning - emollient
PHENOXYETHANOL	122-99-6	0.50	Preservative
TOCOPHERYL ACETATE	58-95-7	0.20	Antioxidant
BENZALKONIUM CHLORIDE	8001-54-5	0.10	Preservative
POLYSORBATE 20	9005-64-5	0.10	Surfactant - cleansing
ETHYLHEXYLGLYCERIN	70445-33-9	0.10	Skin conditioning
PARFUM (PC-356A(DPG) Lemon fragrance)	Mixture	0.10	Fragrance

FRAGRANCE ALLERGENS

Fragrance allergen LIMONENE, LINALOOL must be declared on the product label in the ingredients section according to EU Cosmetic Regulation.

A.2 Physical chemical characteristics and stability of the cosmetic product

A.2.1 Physical/chemical characteristics of Raw Materials

The raw materials specifications are available upon request.

A.2.2 Physical chemical specifications of the end product

The finished product is a white liquid with lemon odour impregnated in white fabric with the pH of 6.0-8.5.

A.2.3 End product stability

The stability evaluation of the above formula was conducted under different operating conditions in an appropriate packaging at -5°C, -15°C, 25°C, and 40°C for 12 weeks. Light stability and cycling test (45°C/RT/-10°C) were also conducted. The organoleptic, physico-chemical and microbiological examinations (including appearance, colour, odour, pH value, TVC bacteria, appearance of package) were carried out.

The compatibility between the formula and the packaging was also evaluated.

The overall results of these examinations allow it to be stated that the stability tests and compatibility tests are **acceptable**.

A.2.4 Durability (PAO)

It lies with the responsibility of manufacturer or responsible person to determine the product's minimum

durability and period-after-opening (PAO) based on the above results from the product stability testing.

A.3 Microbiological quality

A.3.1 The microbiological specifications of the substance or mixture

The microbiological specifications of all raw materials are available upon request.

A.3.2 The microbiological testing results of end product

The microbiological testing results of end product according to European Pharmacopoeia 9.0 2.6.12 & 2.6.13 were listed below.

Items	Testing Results	Unit
Aerobic Plate Count	<10	CFU/g
Yeasts and Moulds	<10	CFU/g
E. Coli, P. aeruginosa, S. aureus, C. albicans, Bile-tolerant gram-negative bacteria, S. typhimurium, C.tetani	Undetected	/g

According to Appendix 9 of the 12th Revision of the NoG (SCCS/1647/22), the microbiological quality of this product was considered as **acceptable** for **Category 2 products.**

A.3.3 Results of preservation challenge test

The preservation challenge test result of this formulation according to European Pharmacopoeia 10.0 5.1.3 was listed below.

Microorganisms	D7	D14	D28
	Log reduction values		
Escherichia coli	> 5.8	> 5.8	> 5.8
Staphylococcus aureus	> 5.6	> 5.6	> 5.6
Pseudomonas aeruginosa	> 5.4	> 5.4	> 5.4
Candida albicans	> 5.5	> 5.5	> 5.5
Aspergillus niger	> 5.4	> 5.4	> 5.4

According to EP 10.0 5.1.3 Table 5.1.3.-2, the preservation challenge test result of this formulation was considered as **acceptable**.

A.4 Impurities, traces and Information about the Packaging Material

A.4.1 Impurities and Traces of prohibited substances

The potential impurities and traces relevant for the raw materials were controlled via the raw material specifications. And the raw material specification are available upon request. This product does not contain any relevant impurity at significant levels, and the analytical testing results of heavy metals (below table) indicated the content of As, Hg, Pb, Sb, Cd and Ni (soluble) in this product were undetected and considered to be **acceptable** according to German Health Authority BgA recommendations form German Health Journal No.28, July 1985 and German Health Journal No.7/1992,Session 45 from November 14,1991. Furthermore, in conformity with the article 3 of the regulation, the safety evaluation of this impurity and trace of prohibited substances is part of the safety evaluation of the cosmetic product.

Items	Testing Results	German Health Authority BgA(Recommendation form German Health Journal No.28, July 1985)	German Health Journal No.7/1992,Session 45 from November 14,1991
Pb	Not detected	≤20	-
Hg	Not detected	≤1	-
As	Not detected	≤5	-
Sb	Not detected	≤10	-
Cd	Not detected	≤5	-
Ni (soluble)	Not detected	-	≤10

A.4.2 Information about the Packaging Material

The relevant characteristics of packaging material and in-depth knowledge of its raw materials is based on supplier data. The material information of packaging was listed below.

No.	Part	Material
1	Sealing sticker	PP
2	Plastic film	PET
3	Non-woven fabrics	Polyester and polyester fibers

The analytical testing results of immediate container indicated Pb, Cd, Hg and Cr (VI) were undetected with total amount less than 100 ppm.

A.5 Normal and Reasonably Foreseeable Use

The normal use and reasonably foreseeable uses of the product are described for the product type and determine the exposure and hazards used in the safety assessment. Product misuse is not considered.

A.5.1 Normal use and reasonably foreseeable use conditions:

The normal use of this product is intended to be applied as wipes by the population of 3 years old and above. Other usage is not foreseeable.

A.5.2 Warning and other explanation in the product labelling of the product category relevant for safety evaluation.

According to the Regulation, it shall be labelled “Avoid contact with eyes” due to the presence of Benzalkonium chloride.

A.6 Exposure to the product

The exposure to the cosmetic product is described by the following items:

A.6.1 Product Type

This cosmetic product is applied as wet wipes

Product Type: Leave-on

A.6.2 Target Group

The target users for this product are: the population of 3 years old and above. And the default body weight use for margin of safety calculation is 15.1 kg.

A.6.3 Area of application

The following exposure areas have been used in the Exposure calculations:

Area of application: hands and body skin

Application Surface area: 305 cm^2

A.6.4 Routes of Exposure

The following exposure routes have been used in the Exposure calculations:

Routes of Exposure: Dermal

A.6.5 Amount per daily application

The following product quantity used per application has been used in the Exposure calculations:

Product Exposure: 2 g per day (200 mg lotion transfer X average wipes 10)

A.6.6 Duration and Frequency

The following product use conditions have been used in the Exposure calculations:

Frequency of use: 10 times per day

Exposure duration: Leave-on

A.7 Exposure to the substances/impurities

Exposure to the substances/impurities has been calculated taking into account the potential exposure of product and the concentration of substances/impurities in the product. And exposure to aqua and sea water is not calculated as it is an innocuous and ubiquitous substance.

A.7.1 Exposure to the substance

INCI Name	Inclusion level (% w/w)	Total Systemic (SED) mg/kg bw/day	Local Dermal (CEL) μg/cm2
AQUA	93.90	124.37055	6157
GLYCERIN	2.00	2.649	131
PROPYLENE GLYCOL	2.00	2.649	131
ALOE BARBADENSIS LEAF EXTRACT	1.00	1.3245	66
PHENOXYETHANOL	0.50	0.66225	33
TOCOPHERYL ACETATE	0.20	0.2649	13
BENZALKONIUM CHLORIDE	0.10	0.13245	7
POLYSORBATE 20	0.10	0.13245	7
ETHYLHEXYLGLYCERIN	0.10	0.13245	7
PARFUM (PC-356A(DPG) Lemon fragrance)	0.10	0.13245	7

A.7.2 Exposure to impurities

As there is no impurity at significant levels, there is no exposure calculation.

A.8 Toxicological Profile of the Substances

Toxicological Profiles are provided for all substances apart from those that are fragrances, aqua or

substances present at levels below a threshold of toxicological concern.

Accordingly, toxicological profiles of GLYCERIN, PROPYLENE GLYCOL, ALOE BARBADENSIS LEAF EXTRACT, TOCOPHERYL ACETATE, POLYSORBATE 20, ETHYLHEXYLGLYCERIN and PARFUM (PC-356A(DPG) Lemon fragrance) are included here.

Toxicological profile of GLYCERIN (CAS# 56-81-5)

Toxicological endpoints:

Acute toxicity: Its acute toxicity was practically non-toxic [1, 2]. The oral LD_{L0} of glycerin was reported to be 1428 mg/kg for humans [3].

Skin irritation: It's not considered to be a skin irritant [1].

Eye irritation: It is not considered as an eye irritant [1].

Skin sensitization: Based on the available information, there is no human or animal data that indicates glycerol to be a skin sensitiser.

Phototoxicity: Weight of evidence indicated it was not phototoxic.

Repeated dose toxicity: Repeated oral exposure to glycerin does not induce adverse effects other than local irritation of the gastro-intestinal tract. And in one 2-year chronic diet feeding study in rats, NOAEL was considered as10,000 mg/kg bw/day (20% in diet) [1-3].

Mutagenicity/Genotoxicity: It's not considered to possess genotoxic potential.

Carcinogenicity: Glycerin administered in the feed of rats at concentrations up to 20% for 2 years did not increase the incidence of tumors. Hence, it's considered to be of no concern with regard to carcinogenicity [1-3].

Reproductive toxicity: No effects on fertility and reproductive performance were observed in a two generation reproductive toxicity study with glycerin administered by gavage (NOAEL 2000 mg/kg bw/day) [1-3].

Critical Point of Departure Value for MoS calculation

Critical Point of Departure Value	10000 mg/kg bw/d
Exposure Estimate	2.65 mg/kg bw/d
Margin of Safety (MoS)	3775

Regulatory Status: Not Regulated in Regulation (EC) No 1223/2009 with the assessment opinion from CIR that it can be safely used in leave-on and rinse-off cosmetics at the concentration up to 79.2% and 99.4% respectively [3]. Glycerin was on the restriction list of Cosmetic Ingredient Hotlist in Canada and Conditions of Use was "Manufacturers of oral and leave-on products containing glycerin must ensure the raw material used is within the specifications of an accepted pharmacopoeia with respect to diethylene glycol (DEG) impurities (e.g. Glycerin Official Monograph in the most current edition of the USP)".

Conclusion

Glycerin is a clear, syrupy liquid and is naturally occurring in all animals and plant matter in combined form as glycerides in fats and oils, or, in intracellular spaces as lipids. Natural glycerin is obtained as a byproduct in the conversion of fats and oils to fatty acids or fatty acid methyl esters. The U.S. Pharmacopeia-National Formulary (USP-

NF) standards state that the amount of any individual impurity in glycerin cannot exceed 0.1%, and that the total for all impurities, including diethylene glycol and ethylene glycol, must not exceed 1%. Glycerin is considered generally recognized as safe (GRAS) by the FDA for its use in food packaging and it is a multiple-purpose GRAS food substance when used in accordance with good manufacturing practices [21CFR182.90; 21CFR182.1320]. And it is concluded that the currently available data is sufficient to consider it safe to be used as intended in this product.

Reference list:

[1] ECHA. Registration Registration dossier of Glycerol (CAS No. 56-81-5). Last accessed on 2024-09-12@ https://echa.europa.eu/registration-dossier/-/registered-dossier/14481.
[2] OECD SIDS. INITIAL ASSESSMENT PROFILE of Glycerol. SIAM 14 Paris, France, 26-28 March 2002.
[3] CIR Expert Panel. Safety Assessment of Glycerin as Used in Cosmetics. IJT 38(Suppl. 3): 6-22, 2019.

Toxicological profile of PROPYLENE GLYCOL (CAS# 57-55-6)

Toxicological endpoints:

Acute toxicity: Its acute oral toxicity was practically non-toxic with the lowest oral LD_{50} values range between 18 and 23.9 g/ kg bw (5 different species) and the reported dermal LD_{50} is 20.8 g/kg bw in rabbits [1-3].

Skin irritation: In one primary skin irritation test according to OECD TG 404, it was found to be not irritating to the rabbit skin [1-3].

Eye irritation: It was found to be not irritating to eyes in acute eye irritation test in rabbits according to OECD TG 405 [1-3].

Skin sensitization: Based on the several animal studies and the data from human study, it is concluded that its skin sensitization potential was very low.

Phototoxicity: Weight of evidence indicated it was not phototoxic as it was demonstrated not to have significant UV absorption capacity.

Repeated dose toxicity: Repeated exposures of rats to propylene glycol in drinking water or feed did not result in adverse effects at levels up to 10% in water (estimated at about 10 g/kg bw/day) or 5% in feed (dosage reported as 2.5 g/kg bw/d) for periods up to 2 years [1, 3].

Mutagenicity/Genotoxicity: Propylene glycol was not a genetic toxicant as demonstrated by a battery of in vivo (micronucleus, dominant lethal, chromosome aberration) and in vitro (bacterial and mammalian cells and cultures) studies [1, 3, 4].

Carcinogenicity: No increase in tumors was found in all tissues examined when propylene glycol was administered in the diet of rats (2.5 g/kg bw/d for 2 years), or applied to the skin of female rats (100% PG; total dose not reported; 14 months) or mice (mouse dose estimated at about 2 g/kg bw/week; lifetime) [1, 3, 4].

Reproductive toxicity: Based on the absence of adverse effects on reproduction and development in available continuous breeding study and developmental toxicity studies, it shall not be recognized as a reproductive or

developmental toxicant.

Critical Point of Departure Value for MoS calculation

Critical Point of Departure Value	2500 mg/kg bw/d
Exposure Estimate	2.65 mg/kg bw/d
Margin of Safety (MoS)	944

Regulatory Status: **Not** Regulated in Regulation (EC) No 1223/2009 and with the assessment opinion from CIR that it can be safely used in cosmetics at the concentration up to 99% [2].

Conclusion

Propylene glycol (PG)is readily absorbed from the gastrointestinal and is expected to be widely distributed to organs and tissues. The major route of metabolism is oxidation to lactic acid and pyruvic acid. At high concentrations, free propane-1,2-diol is excreted in the urine. It is not acutely toxic. PG is essentially nonirritating to the skin and mildly irritating to the eyes. Numerous studies support that PG is not a skin sensitizer. No treatment-related effects were observed in subchronic and chronic toxicity studies. No adverse effects were reported in a 2-year chronic study in rats with PG (up to 2,500 mg/kg bw per day). The available data did not raise concern with respect to genotoxicity. No adverse effects were observed in the available reproductive and developmental toxicity studies. It is authorised as a food additive in EU and other regions with ADI of 25 mg/kg bw/d set by both EFSA and JECFA. It was recognized to pose no unreasonable risk to human health based on Tier I assessment under the NICNAS IMAP assessment framework. And it is concluded that the currently available data is sufficient to consider it safe to be used as intended in this product.

Reference list:

[1] ECHA. Registration dossier ofPropane-1,2-diol (CAS No. 57-55-6). Last accessed on 2022-10-22@ https://echa.europa.eu/registration-dossier/-/registered-dossier/16001.

[2] CIR Expert Panel. Safety Assessment of Propylene Glycol, Tripropylene Glycol, and PPGs as Used in Cosmetics. IJT 31(Suppl 2):245-260, 2012.

[3] SIDS INITIAL ASSESSMENT PROFILE of Propylene glycol (1,2-dihydroxypropane). SIAM 11, 23-26 January 2001.

[4] EFSA. Re-evaluation of propane-1,2-diol (E 1520) as a food additive. EFSA Journal 2018;16(4):5235.

Toxicological profile of ALOE BARBADENSIS LEAF EXTRACT (CAS# 85507-69-3 / 94349-62-9)

Toxicological endpoints:

Acute toxicity: Its acute toxicity was assumed to be practically non-toxic as Aloe barbadensis–derived ingredients (also known as Aloe vera) were not toxic in acute oral studies using mice (at doses up to 3 g/kg) [1].

Skin irritation: It was not a skin irritant [2].

Eye irritation: It was not an eye irritant [2].

Skin sensitization: It was assumed to be non-sensitizing as one 0.5% Aloe extract was non-photosensitizing [1] and the content of anthraquinone in this ingredient is below 0.2 ppm from the submitted technical data.

Phototoxicity: No data. But it was considered acceptable as it was demonstrated not to have significant UV absorption capacity.

Repeated dose toxicity: No data. But it was considered acceptable as Aloe barbadensis was the food additives permitted for direct addition to food for human consumption as natural flavoring substances (21CFR 172.510) [1]. In addition, in one 13-week repeated dose oral toxicity study in rats, Qmatrix® (a white to light tan powder derived from mucilaginous parenchymal cells found in the inner central area of the Aloe barbadensis leaf) produced no significant adverse effects and the NOAEL was recognized as 2000 mg/kg bw/d [3].

Mutagenicity/Genotoxicity: No data. But it was considered acceptable as Qmatrix® was non-mutagenic in an Ames test and a chromosomal aberration test at concentrations up to 10,000 μg/plate, and in an in vivo bone marrow micronucleus test at doses up to 5000 mg/kg bw/day [3].

Carcinogenicity: No data. But it was considered acceptable the content of anthraquinone in this ingredient is below 0.2 ppm and recognized to lack genotoxicity potential.

Reproductive toxicity: No data and the observed reproductive/developmental toxicity effects in experimental animals were related with the high concentration of anthraquinone. But this ingredient was considered to lack reproductive toxicity potential as the content of anthraquinone in this ingredient is below 0.2 ppm.

Critical Point of Departure Value for MoS calculation

Critical Point of Departure Value	2000 mg/kg bw/d
Exposure Estimate	1.32 mg/kg bw/d
Margin of Safety (MoS)	1510

Regulatory Status: Not regulated in Regulation (EC) No 1223/2009 and with the assessment opinion from CIR that it can be safely used in leave-on cosmetic products at the concentration up to 6% as Aloe extract [1].

Conclusion

Aloe Barbadensis Leaf Extract is an extract of the leaves of the aloe, Aloe barbadensis, Liliaceae. The Aloe Barbadensis plant has a long history of safe use for oral and topical applications. Based on the above information, it is concluded that it is sufficient to consider it safe to be used as intended in this product.

Reference list:

[1] CIR Expert Panel. Final Report on the Safety Assessment of Aloe Andongensis Extract, Aloe Andongensis Leaf Juice, Aloe Arborescens Leaf Extract, Aloe Arborescens Leaf Juice, Aloe Arborescens Leaf Protoplasts, Aloe Barbadensis Flower Extract, Aloe Barbadensis Leaf, Aloe Barbadensis Leaf Extract, Aloe Barbadensis Leaf Juice, Aloe Barbadensis Leaf Polysaccharides, Aloe Barbadensis Leaf Water, Aloe Ferox Leaf Extract, Aloe Ferox Leaf

Juice, and Aloe Ferox Leaf Juice Extract. International Journal of Toxicology, 26(Suppl. 2):1–50, 2007.
[2] SDS of this ingredient from the supplier.
[3] Williams LD, et al. Safety studies conducted on a proprietary high-purity aloe vera inner leaf fillet preparation, Qmatrix. Regul Toxicol Pharmacol. 2010, 57(1):90-8.

Toxicological profile ofTOCOPHERYL ACETATE (CAS# 7695-91-2 / 58-95-7)

Toxicological endpoints:

Acute toxicity: Its acute toxicity was practically non-toxic with oral LD_{50} > 10000 mg/kg bw in rats and dermal LD_{50} > 3000 mg/kg bw in rabbits [1, 2].

Skin irritation:It was found to be not irritating in one primary irritation test in rabbits according to OECD TG 404 [1, 2].

Eye irritation: It was found to be not irritating in one acute eye irritation test in rabbits according to OECD TG 405 [1, 2].

Skin sensitization: Weight of evidence indicated it was not a skin sensitizer [1, 2].

Phototoxicity: A photo-allergenicity test was conducted according to the CTFA Safety Testing Guidelines was carried out in 30 female (20 test and 10 control) Himalayan spotted guinea pig. For the induction of sensitization the undiluted DL-Alpha-Tocopheryl Acetate was applied epicutaneously to a skin area of 8 cm2 (marked previously with 4 intra-dermal injections of Freund's Complete Adjuvant). The test sites were then exposed to 1.8 J/cm_2 UVB and 10 J/cm_2 UVA irradiation. This procedure was repeated 4 times within 2 weeks of the induction phase. Control animals were treated with FCA only. Three weeks after beginning of the induction a challenge was carried out by treating the experimental animals (test and control) epicutaneously on both flanks with the test article at the concentrations of 100% (undiluted), 75%, 50% and 25% (dilutions in ethanol). Treated sites were then either exposed to 10 J/cm UVA irradiation (left flank) or remained un-irradiated (right flank). Cutaneous reactions, i.e. erythema and oedema formation were evaluated at 24, 48 and 72 hrs after the challenge exposure. Two out of 20 test animals were observed with a slight erythematous skin reaction after challenge. No consistent or significant differences were detected between the irradiated and non-irradiated test sites of the animals. The reactions were not clearly dependent on the test article concentration and most likely resulted from cutaneous hyperirritability (angry back) of the animals. No reactions were observed in the control group. Considering the above experimental data, it can be concluded that DL-Alpha-Tocopheryl Acetate does not exhibit photo-allergenic potential in the guinea pig under the study conditions [1, 2].

Repeated dose toxicity: In one subchronic oral toxicity study, the rats were dosed at 125, 500 and 2000 mg/kg. The relative liver weight was significantly increased in high dose females. Administration of 2000 mg/kg bw/d caused hematological changes: prolongation of prothrombin and activated partial thromboblastin (APTT) times and an increase in fibrinogen value, reticulocytosis and a decrease in hematocrit values and hemoglobin concentrations was observed in males; APTT times were also increased in females. Hemorrhagic diathesis was observed in males and females of the high dose group; and increased medullary erythropoiesis was seen in the spleen of one high dose male. The test substance at all dose levels tested caused interstitial inflammation and adenomatous hyperplasia of the

lung. The lung lesions were observed in all vitamin E-treated groups, and the incidence and severity increased in a dose-dependent manner. These lesions were characterized by increased cellularity, vascular congestion, thickened alveolar walls and the presence of foamy macrophages (some of which had undergone cell death and degeneration) in the alveolar spaces. A lipid-like yellow pigmentation was often present within either the macrophages or alveoli. These effects were attributed (as in the other oral gavage 90-day in minipigs study) to local aspiration of the test substance, which would not occur under normal circumstances. Furthermore, these effects were not seen in the chronic feed study (Wheldon, 1978). Therefore, for the NOAEL derivation the effects in the lungs were not considered. Because at 500 mg/kg only APTT values were increased in absence of an increase in PT and fibrinogen value, the NOAEL is set at 500 mg/kg bw/d [1]. In addition, in a 4-month clinical study as well as other well-designed clinical studies conducted in humans with DL-Alpha Tocopheryl acetate. Based on the absence of adverse effects up to the highest dose, the NOAEL was established at a dose of 540 mg alpha-tocopherol equivalents (TE)/day.

Mutagenicity/Genotoxicity:Weight of evidence indicated it lacked genotoxicity potential [2].

Carcinogenicity: Weight of evidence indicated it's unlikely to be carcinogenic [2].

Reproductive toxicity: Weight of evidence indicated it lacked reproductive toxicity potential [1, 2].

Critical Point of Departure Value for MoS calculation

Critical Point of Departure Value	500 mg/kg bw/d
Exposure Estimate	0.26 mg/kg bw/d
Margin of Safety (MoS)	1888

Regulatory Status: Not Regulated in Regulation (EC) No 1223/2009 with the assessment opinion from SCCNFP that alpha-tocopherol acetate does not pose a threat to the health of the consumer and therefore does not propose any restrictions or conditions on the use of alpha-tocopherol acetate in cosmetic products [3]. CIR also concluded that it can be safely used in leave-on and rinse-off cosmetics at the concentration up to 36% and 10% respectively [2].

Conclusion

It is the acetate ester of tocopherol. It is prepared by esterification of dl-α tocopherol with acetic acid. α-TA is mainly used in cosmetics as humectants, skin protectant or conditioning agent up to concentration of ≤36%. Further, it is functionally used as a nutrient, dietary supplement and antioxidant. α-Tocopherol and α-tocopheryl acetate are GRAS food ingredients when used as a nutrient, and a-tocopherol is GRAS as a chemical preservative in food when used in accordance with good manufacturing practices (21CFR182.8890; 21CFR182.8892; 21CFR182.8390). A group ADI of 0.15-2 mg/kg bw/d for dl-alpha-tocopherol and d-alpha-tocopherol concentrate, singly or in combination was set by JECFA. The tolerable upper intake level (UL) for vitamin E from all dietary sources, which were previously established by the Scientific Committee on Food, are 300 mg/day for adults, including pregnant and lactating women, 100 mg/day for children aged 1–3 years, 120 mg/day for 4–6 years, 160 mg/day for 7–10 years, 220 mg/day for 11–14 years and 260 mg/day for 15–17 years. From the currently available data, it was shown to be of low acute and repeated dose toxicity potential together with low skin/eye irritation and sensitization potential. There is no concern that tocopherols are genotoxic, carcinogenic, or teratogenic. Hence it is concluded that the currently available data is

sufficient to consider it safe to be used as intended in this product.

Reference list:

[1] ECHA. Registration dossier of 3,4-dihydro-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)-2H-benzopyran-6-yl acetate (CAS No. 7695-91-2). Last accessed on 2024-09-12@https://echa.europa.eu/registration-dossier/-/registered-dossier/13377.

[2] CIR Expert Panel. Safety Assessment of Tocopherols and Tocotrienols as Used in Cosmetics. IJT 37(Suppl. 2): 61-94, 2018.

[3] SCCNFP. THE USE OF ALPHA-TOCOPHEROL ACETATE IN COSMETIC PRODUCTS. SCCNFP/0494/01, final.

Toxicological profile of POLYSORBATE 20 (CAS No. 9005-64-5)

Toxicological endpoints:

Acute toxicity: Its acute toxicity was considered to practically non-toxic with oral LD_{50} > 5000 mg/kg bw in rats and dermal LD_{50} > 3000 mg/kg bw in rabbits [1, 2].

Skin irritation: It was considered to be non-irritating to skin in one primary skin irritation test in rabbits [1, 2].

Eye irritation: It was considered to be non-irritating to eyes in one acute eye irritation test in rabbits [1, 2].

Skin sensitization: It was considered to be non-sensitizing to skin [1, 2]. In one guinea pig maximisation test according to OECD TG 406, it was found to be not sensitizing [1].

Phototoxicity: No data. But it was considered acceptable as it was demonstrated not to have significant UV absorption capacity.

Repeated dose toxicity: In a 22-month dietary administration of polysorbate 20 (5% or 10% (approximately 7.5 or 15 g/kg body weight/day, respectively)) to mice, mild diarrhea was observed in the 10% treated group. In the 2-year oral carcinogenicity study of polysorbate 80 in mice and rats conducted by NTP, the NOAEL was recognized as 2.5% (ca. 3750 mg/kg bw/d) and 5 % in diet (ca. 2500 mg/kg bw/d) respectively for mice and rats [3].

Mutagenicity/Genotoxicity: It was tested as negative in one bacterial reverse mutation assay, in vitro chromosome aberration test in cultured peripheral human lymphocytes, and TK locus mutation assay in mouse lymphoma L5178Y cells [1, 3], indicating it lacked genotoxicity potential.

Carcinogenicity: It's considered unlikely to be carcinogenic [1, 3].

Reproductive toxicity: Oral administration of polysorbate 20 to 24-25 pregnant rats for 6-15 days (500 and 5,000 mg/kg body weight/day) suppressed weight gain in the 5,000 mg/kg body weight/day group. No changes were observed in ovary weights in both administration groups, there was no difference in the number of corpus lutea and implantations and the death rate of preimplantation embryos per mother animal and no marked difference in the growth and development of fetuses compared with those in the control group. The NOAEL for developmental toxicity was considered as 5000 mg/kg bw/d [1, 3].

Critical Point of Departure Value for MoS calculation

Critical Point of Departure Value	2500 mg/kg bw/d
Exposure Estimate	0.13 mg/kg bw/d
Margin of Safety (MoS)	**18875**

Regulatory Status: Not regulated in Regulation (EC) No 1223/2009 and with the assessment opinion from CIR that it can be safely used in leave-on and rinse-off cosmetics at the concentration up to 9.1% and 19.6% respectively [4].

Conclusion

The Polysorbates are a series of general purpose, hydrophilic, nonionic surfactants. They are obtained by reaction of sorbitol and its anhydrides with ethylene oxide (C_2H_4O) under conditions that cause splitting of water from the sorbitol, leaving sorbitan. A specified molar ratio of ethylene oxide to sorbitol and its mono- and dianhydrides is used in the condensation to effect an oxyethylene copolymerization at the free hydroxyl groups of sorbitan. The resulting polyoxyethylene sorbitans are esterified with 1 or 3 moles of a fatty acid (lauric, palmitic, stearic, oleic) to produce the Polysorbates. Therefore, in summary the Polysorbates are polyoxyethylene (W + X + Y + Z) sorbitan mono- or triesters, where the sum of w + x + y + z is the average number of moles of ethylene oxide per mole of sorbitol, and where R denotes 1 or 3 moles of an esterified fatty acid. It should be noted that the number in ingredients with the nomenclature “polysorbate #” has no relationship to the size of the molecule but to the associated fatty acid from which the ingredient is derived (20, laurate; 40, palmitate; 60, stearate; 80, oleate). Polysorbates 20, 60, and 80 are approved for direct use in all food types as synthetic flavorings (21 CFR 172.515). The Joint Food and Agriculture Organization of the United Nations (FAO)/World Health Organization (WHO) Expert Committee on Food Additives (JECFA) derived an Acceptable Daily Intake (ADI) of 25 mg/kg body weight (bw)/day (group ADI for polysorbates 20, 40, 60, 65 and 80).

Polysorbates are hydrolyzed by pancreatic and blood lipases; the fatty acid moiety is released to be absorbed and metabolized, whereas the polyoxyethylene sorbitan moiety is very poorly absorbed and is excreted unchanged. Acute and long-term oral toxicity in animals indicates a low order of toxicity with oral ingestion of the Polysorbates. Currently available data indicate polysorbates do not give rise to concerns for genotoxicity. The Polysorbates were noncarcinogenic in laboratory animals. And there is no indication they will be specific reproductive or developmental toxicants. Extensive experimental clinical skin testing showed Polysorbates to have little potential or human skin irritation or evidence of skin sensitization or phototoxicity. Due to the adequate margin of safety, hence it can be concluded it is safe to be used as intended in this product.

Reference list:

[1] ECHA. Registration dossier of Sorbitan monolaurate, ethoxylated (CAS No.9005-64-5). Last accessed on 2024-10-05@https://echa.europa.eu/registration-dossier/-/registered-dossier/13525.

[2] CIR Expert Panel. Final Report on the Safety Assessment of Polysorbates 20, 21, 40, 60, 61, 65, 80, 81, and 85. JACT 3(5):1-82, 1984.

[3] EFSA. Scientific Opinion on the re-evaluation of polyoxyethylene sorbitan monolaurate (E 432), polyoxyethylene sorbitan monooleate (E 433), polyoxyethylene sorbitan monopalmitate (E 434), polyoxyethylene sorbitan monostearate (E 435) and polyoxyethylene sorbitan tristearate (E 436) as food additives. EFSA Journal 2015;13(7):4151.

[4] CIR Expert Panel. 2015. Safety Assessment of Polysorbates as Used in Cosmetics.

Toxicological profile of ETHYLHEXYLGLYCERIN (CAS# 70445-33-9)

Toxicological endpoints:

Acute toxicity: Its acute toxicity was very low with both oral LD_{50} and dermal LD_{50} > 2000 mg/kg bw in rats [1].

Skin irritation: It was considered as a mild skin irritant in one primary skin irritation test according to the OECD TG 404 test protocol [1].

Eye irritation: Under the conditions of the in vivo study, it is considered as a severe irritant to the rabbit eye when tested undilutedly [1, 2].

Skin sensitization: In a Guinea Pig Maximisation Test, it was not identified as a skin sensitiser. The sensitization potential of ethylhexylglycerin was not demonstrated in one local lymph node assay at concentrations up to 50% [1, 2].

Phototoxicity: Ethylhexylglycerin was not phototoxic or photoallergic in guinea pigs when tested at concentrations up to 100% in the presence of UV-A/UV-B light [2].

Repeated dose toxicity: Ethylhexylglycerin administered orally to rats, at doses up to 800 mg/kg/d, in a 13-week study did not result in any treatment-related deaths, macroscopic observations, or neurotoxicity. A statistically significant increase in absolute and relative-to-body weight liver weights was observed in males of all dose groups and females of the highest dose group. Generalized hepatocytic hypertrophy was observed at microscopic examination in the highest dose group, a finding that was statistically significant in males. Two summaries of this 13-week showed that a dose of 50 mg/kg bw/d (lowest dose) was the LOAEL in one summary and the NOAEL in the other summary [1, 2]. And in one Repeated Dose 28-Day Oral Toxicity Study of in Ethylhexylglycerin in rats, increased liver and adrenal weights were observed in the highest dose group, and microscopic findings included slight to moderate liver hypertrophy in rats of all 3 dose groups. The NOAEL was recognized as 100 mg/kg bw/d [1, 2].

Mutagenicity/Genotoxicity: Ethylhexylglycerin was nongenotoxic in the Ames test (S typhimurium strains) and in the mouse lymphoma assay in vitro, both with and without metabolic activation. It was also nonclastogenic in the micronucleus assay in vivo [1, 2].

Carcinogenicity: No data, but it is not expected to be a carcinogen as no structural alerts were found in the computational toxicology software DEREK for its carcinogenicity and no genotoxicity hazards are recognized.

Reproductive toxicity: It was not found to be a reproductive or developmental toxicant, based on a prenatal developmental study and a one generation Reproduction Toxicity study in rats [1].

Critical Point of Departure Value for MoS calculation

Critical Point of Departure Value	50 mg/kg bw/d
Exposure Estimate	0.13 mg/kg bw/d

Margin of Safety (MoS)	378

Regulatory Status: Not Regulated in Regulation (EC) No 1223/2009 and with the assessment opinion CIR also concluded it can be safely used in leave-on and rinse-off cosmetics at the concentration up to 2% and 8% respectively [2].

Conclusion

Ethylhexylglycerin (EHG) is an alkyl glyceryl ether that acts as a surfactant or skin conditioning agent in cosmetic products. It reportedly also inhibits the growth and multiplication of odor-causing bacteria and enhances the efficacy of cosmetic preservatives, such as phenoxyethanol, methylisothiazolinone, or methylparaben. And it is concluded that the currently available data is sufficient to consider it safe to be used as intended in this product.

Reference list:

[1] ECHA. Registration dossier of 3-(2-ethylhexyloxy)propane-1,2-diol (CAS No. 70445-33-9). Last accessed on 2024-09-10@https://echa.europa.eu/registration-dossier/-/registered-dossier/16725.

[2] CIR Expert Panel. Safety Assessment of Alkyl Glyceryl Ethers as Used in Cosmetics. IJT 32(Suppl. 3): 5-21, 2013.

Assessment of PARFUM (PC-356A(DPG) Lemon fragrance) was based on the submitted IFRA certificate according to the Standards of the INTERNATIONALFRAGRANCE ASSOCIATION (IFRA-51th Amendment /published June 30, 2023), which indicated it can be safely used in Category 3 products at the concentration up to 18.18%. Based on the above information, it is considered to be safe at the stated concentration in the formulation under normal and reasonably foreseeable conditions of use.

A.9 Undesirable effects and serious undesirable effects

As at the date of this report the product has not yet been commercialized, therefore there are no data available from post marketing surveillance on undesirable effects or serious undesirable effects to the cosmetic product. No relevant data on other cosmetic product are available.

A.10 Information on the Cosmetic Product

This product is indicated to be manufactured by in a manufacturing setting according to ISO 22716:2007, with scope of compliance on manufacturing of general liquid unit, including hair care & cleansing products, skin care liquid products# and gel products#; cream & lotion unit, including skin care & cleansing products# and hair care products; powder unit, including loose powder products and pressed powder products; wax base unit, including wax base products#; eye care products and skincare products for children by third party laboratory (Intertek Certificate SZ2210D6 which is valid until 18 Oct, 2025).

PART B – Cosmetic Product Safety Assessment

B.1 Assessment conclusion

The formulation does not contain forbidden or banned ingredients per European Cosmetics Regulation (EC) No 1223/2009 and its amendments, and the safety assessment has been carried out in accordance with this regulation and its subsequent amendments.

After overall evaluation, this product can be considered as safe to be placed on the market without posing a foreseeable risk to the health of consumers under normal or reasonably foreseeable conditions of use.

B.2 Labelled warnings and instructions of use

As the printed instructions of use and warning is clear to describe the product usage and appropriate enough to avoid misuse, no special warnings or instructions of use are further required.

B.3 Reasoning

B.3.1 Safety Evaluation of the Substances

All of the following ingredients have been assessed as safe for human health under normal and reasonably foreseeable conditions of use.

Substance Name	Conc. (%)	Max. allowed conc. (%)	Margin of Safety	Assessment Conclusion
GLYCERIN	2.00	NA	3775	Safe for human health under normal and reasonably foreseeable conditions of use.
PROPYLENE GLYCOL	2.00	NA	944	Safe for human health under normal and reasonably foreseeable conditions of use.
ALOE BARBADENSIS LEAF EXTRACT	1.00	NA	1510	Safe for human health under normal and reasonably foreseeable conditions of use.
PHENOXYETHANOL	0.50	1	NA	Safe for human health under normal and reasonably foreseeable conditions of use.
TOCOPHERYL ACETATE	0.20	NA	1888	Safe for human health under normal and reasonably foreseeable conditions of use.
BENZALKONIUM CHLORIDE	0.10	0.1	NA	Conforms to regulated usage.
POLYSORBATE 20	0.10	NA	18875	Safe for human health under normal and reasonably foreseeable conditions of use.
ETHYLHEXYLGLYCERIN	0.10	NA	378	Safe for human health under normal and reasonably foreseeable conditions of use.

PARFUM (PC-356A(DPG) Lemon fragrance)	0.10	18.18	NA	Fragrance conforms to IFRA standards

B.3.2 Safety Evaluation of the Product

This product along with all substances contained within the formulation of the product has been evaluated and found to be safe for its normal and reasonably foreseeable use based on submitted product information and other information publicly available.

The product will be produced with certified Good Manufacturing Practices for cosmetics. And the stability, microbiological quality, packaging, warnings and use instructions have been considered and taken into account as part of safety evaluation of this product. These aspects are covered under Sections A2, A3, A4 & A5 of the report.

Based upon the information supplied, unless otherwise stated in this report, it was assumed that neither this product, nor the ingredients used in the product, contained any impurities/contaminants that would cause harm to the health of a consumer. And this evaluation result is valid only to the conditions described herein. And any deviation from the above disclosed conditions will necessitate a new evaluation. Furthermore, if any serious undesirable effects attributed to the use of this product occurred, the safety assessor shall be informed immediately. Under such circumstances, a new safety assessment will be conducted, and conclusions may be revised.

B.4 Assessor´s credentials and approval of part B

Dr. Raul Xin, EUROTOX Registered Toxicologist (ERT)

Authorized external expert of Bureau Veritas

*** End of Report ***