Cosmetic Product Safety Report

Product name:	**Dhiva Shampoo**		
Company name:	**Dhiva Cosmetics**	**Version:**	**1**
Formula number:		**Date:**	**October 2016**

Part A: Cosmetic Product Safety Information

The following information is gathered and managed in the Dhiva Cosmetics product database (the product information file, PIF) under the relevant section.

1. Quantitative and qualitative composition of the cosmetic product, **Dhiva shampoo composition (see Appendix A – Quantitative and qualitative composition of the cosmetic product)**:
2. Physical/chemical characteristics and stability of the cosmetic product: **Stability clearance (see Appendix B – Stability summary)**.
3. **Claim support: (no claim on this product)**.
4. Microbiological quality: **Microbiological clearance (see Appendix B – Stability summary)**.
5. Impurities, traces, information about the packaging material: **Packaging clearance (see Appendix B – Stability summary)**.
6. Normal and reasonably foreseable use: **Label specifications (see below 2. Labelled warnings and instructions of use**).
7. Exposure to the cosmetic product: **(see Appendix C – Exposure assessment)** and assessment **below**
8. Exposure to the substances: **MoS calculation (see Appendix D – Margin of Safety calculations)**.
9. Toxicological profile of the substances **(see Appendix E - Toxicological profiles for ingredients)**.
10. Undesirable effects and serious undesirable effects: **Data from reports on (serious) undesireable effects (see Part B: Cosmetic Product Safety Assessment)**.
11. Information on the cosmetic product: **User Test (see Appendix F – User test)**.

Part B: Cosmetic Product Safety Assessment

1. Assessment conclusion

The cosmetic product **Dhiva Shampoo** can be assessed as **safe** for normal and reasonably foreseeable use in accordance with the European Cosmetics Regulation (EC) No 1223/2009.

2. Labelled warnings and instructions of use

The following warnings and instructions of use are mentioned on the packaging material/label of the product:

Instructions of use: Massage into wet hair until it lathers. Rinse thoroughly. Caution: Avoid contact with eyes. If accidental contact occurs rince immediately with water.

Further labelled warnings and instructions of use are not needed as the product labelling and the general description of the product are sufficient to define the use of the product as a **shampoo**.

There are no ingredients incorporated in the finished product, which require additional directions, specific indications or warnings in accordance to the relevant Annexes of the European Cosmetics Regulation (EC) No 1223/2009 (as amended) or due to their toxicological and/or physical-chemical properties or because of their concentrations in the finished product.

3. Reasoning

The safety assessment of Dhiva shampoo is based on the toxicological profile of each ingredient and evaluation of the PIF[A] collected data on the product. The product is produced using Good Manufacturing Practice for cosmetics and Microbial Quality Management in the production facilities and further along the storage. Procedures also include microbiological control of raw materials, bulk and finished products, packaging material, personnel, equipment and preparation and storage rooms. As this product contains an eye irritating ingredient (Sodium laureth sulfate) in a 10 % concentration, the product is labelled with "Avoid contact with eyes". "If accidental contact occurs rince immediately with water". Other ingredients irritating in 100 % concentration are used in low concentrations in this shampoo and a user test has shown that the final formula is formulated to be non-irritating to the skin, and this is why further labelling is not required.

Physical/chemical characteristics, stability and microbiological quality of the cosmetic product

The stability data of the formula after storage meet the specified characteristics of the product specifications. The data confirm a sufficient stability of the tested formula.

This water based product has a functioning preservation system and the level of preservative is within specifications at the end of shelf life. Based on all the stability results including physical stability, challenge test and other laboratory analyses (microbiological tests, chemical test of level of preservatives):
The shelf life for the final product is **12 months**[B].
The Period After Opening (PAO) is **12 months**.

Impurities, traces and information about the packaging material

No impurities and/or traces were detected in the final product or in the ingredients at levels that may have an impact on the safety of the finished product.

The product packaging material is:
200 ml bottle = HDPE. lid/cap= Polypropylene
The interactions/suitability between the formulation and the packaging was validated in **accelerated stability tests (see packaging clearance in Appendix B).** The packaging material is evaluated to be suitable and safe for use.

Normal and reasonably foreseeable use

The labelling as shampoo in combination with the general description of the product on the label, support the safe use of the product during intended and reasonably foreseeable use. (Unintended) reasonably foreseeable use (not a misuse) is not recognisable.

[A] *Tip: A product information file (PIF) is a paper or electronic dossier where all information on the product and ingredients are stored. Regulation (EC) No 1223/2009 states in Article 11 what the product information file should contain.*
Summary of PIF content

- *A clear connection between the cosmetic product and the product information (traceability).*
- *The cosmetic product safety report (CPSR)*
- *Method of manufacture and GMP statement on compliance with good manufacturing practice (GMP).*
- *Claim support if claims are used*
- *Animal testing information or non-animal testing certificate of the cosmetic product and its ingredients.*

https://www.cosmeticseurope.eu/publications-cosmetics-europe-association/guidelines.html?view=item&id=85

[B] *Tip: The shelflife and PAO is a case to case evaluation made based on the various tests performed. There is no common formula to use.*

Exposure to the cosmetic product and the substances[C]

The calculation of the exposure to the product and to each of the ingredients in the cosmetic product was carried out according to the "SCCS's Notes of Guidance for the testing of cosmetic ingredients and their safety evaluation, 9th revision 2015" (see appendix C). For the exposure calculation, reasonable forseeable use is calculated as the sum of use as shampoo and use as body wash. A retention factor of 0.01 (1 %) is used, as this is a rinse-off product.

Toxicological profile of the substances

All raw materials and ingredients in the finished product were assessed as safe for the use as cosmetic ingredients in the finished product. The safety of the cosmetic product is based on the safety of its ingredients.

The Margin of Safety (MoS) calculated for each of the substances contained in the cosmetic product is above 100, which supports the safety of the cosmetic product. See the calculation of MoS in Appendix D.

The fragrance selected for this shampoo has an IFRA certificate and an IFRA safety assessment certifying the use in rinse-off products in up to 5 % of the product. Allergenic fragrance compounds mandatory to declaration above 0,01 % in the product are declared in the INCI-list on the product.

Undesirable effects and serious undesirable effects

The information about undesirable effects and serious undesirable effects is kept up-to-date and regularly made available to the safety assessor.

This is a fictive product and therefore the product does not have any adverse event reporting .

Information on the cosmetic product

A User Test on the Dhiva shampoo did not indicate any potential for dermal irritation. The dermal tolerance of Dhiva shampoo was tested by a 4-week application test in accordance with international guidelines (fictive study as this is a fictive product). The application test was carried out on 50 volunteers (30 adults and 20 children aged between 10 years and 18 years). The shampoo was used for washing the hair and body at least 3 times a week. During the test and at the end of the test period, none of the subjects showed any skin reaction to the test product or any skin disorders.

4. Assessor's credentials and approval of part B

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Date and signature of the safety assessor.

Proof of the safety assessor's qualification can be found in the safety assessor Curriculum Vitae (normally enclosed).

[C] *Tip; The calculation of exposure should be in accordanc with the labelled use. For common products you can find default values of skin area and amount of product normally used* in SCCS's "Notes of Guidance for the testing of cosmetic ingredients and their safety evaluation, 9th revision 2015". *For products not mentined in this guideline you need to assess the skin area and measure the amount of product used.*

Appendix A – Quantitative and qualitative composition of the cosmetic product

Composition of Dhiva shampoo

INCI name of ingredient	Content in %	Function in product
Aqua	74.95	Solvent
Sodium laureth sulfate	10.00	Detergent
Glycerin	3.85	Humectant
Glycol distearate	2.80	Emollient
Cocamidopropyl betaine	2.50	Detergent
Citric acid	1.80	pH regulator
Perfume[D]	0.60	Fragrance
Sodium chloride	0.50	Viscosity controlling
Coco-Glucoside	0.50	Detergent
Glyceryl Oleate	0.50	Emulsifiying
Hydroxypropyl Guar Hydroxypropyltrimonium Chloride	0.50	Conditioning
Dihydrogenated Palmoylethyl Hydroxyethylmonium Methosulfate	0.50	Conditioning
Phenoxyethanol	0.50	Preservative
Behenoyl PG-Trimonium Chloride	0.25	Conditioning
Sodium bensoate	0.25	Preservative
Total:	100.00	

Further information on the chemical identity of the ingredients is stated in **Appendix E - Toxicological profiles for ingredients.**

[D] *Since this is a fictive product no IFRA certificate, IFRA safety assessment or other assessment is enclosed.*

Appendix B – Stability summary

Product name:	**Dhiva Shampoo**	**Product number in the database:**	
Company name:	**Dhiva Cosmetics**	**Version:**	**1**
Formula number:		**Date:**	**October 2016**

Stability testing ensures that the functionality and aesthetics of the product are not adversely impacted during its intended shelf life and consumer use. Testing can be conductedunder controlled accelerated or real-time conditions. The stability summary includes physical, chemical and microbiological stability along with compatibility between the product and packaging used.

Physical stability summary

Includes stability and physical integrity of the product under appropriate conditions for storage, transport and use.
The physical stability study has been conducted according to stability protocol for shampoo. For this product, an accelerated storage at 40°C for 1 and 3 months has been applied. Samples for this product will also be stored for long term testing.

Appearance / colour / odour
Dhiva shampoo is a white, slightly fragranced shampoo.

After 1 and 3 months of accelerated storage at 40°C, the Dhiva shampoo routine production batch 1/2016 in packaging 300 ml (HDPE) bottle (appearance / odor / color) comply.

pH
The pH values of routine production batch 1/2016 during the stability testing complies with the current specifications at the time of production and shelf life.

pH range remain the same (5.6 +/- 0.2)

Viscosity
The viscosity values of routine production batch 1/2016 during the stability testing conform to the current specifications at the time of production and shelf life.

Viscosity T0 (physica, 45 1/s) : 3000 mPas +/- 500 mPas
Viscosity Shelf life (physica, 45 1/s) : 3000 mPas +/- 500 mPas

Light stability
Cosmetics, for which the packaging may allow the product to be exposed to light, should undergo light stability testing. The light used in the testing should simulate the intensity to which the cosmetic will likely be exposed. All these tests are compliant.

Microbiological stability summary[E]

Dhiva shampoo is classified in Category 2: Other products. It is generally accepted that for cosmetics classified in Category 2, the total viable count for aerobic mesophyllic microorganisms should not exceed 10^3 cfu/g or 10^3 cfu/ml of the product.

Dhiva shampoo is a waterbased shampoo preserved with phenoxyethanol and sodium benzoate to prevent microbiological growth. Raw material review and microbiological risk classification by the microbiological laboratory have assessed this product to be a microbiologically category 2 risk product. Microbiological testing of each batch after filling of Dhiva shampoo conforms to category 2 requirements. A challenge test has been performed to test the efficacy of the preservation of this product. Data from challenge testing of the product conform to specifications/passed for all endpoints, see Challenge test report (example of challenge test attached in Dhiva baby bodylotion report).

Chemical stability

Dhiva shampoo is a waterbased product preserved with phenoxyethanol and sodium benzoate. The level of phenoxyethanol and sodium benzoate was analysed at time 0 and after accelerated storage of 3 month at 40°C with the result: passed. The test methods have been successfully validated for sodium benzoate and phenoxyethanol according to the standards. They meet all test method validation specifications.

Packaging clearance[F]

The packaging material is a 200 ml bottle = HDPE. lid/cap = Polypropylene. This package does not contain hazardous materials that require special markings or labelling. Based on the package testing results, which conform to the package development procedures, it is the opinion of the Packaging Development Department that this package is acceptable for distribution.

Conclusion

The Dhiva shampoo is considered compliant and acceptable for consumers based on the tests of the accelerated stability program in 200 ml HDPE bottles. Compatibility between the product and the packaging employed is ensured by the tests employed. Based on the results from all stability testing, the shelf life is 12 months and the period after opening is 12 months.

Signed by Head of lab

[E] *Tip: For microbiological testing of cosmetic products see the following guidance document http://www2.mst.dk/udgiv/publications/2010/978-87-92668-66-0/pdf/978-87-92668-67-7.pdf For waterbased cosmetics a Microbiological Risk Classification should be performed see ISO 29621:2010 and Stewart SE, Parker MD, Amézquita A, Pitt TL. Microbiological Risk Assessment for Personal Care Products. Int J Cosmet Sci. 2016 May 3. doi: 10.1111/ics.12338. [Epub ahead of print]*

[F] *Tip; If you do not use material specifically certified for cosmetic use you need to ensure that the analysed level of migrating chemicals in your cosmetic product is safe.*

Appendix C – Exposure assessment

Calculation of the Exposure of a Shampoo

In this part, the amount of the substance and the frequency of human exposure to the substance are determined (including specific groups at potential risk, e.g. children, pregnant women, etc.). If the default values fit with the labelled recommended use, then the default values can be used. Otherwise it is necessary to perform an assessment of quantity of product used per day. Here is used the default values for the used quantity per day of the product.

Basic data from The SCCS Notes of Guidance for the testing of cosmetic ingredients and their safety evaluation. 9th Revision, September 2015.

Basic data

Average body weight **K**:	60 kg [1]
Way of exposure:	Dermal [1]
Kind of exposure:	Rinse off product [1]
Quantity per day as body cleanser $\mathbf{G_{BC}}$:	18.67 g/day [1]
Quantity per day as shampoo $\mathbf{G_{SH}}$:	10.46 g/day [1]
Retention factor body cleanser $\mathbf{R_{BC}}$:	0.01 [1]
Retention factor body shampoo $\mathbf{R_{SH}}$:	0.01 [1]
Percutaneous permeation **P**:	Not applicable; see raw material

Dermal exposure (Edermal)

$$\mathbf{E_{dermal} = (G_{BC} + G_{SH}) * R_{BC+SH} / K}$$
$$= (18.67+10.46) * 0.01/ 60$$
$$= 0.0048 \text{ g/kg bw/day}$$
$$\mathbf{= 4.86 \text{ mg/kg bw/day}}$$

Reference

1 The SCCS's Notes of Guidance for the testing of cosmetic ingredients and their safety evaluation. 9th Revision, September 2015.

Appendix D – Margin of Safety calculations

Based on the SCCS Notes of Guidance for the testing of cosmetic ingredients and their safety evaluation. 9th Revision, September 2015.

$$P = dermal \text{ absorption } fraction$$

$$Systemic\ exposure\ dose;\ SED = \left(\frac{Conc}{100}\right) * P * E_{derm}$$

$$MoS = \frac{NOAEL}{SED}$$

It is generally accepted that Margin of Safety (MoS) should, at least, be 100 to declare an ingredient safe for use. This is the case for all the ingredients in this product.

Calculation of Margin of Safety (MoS) for the INCI ingredients of the product

Product name:	Dhiva Shampoo	Ederm [mg/kg/d]=	4,86
Formula number:	Fictive product	Adult hair + body wash	
Product number:			

INCI ingredient	Conc [%]	P	NOAEL [mg/kg/d]	Info	SED [mg/kg/d]	Margin of Safety
Aqua	74,95000	n.r.	n.r.	n.r.	n.r.	>100
Sodium laureth sulfate	10	0,01	225	*	0,00486	46296
Glycerin	3,85	0,8	10000	*	0,149688	66806
Glycol distearate	2,8	1	1000	*	0,13608	7349
Cocamidopropyl betaine	2,5	0,1	150	*	0,01215	12346
Citric acid	1,8	1	1200	*	0,08748	13717
Parfum	0,6	n.r	n.r.	x,¤	n.r	>100
Sodium chloride	0,5	1	200	****	0,0243	8230
Coco-Glucoside	0,50	0,0001	1000	****	0,00000243	411522634
Glyceryl Oleate	0,50	1	1000	****	0,0243	41152
Hydroxypropyl Guar Hydroxypropyltrimonium Chloride	0,50	0	n.r.	****	n.r.	>100
Behenoyl PG-Trimonium Chloride	0,25	0,0001	5	****	0,000001215	4115226
Dihydrogenated Palmoylethyl Hydroxyethylmonium Methosulfate	0,50	0,02	150	****	0,000486	308642
Phenoxyethanol	0,50	1	357	***	0,0243	14691
Sodium benzoate	0,25	0,43	500	***	0,0052245	95703
	100,000					

*: NO(A)EL available from distributor/supplier or from literature

***: Raw Material assessment by EU Scientific Committee on Consumer Safety (SCCS)/SCCNFP. The safety of the raw material is considered safe in the actual use when the maximum concentration in the product is below the SCCS's limit values

****: Calculation of the NO(A)EL reasoned by analogy (for instance food, structure, medical uses etc.)

x: Fragrance ingredient or flavor; raw material safety assessment by the manufacturer should be inclosed to document the safety. Check Annex II and III in the cosmetic safety regulation (EC) No 1223/2009.

n.r.: Data are not relevant for the assessment of the raw material

¤: Refer to IFRA Conformity Certificate and Fragrance Safety Evaluation for the substance

Appendix E[G] - Toxicological profiles for ingredients

Toxicological profile for a cosmetic raw material

The assessment is performed according to the European Cosmetics Regulation (EC) No 1223/2009.

Trade name

Sodium laureth sulfate.

Supplier

General toxicological profile for demonstration purposes.

Composition

INCI name	Chemical Name	Concentration	CAS No	EC No
Sodium Laureth Sulfate	sodium 2-(2-dodecyloxyethoxy)ethyl sulphate	60 %	3088-31-1 / 9004-82-4 / 68891-38-3 / 1335-72-4 / 68585-34-2 / 91648-56-5	221-416-0 / 618-398-5 / 603-752-3 / 500-234-8 / 500-223-8 / 293-918-8
Glycol distearate		20 %	627-83-8	211-014-3
Aqua		20 %	231-791-2	231-791-2

Impurities[H]

- 1,4 dioxane, (Sodium laureth sulfate (SLES), glycol distearate),
- Ethyleneoxid (SLES),
- Ethyleneglycol (glycol distearate).

These impurities are process related and should be kept to a minimum by GMP. Levels of these impurities are established in the specification. If several ethoxylated ingredients are used in combination in the product, a MoS of the sum of each CMR impurity should be performed.

Function

Cleansing, emulsifying, foaming, surfactant (1).

Regulatory status

Not regulated in (EC) No 1223/2009.

[G] *Tip: All toxicological profiles shall be kept updated. It is recommended to update the profiles, when new data is avaiable, using a new supplier or other relevant information. A date for the update shall be noted.*

[H] *Tip: Impurities are batch and supplier dependent and needs to be updated when changing supplier and to be checked for each batch upon arrival. For traces of forbidden substances, safe limits should be established and included into the ingredient's specifications in the PIF.*

Physical-chemical properties[I]

Property	Value	Reference
Molecular weight	376.48	(4)
Description	Colourless and odourless liquid	(4)
Log Pow	1.22	(4)
Water solubility	Soluble	(4)

Toxicological data

The ingredient glycol distearate is assessed elsewhere.

Acute toxicity: Low acute oral toxicity. LD_{50} > 5000 mg/kg (3).

Corrosivity and irritation: Can produce eye and/or skin irritation in experimental animals (2).
Dermal and ocular irritant in concentrate (3).

Skin sensitisation: Not sensitising (3).

Dermal absorption (per substance)

INCI name	Value in % or mg/cm2	Comments / reasoning	Reference
Sodium Laureth sulfate	Rounded value 1 %	In vivo data rat 48 h	(4)

Repeated toxicity: No data, read across to NaC12-14AE2S in group AES (3, 5).
Based on systemic toxicity from the 90 days rat study, behavioural and clinical abnormalities and other general or specific toxic effects, a no adverse effect level (NOAEL) of 225 mg/kg was established.

Mutagenicity/Genotoxicity: Read across to group AES. Negative *in vitro* mutagenicity tests (5) and *in vivo* chromosome aberration tests (5).
Not clastogenic (4).

[I] *Tip: According to SCCS/1564/15, the basic and minimal physical-chemical specifications for any cosmetic ingredient to be evaluated are:*
1) Chemical identity;
2) Physical form;
3) Molecular weight;
4) Characterisation and purity of the chemical including isomer composition;
5) Characterisation of the impurities or accompanying contaminants;
6) Solubility;
7) Partition coefficient (Log Pow);
8) Relevant physical and chemical specifications;
9) Homogeneity and stability.
However, these parameters needs to be adjusted for ingredients obtained directly from nature as most data is not available for these natural UVCB mixtures. In general, physical-chemical specifications should be available from the supplier of the cosmetic ingredient and where relevant they should be attached to batch number.

Carcinogenicity: Not carcinogenic (3, 5).

Reproductive toxicity: Read-across to AES, not reprotoxic (3, 5).

Toxicokinetics: AES is readily absorbed in the gastrointestinal tract in humans and in rats and is excreted primarily through the urine. The length of the ethoxylate portion in an AES molecule seems to have an important impact on the biokinetics of AES in humans and in the rat. AES with longer ethoxylate chains (>7-9 EO units) is excreted at a higher proportion in the faeces. Once absorbed, AES is extensively metabolised by beta- or omega oxidation (5).

Phototoxicity: Not phototoxic (3).

Human data: Known to produce dermal irritation in sensitive persons (2).

Others: Read across between different alcohol ethoxysulphates is acceptable and used by the HERA project and CIR.

NOAEL to use for MoS calculation (per substance)

INCI name	NOAEL (mg/kg bw/day)	NOAEC inhalation
Sodium laureth sulfate	Rat 90 day 225 mg/kg bw/day (5)	No data

Conclusion

It is assessed for this ingredient, Sodium laureth sulfate, which has been extensively assessed by several parties as a group of AES, that the summary of toxicological data of the group and of the actural SLES is sufficient to consider it a safe cosmetic ingredient. The NOAEL from NaC12-14AE2S is assessed to be an acceptable NOAEL for use in the MoS calculation.

Sodium laureth sulfate is assessed to be safe for use as a cosmetic ingredient in this shampoo.

Reference list

1. CosIng EC Regulation v.2
2. CIR Evaluation on SLES (Final Report of the Amended Safety Assessment of Sodium Laureth Sulfate (SLES) and related salts of sulfated ethoxylated alcohols by Valerie C. Robinson et al., International Journal of Toxicology).
3. US EPA Dossier on SLES submitted by Stepan Company.
4. ECHA / REACH Dossier: CAS 3088-31-1
5. HERA Report on Alcohol Ethoxysulfates: http://www.heraproject.com/files/1-HH-04-HERA AES HH web wd.pdf

Toxicological profile for a cosmetic raw material

The assessment is performed according to the European Cosmetics Regulation (EC) No 1223/2009.

Trade name

Glycerin.

Supplier

General toxicological profile for demonstration purposes.

Composition

INCI name	Chemical Name	Concentration	CAS No	EC No
Glycerin	Glycerol, 1,2,3-Propanetriol	95-99.5 % (2)	56-81-5	200-289-5

Impurities[H]

Impurities are water and trace levels of polyglycerol. 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 % (2).

Function

Denaturant, hair conditioning, humectant, masking, oral care, perfuming, skin protection and viscosity control (3).

Regulatory status

Not regulated in (EC) No 1223/2009.

Physical-chemical properties

Property	Value	Reference
Molecular weight	92.09 mg/mol	(1)
Description	Colourless, odourless, sweet-tasting viscous liquid	(2)
Log Kow	-1.76	(1)
Water solubility	Fully soluble	(1)

Toxicological data

Acute toxicity:

Oral LD_{50} in rats 2530 - 58400 mg/kg (1).

Dermal LD_{50} in rats >21 900 mg/kg (2).

Corrosivity and irritation: Minimal potential to irritate eye and skin (1).

Skin sensitisation: Not a skin sensitiser (1).

Dermal absorption (per substance)

INCI name	Value in % or mg/cm2	Comments / reasoning	Reference
Glycerin	80 %	Low Log Pow and molecular weight, lack of specific data	(1)

Repeated toxicity: In a dietary study, groups of 22 rats/sex/treatment received 5, 10 and 20 % glycerol in their diet (males 2000, 4000 and 8000 mg/kg bw; females 2500, 5000 and 10000 mg/kg bw) for 2 years. No adverse effects were observed at up to 10000 mg/kg bw (1).

Mutagenicity/Genotoxicity: Neither mutagenic nor genotoxic (1).

Carcinogenicity: Not carcinogenic (1).

Reproductive toxicity: Not reprotoxic (1).

Toxicokinetics: Data from studies in humans and animals indicate that glycerol is rapidly absorbed in the intestine and the stomach, distributed over the extracellular space (1). Due to low Log Pow (-2.66 to -1.76) and molecular weight (92g/mol) of glycerins and lack of other data, the dermal absorption of glycerin is set to 80 %.

Phototoxicity: No data. Acceptable as glycerin is not presumed to absorb light.

Human data: In a study with 420 excema patients, only one showed evidence of dermal sensitisation to glycerin (4).

Others: Glycerol occurs naturally in fats and other substances, which are in part made up of lipid complexes. Glycerol may be derived from natural sources, primarily triglycerides, or be synthesised by the hydrogenolysis of carbohydrate materials or from products such as propylene. Evidence is available to show that glycerol is metabolised in the body to form glycogen or provide a direct energy source. In addition, long-term studies are available to show that synthetically derived glycerols are biologically similar to naturally derived glycerol (5).

NOAEL to use for MoS calculation (per substance)

INCI name	NOAEL (mg/kg bw/day)	NOAEC inhalation
Glycerin	10000 from the 2-year study in rats (1)	the NOAEC for local irritant effects to the upper respiratory tract is 165 mg/m3 and 662 mg/m3 for systemic effects (1)

Conclusion

It is assessed for this ingredient, which is virtually nontoxic, that the summary of toxicological data is sufficient to consider it a safe cosmetic ingredient. The NOAEL from the 2-year study in rats is assessed to be an acceptable NOAEL for use in the MoS calculation.

Glycerin is assessed to be safe for use as a cosmetic ingredient.

Reference list

1. CIR Final Report, Safety Assessment of Glycerin as Used in Cosmetics. Released 14 January 2015.
2. SIDS Initial Assessment Report For SIAM 14 (2002). GLYCEROL CAS N°: 56-81-5 http://www.inchem.org/documents/sids/sids/56815.pdf.
3. CosIng, European Commission cosmetic database. Search: “glycerol”, date: 29 July, 2015.
4. Hannuksela, M. and Forstrom, L. 1976 cited in REACH dossier.

5. Glycerol and glycerol di-acetate. Twentieth Report of the Joint FAO/WHO Expert Committee on Food Additives, Geneva, 1976, WHO Technical Report Series No. 599, FAO Food and Nutrition Series No. 1.

Toxicological profile for a cosmetic raw material

The assessment is performed according to the European Cosmetics Regulation (EC) No 1223/2009.

Trade name

Glycol distearate.

Supplier

General toxicological profile for demonstration purposes.

Composition

INCI name	Chemical Name	Concentration	CAS No	EC No
Glycol distearate	Ethylene distearate	100 %	627-83-8	211-014-3

Impurities[H]

Free stearic acid (triple-pressed), the mono or diesters, ethylene glycol, and corresponding derivatives of other fatty acids found in stearic acid may be present as well as traces of 1,4 dioxane (1).
These impurities are process related and should be kept to a minimum. If several ethoxylated or ethylene oxide based ingredients are used, a MoS of the sum of each CMR impurity should be performed.

Function

Emollient, emulsifying, opacifying, skin conditioning and viscosity controlling.

Regulatory status

Not regulated in (EC) No 1223/2009.

Physical-chemical properties

Property	Value	Reference
Molecular weight	594.999 mg/mol	(2)
Description	White to cream coloured vaxy solid (flakes)	(1)
Log Pow	16.12 (QSAR	(3)
Water solubility	Insoluble	(3)

Toxicological data

Acute Toxicity: Undiluted glycol distearate LD_{50} = 5000 mg/kg (rat) (1).

Corrosivity and irritation: No evidence of skin irritation or corrosivity in Draize tests (1). No evidence of eye irritation in Draize tests (1).

Skin sensitisation: No evidence of skin sensitisation in guinea pig tests (1).

Dermal absorption (per substance)

INCI name	Value in % or mg/cm2	Comments / reasoning	reference
Glycol distearate	100 %	No data	(1)

Repeated toxicity: Read across 90-day rat study (OECD 408) with C18 and C18 unsaturated epoxidised ester with ethylene glycol (CAS 151661-88-0), NOAEL 1000mg/kg bw/day (3).

Mutagenicity/Genotoxicity: Ames test negative (3), mouse micronucleus test negative (3).

Carcinogenicity: No data. Acceptable as no mutagenicity/genotoxicity is evident.

Reproductive toxicity: Not reprotoxic, read across from decanoic acid reaction products with 1,3-butanediol and octanoic acid (853947-59-8), 2-generation rat study, P, F1 and F2 NOAEL 1000 mg/kg bw/day (3).

Toxicokinetics: Readily absorbed, read across from Propyleneglycol-distearate (3). Due to its action as a surfactant, glycoldistearate may enhance the permeability of drugs through human and animal skin (1).

Phototoxicity: No data. Acceptable, as glycol distearate is not presumed to absorb light.

Human data: HRIPT with 50 % glycol distearate w/v in mineral oil, repeated doses of 0.25g on 125 subjects gave no irritation or hypersensitivity (1).

Others: No data.

NOAEL to use for MoS calculation (per substance)

INCI name	NOAEL (mg/kg bw/day)	NOAEC inhalation
Glycol distearate	1000 mg/kg bw/day (3) read across from C18 and C18 unsaturated epoxidised, ester with ethylene glycol (CAS 151661-88-0)	No data

Conclusion

It is assessed for this ingredient with low acute toxicity that the summary of toxicological data is sufficient to consider it a safe cosmetic ingredient. The NOAEL from the 90-day study with CAS 151661-88-0 in rats is assessed by read across to be acceptable for use in the MoS calculation.

Glycol distearate is assessed to be safe for use as a cosmetic ingredient.

Reference list

1. Final Report on the Safety Assessment of Glycol Stearate, Glycol Stearate SE, and Glycol Distearate. CIR review 1982. JACT 1(2):1-11. Re-reviewed in 2003, not opened
2. http://chem.sis.nlm.nih.gov/chemidplus/rn/627-83-8.
3. REACH dossier glycol distearate

Toxicological profile for a cosmetic raw material

The assessment is performed according to the European Cosmetics Regulation (EC) No 1223/2009.

Trade name

Coco betaine.

Supplier

General toxicological profile for demonstration purposes.

Composition

INCI name	Chemical Name	Concentration	CAS No	EC No
Cocamidopropyl betaine	1-Propanaminium, 3-amino-N-(carboxymethyl)-N,N-dimethyl-, N-coco acyl derivs., hydroxides, inner salts (1)	30 %	61789-40-0	263-058-8
Water		62-66%	7732-18-5	231-791-2
Sodium Chloride		4-6%	7647-14-5	231-598-3

Impurities[H]

- Sodium monochloroacetate (below 5 ppm),
- Sodium dichloroacetate, Sodium glycolate, Amidoamine
- Dimethylaminopropylamine (DMAPA)

As DMAPA and amidoamine are sensitising impurities; it is essential to use highly pure batches of Coco betaine in order to have acceptable impurity profiles (4).

Function

Antistatic, cleansing, foam boosting, hair conditioning, surfactant, viscosity controlling (1).

Regulatory status

Not regulated in (EC) No 1223/2009.

Physical-chemical properties

Property	Value	Reference
Molecular weight	342.516 g/mol	(2)
Description	Clear, pale yellow liquid	(4)
Log Pow	-1.28 to 3.63 (calculated via KOWWIN v1.67 at 25°C) for specific betaines with C8, 10, 12, 14, 16 & 18- fatty acids 8	(3)
Water solubility	Soluble	(4)

Toxicological data

Sodium chloride is assessed, at page 22.

Acute toxicity: The LD_{50} oral in rats is ≥4900 mg/kg bw. The LD_{50} dermal in rats is >2000 mg/kg bw (3).

Corrosivity and irritation: The concentrated as well as the 25 – 30 % active cocamidopropyl betaine are irreversible eye irritant and a skin irritant. At and below 10 % active dilution, mild to moderate and reversible eye irritation and skin irritation are apparent (3).

Skin sensitisation: Cocamidopropylbetaine (CAPB) is not sensitising, but the impurity DMAPA is a moderate sensitiser (3).

Dermal absorption (per substance)

INCI name	Value in % or mg/cm2	Comments / reasoning	Reference
Cocamidopropyl betaine	10 %	Rounded worst case value from ADME study	(3)

Repeated toxicity: In a 90-day study in rats, the NOAEL for cumulative-systemic toxic effects is 1000 mg/kg bw (for the aqueous 30 % active cocamidopropyl betaine solution). Related to 100% active ingredient, a NOAEL of 300 mg/kg bw is established (3).

Mutagenicity/Genotoxicity: Negative (3).

Carcinogenicity: Not carcinogenic (4).

Reproductive toxicity: Not reprotoxic (3).

Toxicokinetics: Lauramidopropyl betaine (50 % component in cocamidopropyl betaine - as a model for cocamidopropyl betaine) is poorly absorbed from the intestinal tract (< 10 %) and through the skin (2-6 %). Following oral or dermal exposure, there is metabolism of the absorbed material (3).

Phototoxicity: Not phototoxic (4).

Human data: CAPB at 6 % active in cleansing cloths was not a sensitiser in a repeated patch test, nor was it a sensitiser in similar studies at lower active concentrations in formulations (4). Not a photosensitiser (4). Slightly irritation in 3 % solution (4).

Others: The formation of nitrosamines is possible. Secondary amides (and the identified impurities) may serve as substrates for N-nitrosation, therefore formulation with N-nitrosating agents should be avoided (4).

NOAEL to use for MoS calculation (per substance)

INCI name	NOAEL (mg/kg bw/day)	NOAEC inhalation
Cocamidopropyl betaine	1000 mg/kg for 30 % of aqueous solution, 300 mg/kg bw for 100 % CAPB. The NOAEL is further reduced to 150 mg/kg bw due to low oral absorption and use of default 50 % oral absorption value (3).	N.A.

Conclusion

It is assessed for this ingredient, assessed by both CIR and HERA, that the summary of toxicological data is sufficient to consider it a safe cosmetic ingredient. The NOAEL from 90-day study in rats is assessed to be acceptable for use in the MoS calculation.

Cocamidopropyl betaine is assessed to be safe for use as a cosmetic ingredient.

Reference list

1. http://ec.europa.eu/consumers/cosmetics/cosing/index.cfm?fuseaction=search.details&id=75231.
2. http://pubchem.ncbi.nlm.nih.gov/compound/20280.
3. HERA, June 2005. http://www.heraproject.com/files/45-hh-e101023f-d12f-6a30-deb0770e9bf8e4d0.pdf
4. CIR Draft Final Amended Report on Cocamidopropyl Betaine and Related Amidopropyl Betaines July 28, 2010.

Toxicological profile for a cosmetic raw material

The assessment is performed according to the European Cosmetics Regulation (EC) No 1223/2009.

Trade name

Citric acid.

Supplier

General toxicological profile for demonstration purposes.

Composition

INCI name	Chemical Name	Concentration	CAS No	EC No
Citric acid	2-Hydroxy-1,2,3-propanetricarboxylic acid	100 %	5949-29-1 (monohydrate) 77-92-9 (anhydrous)	611-842-9 / 201-069-1

Impurities[H]

None of relevance.

Function

Buffering, chelating and masking.

Regulatory status

The ingredient citric acid (CAS NO 77-92-9 (anhydrous); CAS NO 5949-29-1 (monohydrate) is not regulated in the Cosmetics Regulation, but there are two opinions from SCCS; 0370/00 - Position paper on the Safety of alpha-Hydroxy Acids and 0799/04 - Updated position paper concerning consumer safety of alpha-hydroxy acids suggesting labelling as a precaution for products containing AHAs.

Physical-chemical properties

Property	Value	Reference
Molecular weight	192.124 g/mol	(1)
Description	Colouless, odourless crystals with an acid taste	(1)
Log Pow	-1.64	(1)
Water solubility	Soluble	(1)

Toxicological data

Acute toxicity: Rat oral LD_{50} = 3,000-12000 mg/kg bw (2).

Skin irritation: Slightly skin irritating (2).

Eye irritation: Eye irritating in 100% concentration, (2).

Skin sensitisation: Not sensitising (3).

Dermal absorption (per substance)

INCI name	Value in % or mg/cm2	Comments / reasoning	reference
Citric acid	100%	No data	

Repeated toxicity: Rat oral 2-year study with 5 % and 3 % citric acid in feed, slightly decreased growth. NOAEL = 1200 mg/kg bw/d (2).

Mutagenicity/Genotoxicity: Negative (2).

Carcinogenicity: Not a suspected carcinogen (2).

Reproductive toxicity: Not reprotoxic (3).

Toxicokinetic: Citric acid is well absorbed and largely metabolised when administered orally (3).

Phototoxicity: Structurally, citric acid is an α-hydroxy acid (AHA). In the FDA *Guidance for Industry: Labelling for Topically Applied Cosmetic Products Containing Alpha Hydroxy Acids as Ingredients* from 2005, the FDA specifically mentions citric acid containing products, for which the following labelling may be warranted: *Sunburn Alert: This product contains an alpha hydroxy acid (AHA) that may increase your skin's sensitivity to the sun and particularly the possibility of sunburn. Use a sunscreen, wear protective clothing, and limit sun exposure while using this product and for a week afterwards* (4).

Human data: Clinical report; irritant skin dermatitis in waiters and bakers attributed to citric acid. Clinical report; in solution the acid may produce pain if applied to abraded skin (2). Clinical report; severe eye damage in a man splashed in the eye with saturated aq. solution (2). Clinical report; mouth sores, headache, asthma, nasal blockage, general tiredness. Itchiness was reported after the ingestion of foods containing citric acid (2). Clinical report; citric acid might be a skin sensitiser (2).

Others: Citric acid might influence the absorption of other ingredients (4).

NOAEL to use for MoS calculation (per substance)

INCI name	NOAEL (mg/kg bw/day)	NOAEC inhalation
Citric acid	1200 mg/kg bw/d (oral/repeated dose toxicity) (2)	N. A.

Conclusion

It is assessed for this ingredient with low acute toxicity that the summary of toxicological data is sufficient to consider it a safe cosmetic ingredient. The NOAEL from 2-year study in rats is assessed to be acceptable for use in the MoS calculation.
Citric acid is assessed to be safe for use as a cosmetic ingredient.

References list

1. http://pubchem.ncbi.nlm.nih.gov/compound/citric_acid#section=Non-Human-Toxicity-Values.
2. OECD SIDS, 2001. SIDS Initial Assessment Report, Citric Acid.
3. CIR Final report 27th March 2012. Safety Assessment of Citric Acid, Inorganic Citrate Salts, and Alkyl Citrate Esters as Used in Cosmetics.
4. Food and Drug Administration (FDA). Guidance: Labeling for Cosmetics Containing Alpha Hydroxy Acids. Guidance for Industry, Labeling for Topically Applied Cosmetic Products Containing Alpha Hydroxy Acids as an Ingredient. http://www.fda.gov/cosmetics/guidanceregulation/guidancedocuments/ucm090816.htm 2005. Date Accessed 30.07.2015.

Toxicological profile for a cosmetic raw material

The assessment is performed according to the European Cosmetics Regulation (EC) No 1223/2009.

Trade name

Not identified.

Supplier

General toxicological profile for demonstration purposes.

Composition

INCI name	Chemical Name	Concentration	CAS No.	EC No
Sodium chloride	NaCl	100 %	7647-14-5	231-598-3

Impurities[H]

Cosmetic grade purity or higher purity: Thus acceptable.

Function

Bulking, masking, oral care, viscosity controlling (1).

Regulatory status

Not regulated in (EC) No 1223/2009

Physical-chemical properties

Property	Value	Reference
Molecular weight	58.44 g/mol	(3)
Description	Colourless, transparent crystals or white crystalline powder, odourless	(3)
Log Pow	-3.0	(6)
Water solubility	Soluble	(3)

Toxicological data

Acute toxicity: LD_{50} of a 25% solution of sodium chloride in water in rats 3 040 - 4 140 mg/kg bw (2).

Corrosivity and irritation: Undiluted, slightly irritating to skin and eyes (2).

Skin sensitisation: Not sensitising (2).

Dermal absorption (per substance)

INCI name	Value in % or mg/cm2	Comments / reasoning	Reference
Sodium chloride	100 %	No data on dermal absorption, good oral absorption	

Repeated toxicity: NOEL 2 % added salt from a 90-day study in rats (2). For long-term toxicity there is a 2-year study in Fisher344/Slc rats with a calculated LOEL of sodium chloride of approximately 2533 mg/kg/day based on increased blood pressure (4).

Mutagenicity/Genotoxicity: Not mutagenic in Ames test (5). Sodium chloride was positive at concentrations in the range 0.02-1 mol/l in an OECD Guideline 476 Mouse Lymphoma L5178Y thymidine kinase locus assay (2). A statistically significant positive result was obtained with 40 mmole/kg NaCl (2338 mg/kg) in an OECD Guideline 475 (Mammalian Bone Marrow Chromosome Aberration Test) (2).

Carcinogenicity: No data. Acceptable, as this is a food ingredient that has been used safely for a long time.

Reproductive toxicity: No data, but by analogy to calcium chloride; sodium and chloride are both essential constituents for all animals and humans and are ingested daily. Any toxic effect of sodium chloride on mammalian reproduction is not predicted as far as ordinary consumer and occupational exposures are concerned (4).

Toxicokinetic: Sodium chloride is easily dissociated into sodium and chloride ions in water. The absorption, the distribution and the excretion of the ions in animals are regulated separately (4).

Phototoxicity: No data. Acceptable, as sodium chloride is not presumed to absorb light.

Human data: Results from a recently published study show that a sodium chloride intake above 12.5 g/day (208 mg/kg bw for a 60 kg person) increases blood pressure to dangerous levels (5). As a comparison, the normal intake of salt in Sweden is 10-12 grams per day, which is almost double the intake of 6 grams per day (100 mg/kg bw/day for a 60 kg person) recommended by the Swedish National Food Agency.

Others: No data.

NOAEL to use for MoS calculation (per substance)

INCI name	NOAEL (mg/kg bw/day)	NOAEC inhalation
Sodium chloride	200 human data (5)	No data

Conclusion

For this ingredient, it is assessed, that based on relevant human data, the NOAEL from human data is assessed to be acceptable for use in the MoS calculation.

Sodium chloride is assessed to be safe for use as a cosmetic ingredient.

Reference list

1. CosIng, European Commission cosmetic database. Search: “sodium chloride”, accessed 6th of April 2016.
2. REACH dossier sodium chloride http://echa.europa.eu/registration-dossier/-/registered-dossier/15467/1.
3. Pubchem sodium chloride.
4. Imai, S., et al. 1986. Chronic Toxicity Test of KCl and NaCl in F344/Slc Rats. J. Nara Med. Ass., 37, pp. 115-12.
5. Mozaffarian D, Fahimi S, Singh GM, Micha R, Khatibzadeh S, Engell RE, Lim S, Danaei G, Ezzati M, Powles J; Global Burden of Diseases Nutrition and Chronic Diseases Expert Group.2014. Global

sodium consumption and death from cardiovascular causes. N Engl J Med. 2014 Aug 14;371(7):624-34.

6. CHEMINFO by CCOHS accessed 6. June 2016. http://www.chem.utoronto.ca/~pmeindl/labs/msds%20files/sodium%20chloride.htm

Toxicological profile for a cosmetic raw material

The assessment is performed according to the European Cosmetics Regulation (EC) No 1223/2009.

Trade name

Not identified.

Supplier

General toxicological profile for demonstration purposes.

Composition

INCI name	Chemical Name	Concentration	CAS No.	EC No
Coco-glucoside	Alcohols, coco, reaction products with glucose; C8-16 fatty alcohol glucoside	50-60 %	141464-42-8	604-232-9
Aqua		40-50 %	7732-18-5	231-791-2

Impurities[H]

No CMR impurities expected in this cosmetic grade. Thus acceptable.

Function

Cleansing, foaming, surfactant (1).

Regulatory status

Not regulated in (EC) No 1223/2009.

Physical-chemical properties

Property	Value	Reference
Molecular weight	320.42, varies depending on carbon backbone and polymerization.	(2)
Description	Cloudy, viscous pale yellow aquaeous solution. Nonionic surfactant	(2)
Log Pow	7.406 (at 25°C) Arachidyl Glucoside (mono)	(2)
Water solubility	Soluble	(2)

Toxicological data

Acute toxicity: LD_{50} in rats >2000 mg/kg bw (2).

Corrosivity and irritation: Irritating to skin (2). Corrosive to eyes undiluted. The irritation threshold value was 10% for 30% a.i. caprylyl/capryl glucoside and 5% for 60% a.i. caprylyl/capryl glucoside. (2).

Skin sensitisation: Not sensitising (2).

Dermal absorption (per substance)

INCI name	Value in % or mg/cm2	Comments / reasoning	Reference
Coco-glucoside	0.01 %	By analogy to caprylyl/capryl Glucoside	(2)

Repeated toxicity: NOAEL 1000 mg/kg bw/day in a 90-day study in rats by analogy with C12/16 AlkylPolyGlucosides (2).

Mutagenicity/Genotoxicity: Not mutagenic in Ames test (2), negative in chromosome aberration test (2).

Carcinogenicity: No data. Acceptable, as it is derived from coconut oil and glucose having no structural alerts and is not mutagenic or genotoxic.

Reproductive toxicity: Not reprotoxic (2).

Toxicokinetics: Caprylyl glucoside has been shown to increase the absorption of poorly absorbed drugs (e.g., insulin) (2). No consistent relationship between alkyl chain length and penetration enhancement (2).

Phototoxicity: No data. Acceptable, as coco-glucoside is not presumed to absorb light.

Human data: Allergic contact dermatitis caused by alkyl glucosides in cosmetics (and topical pharmaceutical products) does occur. However, the mechanism by which these substances cause sensitisation is not clear (3).

Others: It is assessed that read across is acceptable between all the alkyl glucosides group assessed by CIR.

NOAEL to use for MoS calculation (per substance)

INCI name	NOAEL (mg/kg bw/day)	NOAEC inhalation
Coco-glucoside	1000 from a 90-day study in rats with the analog C12/16 APG (2)	No data

Conclusion

It is assessed for this ingredient, which has been assessed by CIR as a group of alkyl glucosides, that the summary of toxicological data is sufficient to consider it a safe cosmetic ingredient. The dermal absorption is very low and systemic toxicity after dermal application is not expected. The NOAEL from the 90-day study with the analog C12/16 APG is assessed to be acceptable for use in the MoS calculation.

Coco-glucoside is assessed to be safe for use as a cosmetic ingredient.

Reference list

1. CosIng, European Commission cosmetic database. Search: “Coco-glucoside”, accessed 6th of April 2016.
2. CIR safety assessment of Decyl Glucoside and Other Alkyl Glucosides, 2011.
3. Giejbels D et al. 2014. Allergic contact dermatitis caused by alkyl glucosides. Contact Dermatitis, 70, 175–182.

Toxicological profile for a cosmetic raw material

The assessment is performed according to the European Cosmetics Regulation (EC) No 1223/2009.

Trade name

Not identified.

Supplier

General toxicological profile for demonstration purposes.

Composition

INCI name	Chemical Name	Concentration	CAS No.	EC No
Glyceryl Oleate	Oleic acid, monoester with glycerol	>90 %	25496-72-4 / 111-03-5	247-038-6 / 203-827-7

Impurities[H]

Free fatty acids (FFA) <2.5 %, glycerol <1 % (2) and thus acceptable. For further impurities, refer to supplier. Traces of monomers can be expected, but for this ingredient no CMR impurities are expected. A low level of FFA is a sign of high quality.

Function

Emollient, emulsifying, perfuming (1).

Regulatory status

Not regulated in (EC) No 1223/2009.

Physical-chemical properties

Property	Value	Reference
Molecular weight	356.5 g/mol	(3)
Description	Oleic acid, monoester with glycerol	(1)
Log Pow	6.68	(4)
Water solubility	Insoluble	(3)

Toxicological data

Acute toxicity: LD_{50} in rats >2000 mg/kg bw (2).

Corrosivity and irritation: Not irritating to skin (2). Not irritating to eyes (2).

Skin sensitisation: Not sensitising (2).

Dermal absorption (per substance)

INCI name	Value in % or mg/cm2	Comments / reasoning	Reference
Glyceryl Oleate	100 %	No data on dermal absorption, good oral absorption	

Repeated toxicity: In a 28-day study of glycerides, C8-18 and C18-unsatd. mono- and di-, acetates in rats, the NOAELs were 1000 mg/kg bw/day (2).

Mutagenicity/Genotoxicity: Not mutagenic in Ames test (2).

Carcinogenicity: Not carcinogenic (2).

Reproductive toxicity: Not reprotoxic, the NOAELs for systemic toxicity (males and females), fertility (males and females), and development (F1 generation) were 1000 mg/kg bw/day (2).

Toxicokinetics: The metabolic products of Glyceryl Oleate are glycerol and oleic acid, both well absorbed orally (2).

Phototoxicity: Not phototoxic or photosensitising (2).

Human data: Two aqueous Glyceryl Oleate preparations (15 % and 30 % concentrations) and a fragrance preparation containing 19.0 % Glyceryl Oleate were negative for cutaneous irritation when tested on human skin using single insult occlusive patch tests (2).

Others: It is assessed that read across is acceptable between all monoglycerides assessed by CIR as the monoglyceryl monoesters are structurally constituted of the esterification products of one equivalent of glycerin and one equivalent of a carboxylic acid, usually a fatty acid. These ingredients vary only in the identity of those acids (e.g., variable length, branching, and unsaturation of those acid residues).

NOAEL to use for MoS calculation (per substance)

INCI name	NOAEL (mg/kg bw/day)	NOAEC inhalation
Glyceryl Oleate	1000 from a 28-day study in rats with the analog, glycerides, C8-18 and C18-unsatd. mono- and di-, acetate (2). It is assessed that it is not necessary to add a further safety factor of 3 due to the use of a 28-day study as no clinical signs of toxicity was seen at the highest dose tested is this study.	No data

Conclusion

It is assessed for this ingredient with low oral toxicity that the summary of toxicological data is sufficient to consider it a safe cosmetic ingredient. The NOAEL from an 28-day study in rats with the analogue glycerides, C8-18 and C18-unsatd. mono- and di-acetate, is assessed to be acceptable for use in the MoS calculation.

Glyceryl oleate is assessed to be safe for use as a cosmetic ingredient.

Reference list

1. CosIng, European Commission cosmetic database. Search: “glyceryloleate”, accessed 6th of April 2016.
2. CIR safety assessment of Monoglyceryl Monoesters as Used in Cosmetics, 2015.
3. Pubchem monoolein.
4. Handbook of Cosmeceutical Excipients and their Safeties. K Y Heng,T Y Kei,K J Singh,Li Hairui,Poh Ai-Ling,K Lifeng 2014.

Toxicological profile for a cosmetic raw material

The assessment is performed according to the European Cosmetics Regulation (EC) No 1223/2009.

Trade name

Not identified.

Supplier

General toxicological profile for demonstration purposes.

Composition

INCI name	Chemical Name	Concentration	CAS No	EC No
Hydroxypropyl Guar Hydroxypropyltrimonium Chloride	Guar gum, 2-hydroxypropyl 2-hydroxy-3-(trimethylammonio)propyl ether, chloride	85 %	71329-50-5	615-280-5

Impurities[H]

Inorganic salts up to 8.7 % do not give rise to safety concern. Residues of plant protection agents and heavy metals should be monitored.

Function

Antistatic, hair conditioning (1).

Regulatory status

Not restricted in (EC) No 1223/2009.

Physical-chemical properties

Property	Value	Reference
Molecular weight	High (polymer)	(2)
Description	Cationic guar, light ivory to yellow fine powder	(2)
Log Pow	No data	
Water solubility	Soluble	(2)

Toxicological data

Acute toxicity: The oral LD_{50} value in rats is 12 g/kg bw (2).

Corrosivity and irritation: Not skin irritating (2). Not eye irritating (2).

Skin sensitisation: No data.

Dermal absorption (per substance)

INCI name	Value in % or mg/cm2	Comments / reasoning	Reference
Hydroxypropyl Guar Hydroxypropyltrimonium Chloride	0	Large molecule	(2)

Repeated toxicity: No data. Acceptable, as Hydroxypropyl Guar Hydroxypropyltrimonium Chloride is not likely to be absorbed through the skin (2).

Mutagenicity/Genotoxicity: Not mutagenic (2).

Carcinogenicity: Not carcinogenic (2).

Reproductive toxicity: Not teratogenic by analogy to guar gum (2).

Toxicokinetics: Not likely to be absorbed through the skin (2).

Phototoxicity: No data. Acceptable, as Hydroxypropyl Guar Hydroxypropyltrimonium Chloride is not presumed to absorb light.

Human data: A leave-on hair styling product containing 2 % hydroxypropyl guar was evaluated in a RIPT involving 111 human subjects (ages not stated). There was no evidence of skin reactivity in any of the subjects during the study (2).

Others: The prevalence of occupational asthma and immunologic sensitisation to Cyamopsis tetragonoloba (guar) gum was evaluated in 162 employees of a carpet-manufacturing plant where this gum was used to adhere dye to the fiber. It was concluded that the prevalence of IgE sensitisation to guar gum was between 5 % and 8.3 % (2).

NOAEL to use for MoS calculation (per substance)

INCI name	NOAEL (mg/kg bw/day)	NOAEC inhalation
Hydroxypropyl Guar Hydroxypropyltrimonium Chloride	Not relevant no dermal absorption	No data

Conclusion

It is assessed for this ingredient that human dermal test data are the most important, as the dermal absorption is set at zero and no systemic toxicity is expected. No NOAEL is available and is not needed for the MoS calculation.

Hydroxypropyl Guar Hydroxypropyltrimonium Chloride is assessed to be safe for use as a cosmetic ingredient.

Reference list

1. CosIng, European Commission cosmetic database. Search: “Hydroxypropyl Guar Hydroxypropyltrimonium Chloride” Accessed 24 February 2016.
2. CIR Final report on the Safety Assessment of Galactomannans as Used in Cosmetics.

Toxicological profile for a cosmetic raw material

The assessment is performed according to the European Cosmetics Regulation (EC) No 1223/2009.

Trade name

Not identified.

Supplier

General toxicological profile for demonstration purposes.

Composition

INCI name	Chemical Name	Concentration	CAS No	EC No
Dihydrogenated Palmoylethyl Hydroxyethylmonium Methosulfate	Ethanaminium, 2-hydroxy-N,N-bis(2-hydroxyethyl)-N-methyl-, esters with C16-18 and C18-unsatd. fatty acids, Me sulfates (salts)	Not known but usually >80%	157905-74-3	605-113-4

Impurities[H]

Residual solvents (3). Not a problem if produced according to GMP.

Function

Antistatic, hair conditioning (1).

Regulatory status

Not restricted in (EC) No 1223/2009.

Physical-chemical properties

Property	Value	Reference
Molecular weight	733.5 average	(4)
Description	Cationic esterquat appears as straw-coloured paste at 20°C	(2)
Log Pow	>6.5 (est.)	(4)
Water solubility	Soluble	(4)

Toxicological data

Acute toxicity: Oral LD_{50} >4250 mg/kg bw (conc. corrected value) for TEA EQ (2). Dermal LD_{50} TEA-based esterquat (EQ) 157905-74-3 100 % active >2000 mg/kg bw (2).

Corrosivity and irritation: At concentrations < 30 %, EQ did not produce an irritation response that would justify a classification as R38 (2). Concentrated solutions moderately irritating (2).
At active levels larger than 80 % EQ might produce moderate eye irritation (2).

Skin sensitisation: Not sensitising (2).

Dermal absorption (per substance)

INCI name	Value in % or mg/cm2	Comments / reasoning	Reference
Dihydrogenated Palmoylethyl	2 %	Large molecule, rounded value by	(2)

Hydroxyethylmonium Methosulfate		analogy to other esterquats	

Repeated toxicity: 90-day study with SD rats, 10/10 per group, 0, 100, 300, 1000; oral (gavage) with EQ with CAS No 93334-15-7. NOEL 300 mg/kg bw/day (2).

Mutagenicity/Genotoxicity: Not mutagenic or genotoxic both *in vitro* and *in vivo* data (2).

Carcinogenicity: No data. Acceptable as a full battery of genotoxiticity test is negative.

Reproductive toxicity: Not embryotoxic or teratogenic (2) No further data on reproduction (2).

Toxicokinetics: EQ are absorbed through the skin between 0.2 and 2 % (2).

Phototoxicity: No data. Acceptable, as Dihydrogenated Palmoylethyl Hydroxyethylmonium Methosulfate is not presumed to absorb light.

Human data: The exposure to EQ in concentrations up to 10% resulted in only mild and transient dermal irritation (2).

Others: No data.

NOAEL to use for MoS calculation (per substance)

INCI name	NOAEL (mg/kg bw/day)	NOAEC inhalation
Dihydrogenated Palmoylethyl Hydroxyethylmonium Methosulfate	300 mg/kg bw/day (value not corrected to 100% purity as purity of the study substance is not known) from a 90-day study with TEA-based EQ 93334-15-7. The oral absorption is estimated to be moderate why the NOAEL is corrected to 150 mg/kg bw/day to correspond to a 50% oral absorption.	No data

Conclusion

It is assessed for this ingredient, belonging to the group esterquats, that the summary of toxicological data is sufficient to consider it a safe cosmetic ingredient. The NOAEL from a 90-day study in rats with the analogue EQ (93334-15-7) is assessed to be acceptable for use in the MoS calculation.

Dihydrogenated Palmoylethyl Hydroxyethylmonium Methosulfate is assessed to be safe for use as a cosmetic ingredient.

Reference list

1. CosIng, European Commission cosmetic database. Search: “Dihydrogenated Palmoylethyl Hydroxyethylmonium Methosulfate” Accessed 2 March 2016.
2. HERA Esterquats Human Health Risk Assessment Report. Edition 1.0. November 2009.
3. Masoumi HRS, Kassim A, Basri M, Abdullah DK and Haron DJ. (2011). Multivariate Optimization in the Biosynthesis of a Triethanolamine (TEA)-Based Esterquat Cationic Surfactant Using an Artificial Neural Network. Molecules, 16, 5538-5549.
4. NICNAS FULL PUBLIC REPORT AE 425/03 (Dioleoylethyl hydroxyethylammonium methosulfate) File No: STD/1258 December 2007.

Toxicological profile for a cosmetic raw material

The assessment is performed according to the European Cosmetics Regulation (EC) No 1223/2009.

Trade name

Not identified.

Supplier

General toxicological profile for demonstration purposes.

Composition

INCI name	Chemical Name	Concentration	CAS No	EC No
Behenoyl PG-Trimonium Chloride	2-Hydroxy-3-[(1-oxodocosyl)oxy]propyltrimethylammonium chloride	100 %	69537-38-8	274-033-6

Impurities[H]

Max 2 % amines, 25 ppb nitrosamines, heavy metals <10ppm and methylene chloride < 1ppm (1). This level of impuities is acceptable.

Function

Antistatic, hair conditioning (2).

Regulatory status

Not restricted in (EC) No 1223/2009.

Physical-chemical properties

Property	Value	Reference
Molecular weight	497 Da	(5)
Description	Cationic surfactant, quaternary ammonium salt, Glycol Trimonium Compound. White to yellowish, waxy solid	(2,5)
Log Pow	5.3	(4)
Water solubility	Partially soluble	(3)

Toxicological data

Acute toxicity: Oral LD_{50} in rats 3700 mg/kg (1). Dermal LD_{50} for rabbits was reported to be 13,000 mg/kg (1).

Corrosivity and irritation: Skin and ocular irritant in concentrate (1).

Skin sensitisation: Not considered a skin sensitiser (1).

Dermal absorption (per substance)

INCI name	Value in % or mg/cm2	Comments / reasoning	Reference
Behenoyl PG-Trimonium Chloride	0.01 %	Large molecule, low oral absorption, similar compounds not absorbed or minimally absorbed	(1)

Repeated toxicity: By analogy from a one-year study in SD rats with cetrimonium bromide, a NOAEL of 10 mg/kg bw/day is set(3).

Mutagenicity/Genotoxicity: Not mutagenic (1).

Carcinogenicity: Not carcinogenic (1).

Reproductive toxicity: By being analog to cetrimonium chloride, the ingredient is not reprotoxic as cetrimonium chloride was found to be non-foetotoxic and non-teratogenic (3) in a dermal test in rabbits, and steartrimonium chloride was found to be non-foetotoxic and non-teratogenic in a dermal test in rats (3).

Toxicokinetics: Low oral absorption in rats 3.5 % (1).

Phototoxicity: No data. Acceptable, as Behenoyl PG-Trimonium Chloride is not presumed to absorb light.

Human data: The irritancy potential of a formulation containing behentrimonium chloride (5.0 %, vehicle not provided) was tested in subjects (n = 51; 5 male and 46 female subjects) using a Finn Chamber applied to the subjects' backs with occlusion for 24 hours; conclusion: not a skin irritant (1).

Others: No data.

NOAEL to use for MoS calculation (per substance)

INCI name	NOAEL (mg/kg bw/day)	NOAEC inhalation
Behenoyl PG-Trimonium Chloride	10 mg/kg bw/day from a one-year study with cetremonium bromide by analogy. The oral absorption is low why the NOAEL is corrected to 5 mg/kg bw/day to correspond to a 50 % oral absorption.	No data

Conclusion

It is assessed for this ingredient, belonging to the group of trimoniums, that the summary of toxicological data is sufficient to consider it a safe cosmetic ingredient. The NOAEL from a one-year study in rats with the analogue cetrimonium bromide is assessed to be acceptable for use in the MoS calculation.

Behenoyl PG-Trimonium Chloride is assessed to be safe for use as a cosmetic ingredient.

Reference list

1. CIR Final report on Safety Assessment of Trimoniums as Used in Cosmetics 2012.
2. CosIng, European Commission cosmetic database. Search: "Behenoyl PG-Trimonium Chloride", date: 24 February 2016.

3. Opinion of the SCCS on Alkyl (C16, C18, C22) trimethylammoniumchloride, other uses than as a preservative, 8 December 2009. http://ec.europa.eu/health/scientific_committees/consumer_safety/docs/sccs_o_012.pdf
4. Arbejdsrapport fra Miljøstyrelsen, 10/2004 Substitution af overflade aktive stoffer i kosmetiske produkter.
5. Technical Data Sheet QUARTAMIN BTC 131 Kao Chemicals GmbH

Toxicological profile for a cosmetic raw material

The assessment is performed according to the European Cosmetics Regulation (EC) No 1223/2009.

Trade name

Phenoxyethanol

Supplier

General toxicological profile for demonstration purposes.

Composition

INCI name	Chemical Name	Concentration	CAS no	EC No
Phenoxyethanol	2-phenoxyethanol	> 99.9 %	122-99-6	204-589-7

Impurities

None relevant cosmetic quality
Phenol <10 ppm, Ethylene oxide <2 ppm

Function

Preservative (1)

Regulatory status

Regulated in (EC) No 1223/2009, V/29.

Physical-chemical properties

Property	value	reference
Molecular weight	138.17	(2)
Description	Oily, slightly viscous liquid	(2)
Log Pow	1.2 at 23 ºC, pH 7	(2)
Water solubility	Soluble	(2)

Toxicological data

Acute toxicity: The rat oral LD50 values in females and males were determined to be 1840 mg/kg bw and 4070 mg/kg bw, respectively (2).

Corrosivity and irritation: Mild skin irritant and eye irritant (2).

Skin sensitisation: Not a skin sensitiser (OECD 406) (2).

Dermal absorption (per substance)

INCI name	Value in % or mg/cm2	Comments / reasoning	reference
Phenoxyethanol	91 %	Measured data for a 0.2% solution + 1SD.	(2)

Repeated toxicity: From an oral 90-day study in rats NOAEL is considered to be 5000 ppm corresponding to 369 mg/kg/day in males and 652 mg/kg/day in females based on effects on red blood cell parameters and the histopathological changes in the kidney and urinary bladder which occurred at doses ≥ 10,000 ppm (3). Based on the lack of treatment-related effects on body weight, organ weights, haematological and clinical chemistries and gross and histopathological examinations in a dermal 90-day study in rabbits, the no-observed-adverse-effect level (NOAEL) for systemic toxicity was concluded to be 500 mg/kg bw/day

under the conditions of this study. To account for the dosing schedule used in this study, the NOAEL should be multiplied by a factor of 5/7 to give an adjusted NOAEL of 357 mg/kg bw/day.

Mutagenicity/Genotoxicity: Not mutagenic or genotoxic (2).

Carcinogenicity: Not carcinogenic in rat and mouse studies (2).

Reproductive toxicity:

From a 2-generation study in mice it can be concluded that fertility was only minimally affected at the highest dose, but evidence of significant toxicity to the offspring was observed when 2-phenoxyethanol was administered at the mid- and high-dose level. For males, a NOAEL of 400 mg/kg bw/day was calculated. For females, the NOAEL was approximately 950 mg/kg bw/day.
Not a developmental toxicant (2).

Toxicokinetic

Data in rats suggest higher systemic availability of 2-phenoxyethanol after dermal exposure than after oral exposure (2). In humans single oral exposure of phenoxyethanol results in rapid first pass metabolism in the liver why oral exposure is not considered relevant to dermal exposure (2).

Phototoxicity

No experimental data available, but human epidemiological data do not suggest that phenoxyethanol is phototoxic or photo allergenic (2).

Human data

Contact sensitisation in humans has been documented but from the available studies, it can be concluded that this is rare. The risk of sensitization is very low (2).

Others

Given the much higher capacity of humans to metabolise 2-phenoxyethanol compared with rabbits, the toxicokinetic default factor of 4.0 can be reduced to 1.0 yielding a minimum Margin of Safety (MoS) of 25 instead of 100 for the safety assessment of 2-phenoxyethanol (2).

NOAEL to use for MoS calculation (per substance)

INCI name	NOAEL (mg/kg bw/day)	NOAEC inhalation
Phenoxyethanol	an adjusted NOAEL of 357 mg/kg bw/day from a 90-day dermal study in rabbits will be used for the MoS calculation (2).	

Conclusion

It is assessed for this ingredient, that the summary of toxicological data is sufficient to consider it a safe cosmetic ingredient. The adjusted NOAEL from a the dermal 90-day study in rabbits is assessed to be acceptable for use in the MoS calculation.

Phenoxyethanol is assessed to be safe for use as a cosmetic ingredient.

Reference list

1. CosIng, European Commission cosmetic database. Search: “Phenoxyethanol” Accessed 28 September 2016.
2. SCCS (Scientific Committee on Consumer Safety), Opinion on Phenoxyethanol, 16 March 2016, SCCS/1575/16

Toxicological profile for a cosmetic raw material

The assessment is performed according to the European Cosmetics Regulation (EC) No 1223/2009.

Trade name

Sodium benzoate

Supplier

General toxicological profile for demonstration purposes.

Composition

INCI name	Chemical Name	Concentration	CAS no	EC No
Sodium benzoate	Sodium benzoate	100 %	532-32-1	208-534-8

Impurities

None relevant cosmetic quality.

Function

Preservative (1).

Regulatory status

Regulated in (EC) No 1223/2009, Annex V/1.

Physical-chemical properties

Property	value	reference
Molecular weight	114.11	(3)
Description	White granules	(2)
Log Pow	-2.269	(2)
Water solubility	Soluble	(3)

Toxicological data

Acute toxicity

Oral LD50 in rats is between 2 100 and 4 070 mg/kg bw as acid (3).

Corrosivity and irritation

Not a skin irritant (3).
Slightly irritating to rabbit eye (3).

Skin sensitisation

Benzoic acid not sensitising in mouse ear swelling test (2).

Dermal absorption (per substance)

INCI name	Value in % or mg/cm2	Comments / reasoning	reference
Sodium benzoate	43 %		(3)

Repeated toxicity

From a 90-day study in rats a NOAEL of 1 300 mg/kg bw for males and females respectively could be established (2).

Mutagenicity/Genotoxicity
No evidence of mutagenic or genotoxic activity for benzoic acid (2). For sodium benzoate not mutagenic in Ames tests, but some positive results occur in *in vitro* chromosome aberration tests and it cannot be ruled out that sodium benzoate is genotoxic in vitro (3).

Carcinogenicity
No carcinogenic effects from sodium benzoate in rat and mouse studies (2).

Reproductive toxicity
In a 4-generation reproduction toxicity test in rats with benzoic acid given by gavage, the NOAEL for all endpoints was 500 mg/kg bw/day (2).

Toxicokinetic
Extensive oral absorption (3).

Phototoxicity
Benzoic acid absorbs UV light below 300 nm. Benzyl benzoate produced no photoirritation or phototoxicity after 3 irradiations, a slight phototoxicity after 4 irradiations (2).

Human data
Sodium Benzoate showed positive allergenicity reactions in 1.9% of 465 selected patients (2).

Others
Extrapolation of data from benzoic acid to sodium benzoate and vice versa is considered acceptable since the relevant moiety is the benzoic anion, and re-dissociation to benzoic acid can be expected.

NOAEL to use for MoS calculation (per substance)

INCI name	NOAEL (mg/kg bw/day)	NOAEC inhalation
Sodium benzoate	A NOAEL of 500 mg/kg bw from the four-generation reproductive toxicity study in rats with benzoic acid can be used to calculate the MoS.	

Conclusion
It is assessed for this ingredient, Sodium benzoate that is allowed as a preservative in up to 2.5% (acid) in cosmetic rinse-off products and in up to 0.5 % in leave-on products and up to 1.7 % in oral care products, that the summary of toxicological data is sufficient to consider it a safe cosmetic ingredient. The NOAEL from a four-generation reproductive toxicity study in rats with benzoic acid is assessed to be an acceptable NOAEL for use in the MoS calculation.

Sodium benzoate is assessed to be safe for use as a cosmetic ingredient.

Reference list

1. CosIng, European Commission cosmetic database. Search: “Sodium benzoate” Accessed October 2016.
2. CIR Amended Final Safety Assessment Benzyl Alcohol, and Benzoic Acid and its Salts and Benzyl Ester October 17, 2011
3. SCCNFP/0532/01, final OPINION OF THE SCIENTIFIC COMMITTEE ON COSMETIC PRODUCTS AND NON-FOOD PRODUCTS INTENDED FOR CONSUMERS CONCERNING BENZOIC ACID AND SODIUM BENZOATE adopted by the SCCNFP during the 20th plenary meeting of 4 June 2002.

Appendix F – User test

Product name:	**Dhiva Shampoo**	**Product number in the database:**	
Company name:	**Dhiva Cosmetics**	**Version:**	**1**
Formula number:		**Date:**	**October 2016**

Below is a brief description of the user test for the product Dhiva Shampoo. This product is a fictive product for demonstration purposes with no actual claims and therefore no label is available.

A safety-in-use test on Dhiva Shampoo has been performed. The user acceptance and dermal tolerance of Dhiva Shampoo were tested in a 4-week application test in accordance with international guidelines. The application test was carried out on 50 volunteers (30 adults and 20 children aged between 10 years and 18 years). The shampoo was used for hairwash and body wash at least 3-4 times weekly. During the test and at the end of the test period, none of the subjects showed any skin or scalp reaction to the test product or showed any skin disorders. The User Test on the Dhiva Shampoo had a favourable acceptance by the users and did not indicate any potential for dermal irritation.

Conducted in Denmark with 50 participants, Dec. 2015-Jan. 2016. See PIF for full study report (fictive report).

Document signed by R&D Team