Cosmetic Product Safety Report

Product name:	**Dhiva baby body lotion**		
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 baby body lotion (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 claims 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 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: **(See MoS calculation in 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 baby body lotion** 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: **Warnings and instructions of use: "Keep out of reach of children. For external use only".**

Further labelled warnings and instructions of use are not needed as the product labelling and the general description of the product is sufficient to define the use of the product as a **Baby body lotion** for daily use.

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 baby body lotion 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. Some ingredients are irritating undiluted. These ingredients are used in low concentrations and a user test has shown that the final formula is non-irritating.

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

Normal and reasonably foreseeable use

The labelling as Baby body lotion 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 Notes of Guidance for the testing of cosmetic ingredients and their safety evaluation, 9th revision 2015"(see **Error! Reference source not found.**).
As this is a baby body lotion for use on the whole body with intact skin one time per day, and as we have calculated the MoS for a newborn baby, it is considered not to be necessary to increase any of the safety factors.

Toxicological profile of the substances

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

Concerning the safety of the ingredients for babies <3 years of age, the following parameters were taken into account for the safety assessment:
a) the type of cosmetic product,
b) the pH-value of the cosmetic product, if applicable,
c) the conditions for use of the cosmetic product,
d) the level of exposure to the ingredient,
e) the permissible maximum concentration of the assessed ingredient, and
f) possible indications, directions, and/or warnings due to the toxicological profile of single 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 C.
No specific fragrance has been added to 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 baby body lotion did not indicate any potential for dermal irritation. The dermal tolerance of Dhiva baby body lotion was tested by a 4-week application test in accordance with international guidelines. The application test was carried out on 50 volunteers (20 adults and 30 babies/children aged between 6 months and 3 years). The lotion was used for skin care at least once daily. 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.

[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 cream 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 cream used.*

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).

Appendix A – Quantitative and qualitative composition of the cosmetic product

Composition of Dhiva baby body lotion

INCI name of ingredient	Content in %	Function on product
Aqua	85.07	Solvent
Isopropylpalmitate	3.72	Emollient
Glycerin	3.506	Humectant
Paraffinum Liquidum	3.05	Emollient
Stearyl Alcohol	1.4	Emollient
Behenyl alcohol	0.7	Emollient
Dimethicone	0.52	Skin conditioner
Carbomer	0.5	Thickener
Phenoxyethanol	0.4	Preservative
Sodium benzoate	0.25	Preservative
Hydrogenated Palm Glycerides	0.24	Emulsifier
Potassium Cetyl Phosphate	0.24	Emulsifier
Beheneth-25	0.15	Emulsifier
Disodium EDTA	0.1	Chelating agent
Bisabolol	0.1	Skin conditioner
Polysorbat 80	0.05	Thickener
Tocopherol	0.004	Antioxidant
Total:	**100.00**	

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

Appendix B - Stability summary

Product name:	**Dhiva Baby body lotion**	**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 conducted under 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

This part 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 the stability protocol for baby lotion. For this product, an accelerated storage at 40°C for 1 and 3 months has been applied. Samples of this product will also be stored for long term testing.

Appearance / colour / odour
Dhiva baby body lotion is a white lotion without specifically added perfume.
After 1 and 3 months of accelerated storage at 40°C, the Dhiva baby body lotion routine production batch 1/2015 in packaging 300 ml (HDPE) bottle (appearance / odour / colour) complies.

pH
The pH values of routine production batch 1/2015 during the stability testing complies with the current specifications of time of production and shelf life.

pH range remains the same (5.5 +/- 0.2)

Viscosity
The viscosity values of routine production batch 1/2015 during the stability testing conform to the current specifications at the time of production and shelf life.
Viscosity T0 (physica, 45 1/s) : 2000 mPas +/- 500 mPas
Viscosity Shelf life (physica, 45 1/s) : 2000 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 testing should simulate the intensity to which the cosmetics will likely be exposed. All these tests are compliant (normally enclosed).

Microbiological stability summary[D]

Dhiva baby body lotion is classified in Category 1: Products specifically intended for children under 3 years, to be used in the eye area and on mucous membranes (EC No 1223/2009). It is generally accepted that for

[D] *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]*

cosmetics classified in Category 1, the total viable count for aerobic mesophyllic microorganisms should not exceed 10^2 cfu/g or 10^2 cfu/ml of the product (cfu = colony forming unit). Microbiological testing of each batch after filling of Dhiva baby body lotion conforms to category 1 requirements.

Dhiva baby body lotion is a waterbased lotion 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. A challenge test has been performed to test the efficacy of the preservation of this product. Data from the challenge testing of the product conform to specifications/passed for all endpoints, see Challenge test report No. 16/000000601 (**Appendix G – Challenge test report No. 16/000000601**).

Chemical stability[E]

Dhiva baby body lotion is a waterbased lotion preserved with phenoxyethanol and sodium benzoate. The levels of phenoxyethanol and sodium benzoate were 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 300 ml bottle = HDPE, cap/lid = 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 of the product.

Conclusion

The Dhiva baby body lotion is considered compliant and acceptable for consumers based on the tests of the accelerated stability program in 300 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 month and the period after opening is 12 months.

Signed by Head of lab

[E] *Tip: If you use preservatives, check with a chemical analysis that the amount of preservative in your product is according to recipe also at end of shelf life.*

[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 Baby body lotion

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, 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 data for the use on the entire body of a child below the age of 3.

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 baby **K**:	3.4 kg [1, 3]
Way of exposure:	Dermal [2]
Kind of exposure:	Leave-on-product [2]
Quantity per application **G**:	1.1 [3]
Quantity per skin surface area $\mathbf{G_A}$:	0.5 mg/cm^2 (from adult data in ref 2, 7.82g/15670cm^2)
Frequency of Application **F**:	1 [3]
Surface area per application **A**:	2200 cm^2 [1]
Retention factor **R**:	1 [2]
Percutaneous permeation **P**:	Not applicable here as Mos is calculated per ingredient, see each toxprofile

Dermal exposure (Edermal)

$$\mathbf{E_{dermal} = (G_A * A * F * R) / K}$$

$$= (0.5 * 2200 * 1 * 1) / 3.4$$

$$\mathbf{= 323.5\ mg/kg\ bw/d}$$

Reference

1. Body surface area calculator http://www.cato.eu/body-surface-area-children-1.html
2. The SCCS Notes of Guidance for the testing of cosmetic ingredients and their safety evaluation. 9th Revision, September 2015.
3. Internal usage data

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.

$$P = Dermal\ absorption\ fraction$$

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

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

It is generally accepted that Margin of Safety (MoS) should, at least, be 100 to declare an ingredient safe for use (1).

This product is a baby body lotion for use on the entire body one time per day. The calculated MoS is performed for a newborn baby. Thus, it has not been seen necessary to increase the MoS. In general, there is no need for an additional uncertainty factor for children when intact skin is involved (1).

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

Product name:	Dhiva baby bodylotion	Ederm [mg/kg/d]=	323,5
Formula number:	Fictional product	Baby body lotion	
Product number:			

INCI ingredient	Conc [%]	P	NOAEL [mg/kg/d]	Info	SED [mg/kg/d]	Margin of Safety
Aqua	85,07000		n.r.	n.r.		>100
Paraffinum Liquidum	3,05	0,001	600	*	0,00986675	60810
Glycerin	3,506	0,8	10000	*	9,073528	1102
Isopropylpalmitate	3,72	0,1	1000	*	1,20342	831
Hydrogenated Palm Glycerides	0,24	0,1	7500	*	0,07764	96600
Potassium Cetyl Phosphate	0,24	0,03	800	*	0,023292	34347
Disodium EDTA	0,1	0,00001	250	*	0,000003235	77279753
Phenoxyethanol	0,4	1	357	**	1,294	276
Sodium benzoate	0,25	0,43	500	***	0,3477625	1438
Carbomer	0,5	0,01	1500	*	0,016175	92736
Dimethicone	0,52	0,01	500	****	0,016822	29723
Stearyl Alcohol	1,40	0,1	500	****	0,4529	1104
Polysorbat 80	0,050	0,01	1000	*	0,0016175	618238
Bisabolol	0,100	1	850	*	0,3235	2628
Behenyl alcohol	0,70	0,1	500	*	0,22645	2208
Beheneth-25	0,15	0,02	400	****	0,009705	41216
Tocopherol	0,004	1	125	*	0,01294	9660
	100,000					

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

** A new SCCS opinion on Phenoxyethanol, SCCS/1575/16. In summary, SCCS evaluates that Phenoxyethanol up to 1% is safe also for children <3 years even if MoS is below 100 from aggregate exposure.

***: 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

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

Not identified.

Supplier

General toxicological profile for demonstration purposes.

Composition

INCI name	Chemical Name	Concentration	CAS No	EC No
Isopropyl palmitate	Isopropyl palmitate	100 %	142-91-6	205-571-1

Impurities[H]

Major impurity is methyl oleate (3). There is a Ph. Eur. specification for this ingredient that is acceptable for cosmetic use.

Function

Binding, emollient, masking, perfuming (1).

Regulatory status

Not regulated in (EC) No 1223/2009.

Physical-chemical properties[I]

Property	Value	Reference
Molecular weight	298.51 g·mol^{-1}	(2)
Description	Colouless liquid alkyl ester	(2)

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

[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.*

[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 need to be adjusted for ingredients obtained directly from nature as most data are not available for the 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 the batch number.

Property	Value	Reference
Log Pow	8.16	(2)
Water solubility	Insoluble	(2)

Toxicological data

Acute toxicity: LD_{50} in rats >5000 mg/kg bw (2).

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

Skin sensitisation: Not sensitising by analogy to isopropyl myristate (2).

Dermal absorption (per substance)

INCI name	Value in % or mg/cm2	Comments / reasoning	Reference
Isopropyl palmitate	10 %	Large molecule, high log_{pow}. QSAR predicts low dermal penetration	(2)

Repeated toxicity: By analogy a NOAEL of 1000 mg/kg bw/day from a 28-day study in rats with isopropyl myristate (2).

Mutagenicity/Genotoxicity: Not mutagenic in Ames test by analogy with isopropyl myristate (2).

Carcinogenicity: No data. Acceptable, as isopropyl palmitate is expected to be nontoxic in view of the hydrolysis to palmitic acid and to isopropanol. Similar alkylesters are not mutagenic and used as food additives (5)

Reproductive toxicity: Not reprotoxic by analogy to butylmyristate (2).

Toxicokinetics: From a dermal penetration study, most of the isostearyl isostearate was located at the surface of the stratum corneum (3).

Phototoxicity: Not phototoxic (4).

Human data: A total of 235 subjects participated in a 12-week trial where ethyl oleate in a milk-based beverage was given in doses up to 16 g/day without clinically or toxicologically significant negative effects (5).

Others: No data.

NOAEL to use for MoS calculation (per substance)

INCI name	NOAEL (mg/kg bw/day)	NOAEC inhalation
Isopropyl palmitate	1000 mg/kg bw/day by analogy to isopropyl myristate	No data

Conclusion

It is assessed for this ingredient (assessed by CIR in a group assessment of alkylesters), that the summary of toxicological data on the group and on the actual isopropyl palmitate is enough to consider it a safe cosmetic ingredient. The NOAEL from the analogue isoprolyl myristate is assessed to be an acceptable replacement for use in the MoS calculation.

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

Reference list

1. CosIng, European Commission cosmetic database. Search: “Isopropyl palmitate” Accessed 7 March 2016.
2. REACH dossier Isopropyl palmitate.
3. CIR Re-review of Alkyl esters 2012.
4. Final Report on the Safety Assessment of Octyl Palmitate, Cetyl Palmitate and Isopropyl Palmitate. 1982. International Journal of Toxicology vol. 1 no. 2 13-35.
5. Bookstaff, R.C. et al. (2003) The safety of the use of ethyl oleate in food is supported by metabolism data in rats and clinical safety data in humans. Regul Toxicol Pharmacol.; 37(1):133-48.

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[I]

Property	Value	Reference
Molecular weight	92.09 mg/mol	(2)
Description	Colourless, odourless, sweet tasting alcohol.	(2)
Log Pow	-1.75	(4)
Water solubility	Fully soluble	(4)

Toxicological data

Acute toxicity:

Oral LD_{50} in rats 2530 - 58400 mg/kg (2).

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 (1,2).

Dermal absorption (per substance)

INCI name	Value in % or mg/cm2	Comments / reasoning	Reference
Glycerin	80 %	Low Log Pow and molecular weight. Glycerol has a measured permeability coefficient (Kp) of 1.4e-04 cm/h for full thickness nude mouse skin.	(5)

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 glycerins low Log Pow (-1.75) and molecular weight (92g/mol) and a general 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: Glycerin (50 % in water) was not irritating to subjects with dermatitis (n = 420) when administered for 20-24 h under occlusion (1).

Others: Food additive with an ADI 'not specified' established at the 20th JECFA (1976).

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 (2)	the NOAEC for local irritant effects to the upper respiratory tract is 165 mg/m3 and 662 mg/m3 for systemic effects (2)

Conclusion

It is assessed for this ingredient with low toxicity that the summary of toxicological data is sufficient to consider it a safe cosmetic ingredient. The NOAEL from a 2-year study in rats is assessed to be acceptable 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. CIR 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. REACH dossier glycerol
5. Ackermann, C.; Flynn, G. (1987) Ether-water partitioning and permeability through nude mouse skin in vitro. I. Urea, thiourea, glycerol and glucose. Int. J. Pharmacol. 36:61-66.

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
Paraffinum liquidum	Paraffin oils. Liquid hydro-carbons from petroleum	>99.9 %	8012-95-1 / 8042-47-5	232-384-2/232-455-8

Impurities[H]

Residual Solvents and polycyclic aromatic hydrocarbons PAHs should comply with the European Pharmacopoeia. Heavy metals; Arsenic, Lead, Nickel, Cadmium and Mercury, not more than 1 mg/kg each (JECFA, 1995).

Function

Antistatic, emollient, skin protecting, solvent (1).

Regulatory status

Not regulated in (EC) No 1223/2009.

Physical-chemical properties[I]

Property	Value	Reference
Molecular weight	>500 Da	(2)
Description	Clear liquid	(2)
Log Pow	>6	(4)
Water solubility	Insoluble	(4)

Toxicological data

Acute toxicity: LD_{50} >5 g/kg bw (3).

Corrosivity and irritation: Not skin irritating (3). Mild eye irritation from product formulated with 50% paraffin (3).

Skin sensitisation: No data but not likely a sensitiser as dermal absorption is low (see the following section; Dermal absorption)

Dermal absorption (per substance)

INCI name	Value in % or mg/cm2	Comments / reasoning	Reference
Paraffinum liquidum	0.1 %	Chemically inert substance with high molecular weight	(2)

Repeated toxicity: NOAEL 2100 mg/kg bw in a 90-day study in rats with P70 oil, highest dose tested (2). High viscosity (P-100) and Class I medium viscosity (P-70) white oils were tested in a chronic 2-year study in F344 rats. The NOAEL is 1200 mg/kg bw/day, the highest dose tested for both oils (2).

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

Carcinogenicity: Not carcinogenic (2).

Reproductive toxicity: Not reprotoxic or teratogenic by analogy to low viscosity mineral oil (2).

Toxicokinetics: Not likely to be absorbed through the skin (2). Oral absorption 2-3% (2).

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

Human data: A general conclusion from the literature of human mineral oil tissue deposition and concurrent histopathological changes is that none of the investigations have clearly demonstrated any clinical significance due to the pathological changes and presence of oil (2).
Essentially non-irritating and non-sensitising in human dermal tests, both 100% and in formulated products (3).

Others: No data.

NOAEL to use for MoS calculation (per substance)

INCI name	NOAEL (mg/kg bw/day)	NOAEC inhalation
Paraffinum liquidum	1200 mg/kg bw/day from the 2-year carc/chronic study in rats (2). Since the oral absorption is low the NOAEL is corrected for a 50 % oral absorption to 600 mg/kg bw/day.	No data

Conclusion

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

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

Reference list

1. CosIng, European Commission cosmetic database. Search: “Paraffinum liquidum” Accessed 24 February 2016.
2. EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS); Scientific Opinion on the use of high viscosity white mineral oils as a food additive on request from the European Commission. EFSA Journal 2009;7(11):1387. [39 pp.]. doi:10.2903/j.efsa.2009.1387. Available online: www.efsa.europa.eu
3. Cir Published report Paraffin JACT 3(3):43-99, 1984.
4. REACH dossier Paraffin oils

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 toxprofile for demonstration purposes.

Composition

INCI name	Chemical Name	Concentration	CAS No.	EC No
Stearyl alcohol	Octadecan-1-ol (C18)	>98 %	112-92-5	204-017-6

Impurities[H]

Highly lipophilic contaminants, dioxins and PCBs should be monitored.

Function

Emollient, emulsifying, emulsion stabilising, foam boosting, masking, opacifying, refatting, surfactant, viscosity controlling (1).

Regulatory status

Not regulated in (EC) No 1223/2009.

Physical-chemical properties[I]

Property	Value	Reference
Molecular weight	270.5	(2)
Description	Long-chain (C18) aliphatic alcohol, white waxy solid	(2)
Log Pow	7.19	(5)
Water solubility	0.001 mg/L at 25°C, insoluble	(5)

Toxicological data

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

Corrosivity and irritation: Not a skin irritant (2). Not an eye irritant (2).

Skin sensitisation: Not sensitising by analogy to cetyl alcohol (2).

Dermal absorption (per substance)

INCI name	Value in % or mg/cm2	Comments / reasoning	Reference
Stearyl alcohol	10 %	Rounded value by analogy to cetylalchohol (C 14) approx. 1-2 % were absorbed depending on conc. and vehicle	(5)

Repeated toxicity: Oral NOAEL in CD rats >1000 mg/kg bw/day in a 26-week study with behenyl alcohol (3).

Mutagenicity/Genotoxicity: Not mutagenic nor genotoxic (3).

Carcinogenicity: Not carcinogenic (2).

Reproductive toxicity: Not reprotoxic (3, 4).

Toxicokinetics: Stearyl Alcohol is poorly absorbed from the gastrointestinal tract (2).

Phototoxicity: Not phototoxic by analogy to Octyl Dodecanol (2).

Human data: No data.

Others: No data

NOAEL to use for MoS calculation (per substance)

INCI name	NOAEL (mg/kg bw/day)	NOAEC inhalation
Stearyl alcohol	By analogy 1000 mg/kg bw/day from a 6 months study in rats with behenyl alcohol (3). Since the oral absorption is low the NOAEL is corrected for a 50 % oral absorption to 500 mg/kg bw/day.	No data

Conclusion

It is assessed for this ingredient with low toxicity that the summary of toxicological data is sufficient to consider it a safe cosmetic ingredient. The NOAEL by analogy to behenyl alcohol from a 6-month study in rats is assessed to be acceptable for use in the MoS calculation.

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

Reference list

1. CosIng, European Commission cosmetic database. Search: “Stearyl alcohol” Accessed 10 March 2016.
2. CIR Final report on the Safety Assessment of Stearyl Alcohol, Oleyl Alcohol, and Octyl Dodecanol. J. Am. Coll. Toxicol. Vol 4, No 5, 1985.
3. Iglesias G, Hlywka J, Berg JE, Khalil MH, Pope LE and Tamarkin D. The toxicity of behenyl alcohol. I. Genotoxicity and subchronic toxicity in rats and dogs. Regul Toxicol Pharmacol. 2002 Aug;36(1):69-79.
4. SIDS Long chain alcohols 2006.
5. REACH dossier Behenyl alcohol.

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
Behenyl Alcohol	Docosan-1-ol (C22)	72-80 %	661-19-8	211-546-6
Stearyl Alcohol,	Octadecan-1-ol (C18)	20-30 %	112-92-5	204-017-6

Impurities[H]

The highly lipophilic contaminants, dioxins and PCBs, should be monitored.

Function

Binding, emollient, emulsion stabilising, viscosity controlling (1).

Regulatory status

Not regulated in (EC) No 1223/2009.

Physical-chemical properties[I]

Property	Value	Reference
Molecular weight	326.61	(2)
Description	Long-chain (C22) aliphatic alcohol, white waxy solid.	(2)
Log Pow	8.3	(5)
Water solubility	Insoluble <1mg/L	(5)

Toxicological data

Stearyl alkolhol is assessed elsewhere in another toxicological profile.

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

Corrosivity and irritation: Not a skin irritant (2). Not an eye irritant (2).

Skin sensitisation: Not sensitising by analogy to cetyl alcohol (2).

Dermal absorption (per substance)

INCI name	Value in % or mg/cm2	Comments / reasoning	Reference
Behenyl alcohol	10 %	Rounded value by analogy to cetylalchohol (C 14) approx. 1-2 % were absorbed depending on conc. and vehicle	(5)

Repeated toxicity: Oral NOAEL in CD rats >1000 mg/kg bw/day in a 26-week study (3).

Mutagenicity/Genotoxicity: Not mutagenic nor genotoxic (3).

Carcinogenicity: Not carcinogenic (2).

Reproductive toxicity: Not reprotoxic (3, 4).

Toxicokinetics: Stearyl alcohol is poorly absorbed from the gastrointestinal tract (2). It is likely that behenylalcohol is slightly less absorbed than stearyl alcohol as behenylalcohol has a longer carbon chain.

Phototoxicity: Not phototoxic by analogy to Octyl Dodecanol (6).

Human data: No data.

Others: Of vegetable origin (rapeseed).

NOAEL to use for MoS calculation (per substance)

INCI name	NOAEL (mg/kg bw/day)	NOAEC inhalation
Behenyl alcohol	1000 mg/kg bw/day from a 6 months study in rats (3). Since the oral absorption is low the NOAEL is corrected for a 50 % oral absorption to 500 mg/kg bw/day.	No data

Conclusion

It is assessed for this ingredient with low toxicity that the summary of the toxicological data is sufficient to consider it a safe cosmetic ingredient. The NOAEL from a 6-month study in rats is assessed to be acceptable for use in the MoS calculation.

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

Reference list

1. CosIng, European Commission cosmetic database. Search: “Behenyl alcohol” Accessed 10 March 2016.
2. CIR Final report on the Safety Assessment of ceterayl alcohol, cetyl alcohol, isostearyl alcohol, myristyl alcohol and behenyl alcohol JACT 7(3):359-413, 1988.
3. Iglesias G, Hlywka J, Berg JE, Khalil MH, Pope LE and Tamarkin D. The toxicity of behenyl alcohol. I. Genotoxicity and subchronic toxicity in rats and dogs. Regul Toxicol Pharmacol. 2002 Aug;36(1):69-79.
4. SIDS Long chain alcohols 2006.
5. REACH dossier Behenyl alcohol.
6. CIR Final report on the Safety Assessment of Stearyl Alcohol, Oleyl Alcohol, and Octyl Dodecanol. J. Am. Coll. Toxicol. Vol 4, No 5, 1985.

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
Dimethicone	polymethylsiloxane	100 %	63148-62-9 / 9006-65-9 / 9016-00-6 (1)	613-156-5 / 618-433-4 / 618-493-1

Impurities[H]

- Heavy metals <5ppm (3)
- D4/D5 cyclomethicone <1 % (3)
- octamethylcyclotetrasiloxane < 0.1 % (3)
- Catalyst residues content (Neutralised acidic clay) < 0.05 % (3)

These levels of impurities are considerd acceptable.

Function

Antifoaming, emollient, skin conditioning, skin protecting (1).

Regulatory status

General toxicological profile for demonstration purposes

Physical-chemical properties[I]

Property	Value	Reference
Molecular weight	Depending on degree of polymerisation but usually >1100 Da.	(6)
Description	Fully methylated linear siloxane polymers end-blocked with trimethylsiloxy units. Clear colourless viscous liquid.	(2)
Log Pow	2.86 @ MW 1200 4.25 @ MW 56 000	(6)
Water solubility	Practically insoluble in water	(6)

Toxicological data

Acute toxicity: Not acutely toxic (2).

Corrosivity and irritation: Not skin irritating (2). Eye irritating in 100 % concentration (2).

Skin sensitisation: Not sensitising (2).

Dermal absorption (per substance)

INCI name	Value in % or mg/cm2	Comments / reasoning	Reference
Dimethicone	1 %	Large molecule > or >> than 1000 Da, experimental data	(2,6)

Repeated toxicity: 2 years feeding study in rats, Wacker-Belsil ®DM 100, NOAEL 1000 mg/kg bw/d (3).

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

Carcinogenicity: Not carcinogenic (2).

Reproductive toxicity: Not reprotoxic or teratogenic (2).

Toxicokinetics: Not likely to be absorbed through the skin or through orally exposure (2,6). Experimental data with human skin (Franz cell) show very low dermal absorption, dermal flux rates for 350 cSt PDMS were 0.3 and 2 ng/cm^2/h for abdominal skin and vaginal tissue respectively at infinite dose of 10 mg/cm^2 (6). This study shows that including residual radioactivity as absorbed, less than 0.5 % of the applied dose is absorbed through skin or vaginal tissue (6).

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

Human data: Human Repeated Insult Patch Test (HRIPT) 5 % dimethicone not irritating or sensitising (2).

Others: An ADI of 0-1.5 mg/kg bw was established for polydimethylsiloxane (synonyme: dimethicone) at the 74th meeting of the Joint FAO/WHO Expert Committee on Food Additives in 2011 (4, 5).

NOAEL to use for MoS calculation (per substance)

INCI name	NOAEL (mg/kg bw/day)	NOAEC inhalation
Dimethicone	1000, from a 2-year study in rats (3). Since the oral absorption is low the NOAEL is corrected for a 50 % oral absorption to 500 mg/kg bw/day.	No data

Conclusion

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

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

Reference list

1. CosIng, European Commission cosmetic database. Search: “Dimethicone” Accessed 24 February 2016.
2. CIR Final report on the Safety Assessment of Final report on the safety assessment of stearoxy dimethicone, dimethicone, methicone, amino bispropyl dimethicone, aminopropyl dimethicone, amodimethicone, amodimethicone hydroxystearate, behenoxy dimethicone, C24-28 alkyl methicone, C30-45 alkyl methicone, C30-45 alkyl dimethicone, cetearyl methicone, cetyl dimethicone, dimethoxysilyl ethylenediaminopropyl dimethicone, hexyl methicone, hydroxypropyldimethicone, stearamidopropyl dimethicone, stearyl dimethicone, stearyl methicone, and vinyldimethicone. Int J Toxicol. 2003;22 Suppl 2:11-35.
3. Product dossier Product Name: Wacker-Belsil DM fluids 5-1 000 000. Version 2.3 14.02.06.
4. WHO, 2009. Safety evaluation of certain food additives. Prepared by the 69th meeting of the Joint FAO/WHO Expert Committee on Food Additives (JECFA). WHO Food Additives Series 60. p 165-183.
5. FAO, 2011. Specification monograph 11 for polydimethylsiloxane. JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES Seventy-fourth meeting Rome, 14–23 June 2011. http://www.fao.org/3/a-at873e.pdf.
6. ECETOC Linear polydimethylsiloxanes CAS 63148-62-9 Second Ed. JACC No 55. Brussel 2011.

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
Carbomer	2-Propenoic acid, polymer with 2,2-bis(hydroxymethyl)propane-1,3-diol 2-propenyl ether	100 %	9007-20-9 / 9003-01-4 /54182-57-9 / 76050-42-5 / 9062-04-8 / 9007-16-3 / 9007-17-4	618-435-5/618-347-7 /611-106-7/ 616-286-0/ 618-594-0

Impurities[H]

Free acrylic acid (0.25 %); benzene (2 mg/mL); sulfated ash(4 %);heavy metals (20 mg/mL) are acceptable according to Ph.Eur.

Function

Emulsion stabilising, gel forming, viscosity controlling (3).

Regulatory status

Not regulated in (EC) No 1223/2009.

Physical-chemical properties[I]

Property	Value	Reference
Molecular weight	1-4 mio Da varying depending on polymerisation.	(4)
Description	Synthetic, high molecular weight, nonlinear polymers of acrylic acid, cross-linked with a polyalkenyl polyether. White fluffy powder or neutralised as liquid.	(2)
Log Pow	No data	
Water solubility	Not soluble in water	(4)

Toxicological data

Acute toxicity: Carbomer-910, 30 % w/v susp. in corn oil given to a total of 16 albino rats resulted in a LD_{50} of 10.250 ±1.203 g/kg bw (2).

Corrosivity and irritation: Carbomer-934 two samples of 100 % solution gave primary irritation scores in a Draize test for both samples of 0.2, indicating minimal irritation (2).
Eye irritation: Since Carbomers are hydroscopic gel-forming polymers, they are expected to draw out water from the eye tissue in such a way that it results in some irritation (2). 100 % carbomer is irritating to eyes and 0.5 % water solution is a mild irritant (2).

Skin sensitisation: No data. Acceptable as Hript data show low sensitising ability (2).

Dermal absorption (per substance)

INCI name	Value in % or mg/cm2	Comments / reasoning	Reference
Carbomer	<1 %	Large molecule, low absorption after oral exposure	(2)

Repeated toxicity: From an oral feeding study of a crosslinked, high-molecular-weight polyacrylate polymer (PA) following exposure to either 0, 300, 1000, or 3000 mg PA/kg/day for 93 days no adverse histopathology, hematology, body weight, or clinical chemistry effects were seen in rats. NOAEL 3000 mg/kg bw/day (2).

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

Carcinogenicity: Not carcinogenic (4).

Reproductive toxicity: No data. Mating results from chronic dog study, no effects were observed in the puppies (4). Acceptable as both oral and dermal absorption is low (2).

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

Phototoxicity: Not phototoxic (2).

Human data: HRIPT and other studies show low irritant and sensitising ability (2). Human studies show that carbomers are unlikely to present a risk of phototoxicity under conditions of normal intended use (2).

Others: No data.

NOAEL to use for MoS calculation (per substance)

INCI name	NOAEL (mg/kg bw/day)	NOAEC inhalation
Carbomer	3000 from the 90-day study in rats (1). Since the oral absorption is low the NOAEL is corrected for a 50 % oral absorption to 1500 mg/kg bw/day.	No data

Conclusion

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

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

Reference list

1. Lindenschmidt RC et al; Fundam Appl Toxicol 17 (1): 128-35 (1991).
2. CIR Final report on Carbomers -934, -910, -934P, -940, -941, and -962. JACT 1(2):109-141, 1982.
3. CosIng, European Commission cosmetic database. Search: "Carbomer", date: 22 February 2016.
4. HSDB Carbomer, accessed 22 February 2016: http://toxnet.nlm.nih.gov/cgi-bin/sis/search/a?dbs+hsdb:@term+@DOCNO+7826

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
Hydroxygenated palm glycerides	N.A.	100 %	91744-66-0	294-631-0

Impurities[H]

Residual solvents, heavy metals, PAHs and organochlorine pesticides should be monitored (2, 3).

Function

Emollient, skin conditioning, viscosity controlling, emulsifying (1).

Regulatory status

Not regulated in (EC) No 1223/2009.

Physical-chemical properties[I]

Property	Value	Reference
Molecular weight	Average for palm oil 837 g/mol based on the known fatty acid composition of palm oil	(6)
Description	Glycerides, palm-oil mono-, di- and tri-, hydrogenated. Solid at room temperatur. Not soluble in water	(1)

Toxicological data

Acute toxicity: LD_{50} Rat: > 18 g/kg b.w. (IUCLID, 2000 palm oil) (2).

Corrosivity and irritation: Not a skin irritant (2, 3). Not an eye irritant (2, 3).

Skin sensitisation: Not sensitising in Guinea pig maximization test (GPMT) (3).

Dermal absorption (per substance)

INCI name	Value in % or mg/cm2	Comments / reasoning	Reference
Hydroxygenated palm glycerides	10 %	By analogy to vegetable oil	(5)

Repeated toxicity: Up to 15 % palm oil both crude and heated in the diet produced no effects in rats in a 90-day study (3). NOAEL is approx. 7500 mg/kg bw/day (4).

Mutagenicity/Genotoxicity: Not mutagenic or clastogenic by analogy to palm oil (2).

Carcinogenicity: Not carcinogenic (2).

Reproductive toxicity: Not reprotoxic (2).

Toxicokinetics: Dermal absorption set at 10 % by analogy to other vegetable oils (5).

Phototoxicity: Not phototoxic (3).

Human data: Not irritating and not sensitising in RIPT and other tests (3).

Others: No data.

NOAEL to use for MoS calculation (per substance)

INCI name	NOAEL (mg/kg bw/day)	NOAEC inhalation
Hydroxygenated palm glycerides	7500 mg/kg bw/day from a 90-day study in rats with palm oil (3)	No data

Conclusion

It is assessed for this ingredient with low toxicity 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 palm oil is assessed to be acceptable for use in the MoS calculation.

Hydroxygenated palm glycerides is assessed to be safe for use as a cosmetic ingredient.

Reference list

1. CosIng, European Commission cosmetic database. Search: “Hydroxygenated palm glycerides” Accessed 7 March 2016.
2. CIR Final report of Plant-Derived Fatty Acid Oils as Used in Cosmetics 2011.
3. CIR Published report on Elaeis Guineensis (Palm) Oil IJT 19(S2):7-28, 2000.
4. Food additives Guidelines for the preparation of toxicological working papers for the Joint FAO/WHO Expert Committee on Food Additives Geneva, December 2000.
5. Lee EJ, Gibson RA, Simmer K. (1993) Transcutaneous application of oil and prevention of essential fatty acid deficiency in preterm infants. Arch Dis Child 68:27-8.
6. Baroutian S et al. 2009. RBD Palm olein-based methyl/ethyl esters. Journal of Oil Palm Research Vol. 21 December 2009 p. 659-666.

Toxicological profile for a cosmetic raw material

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

Trade name

Amphisol K., AakoEmu PCP

Supplier

General toxicological profile for demonstration purposes.

Composition

INCI name	Chemical Name	Concentration	CAS No.	EC No
Potassium cetyl phosphate	1-Hexadecanol, dihydrogen phosphate, monopotassium salt	100 %	19035-79-1, 84861-79-0	242-768-1, 284-374-2

Impurities[HJ]

Data to be requested from supplier. Published data not available.

Function

Emulsifying, surfactant (1).

Regulatory status

Not regulated in (EC) No 1223/2009.

Physical-chemical properties[I]

Property	Value	Reference
Molecular weight	360.4	(3)
Description	Anionic O/W emulsifier, White to off-white powder or flakes	(3)
Log Pow	No data	
Water solubility	Soluble in hot water	(3)

Toxicological data

Acute toxicity: LD_{50} in rats >5000 mg/kg bw (2).

Corrosivity and irritation: Not irritating to skin (2). Corrosive to eyes in 100 % conc. (2).

Skin sensitisation: Not sensitising (2).

Dermal absorption (per substance)

INCI name	Value in % or mg/cm2	Comments / reasoning	Reference
Potassium cetyl phosphate	3 % For MoS calculation a rounded value of 10 % will be used	Read across from 36653-82-4 cetylalcohol	(2)

[J] *For a detailed impurity profile, batch data from supplier needed. As this is a fictive product, these data are not available. For traces of forbidden substances, safe limits should be established and included into the ingredient's specifications included in the PIF.*

Repeated toxicity: NOAEL 800 mg/kg bw/day in a 90-day study in rats (2).

Mutagenicity/Genotoxicity: Not mutagenic in Ames test, in a mammalian cell gene mutation assay and chromosom aberration study (2).

Carcinogenicity: No data. Acceptable as substance is not mutagenic.

Reproductive toxicity: Not reprotoxic by analogy to potassium C9-15 alkyl phosphate and C20-22 alkyl phosphate (4).

Toxicokinetics: By analogy, phosphoric acid, 2- ethylhexyl ester was efficiently absorbed, metabolized, and excreted quantitatively by the body after oral intake in rats (4).

Phototoxicity: Not photoallergenic (5).

Human data: By analogy, HRIPT with C20-22 alkyl phosphate 5 % in an emulsion (emulsion not defined) tested on 49 subjects was not an irritant or a sensitiser (4)

Others: No data.

NOAEL to use for MoS calculation (per substance)

INCI name	NOAEL (mg/kg bw/day)	NOAEC inhalation
Potassium cetyl phosphate	800 from the 90-day study in rats (2)	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 a 90-day study in rats is assessed to be acceptable for the use in the MoS calculation.

Potassium cetyl phosphate is assessed to be safe for use as a cosmetic ingredient.

Reference list

1. CosIng, European Commission cosmetic database. Search: “Potassium cetyl phosphate”, accessed 7 March 2016.
2. REACH dossier Potassium cetyl phosphate; accessed 7 March 2016
3. Technical data sheet Potassium cetyl phosphate AakoEmu PCP
4. CIR Safety Assessment of Alkyl Phosphates as Used in Cosmetics 2015.
5. MSDS Potassium cetyl phosphate M.C.Biotec Inc. Version 2.0 Revision Date 12.30.2010

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
Beheneth-25	Poly(oxy-1,2-ethanediyl), a-docosyl-w-hydroxy	100 %	26636-40-8	607-974-1

Impurities[H]

Residual chemical	Level in the Raw Material
25 mol EO (average molar ratio)	≤ 1ppm
1,4-Dioxane	≤ 1ppm
Polycyclic aromatic hydrocarbons (PAH)	≤ 2µg/kg
Heavy metals (As, Sb, Pb, Cd, Hg and Ni)	≤ 10 ppm

Remark: A MoS calculation must be done for the sum of EO and dioxane in the formulated product if several ingredients (etoxylated) have a similar impurity profile.

Function

Emulsifying, cleansing, surfactant (1).

Regulatory status

Not regulated in (EC) No 1223/2009.

Physical-chemical properties[I]

Property	Value	Reference
Molecular weight	1427.91	(2)
Description	Docosanol, ethoxylated, 20 mol EO (average molar ratio), white solid	(2)
Log Pow	No data available, log Pow is difficult to measure for surfactants, as surfactants will be located preferentially at the interface(s) in an oil/water system	(4)
Water solubility	Emulsifiable but generally insoluble in water	(4)

Toxicological data

Acute toxicity: Acute oral LD_{50} > 2000 mg/kg bw by analogy to Beheneth-10 (3).

Corrosivity and irritation: Not irritating to skin by analogy to Beheneth 10 (3).

Skin sensitisation: By analogy to other alkyl PEG ethers not sensitising in guinea pig tests (2).

Dermal absorption (per substance)

INCI name	Value in % or mg/cm2	Comments / reasoning	Reference
Beheneth-25	2 %	By analogy with other alkyl PEG ethers	(4)

Repeated toxicity: By analogy to PEG Methyl Ether, Subchronic oral toxicity, 90-day study in rats, 400 mg/kg/d (2).

Mutagenicity/Genotoxicity: By analogy to Beheneth-10 not mutagenic in Ames test (2).

Carcinogenicity: By analogy to Laureth-9 not carcinogenic (2).

Reproductive toxicity: By analogy to Laureth-9 not reprotoxic (2).

Toxicokinetics: Oral absorption >75 % (4).

Phototoxicity: No data on alkyl PEG but the similar structure alkyl PPG ethers are not phototoxic (2).

Human data: HRIPT not sensitising (4).

Others: Beheneth-25 is an alkyl PEG ether like Beheneth-2, Beheneth-5, Beheneth-10, Beheneth-15, Beheneth-20 and Beheneth-30 (3). The CIR Expert Panel describes all alkyl PEG ethers to have fundamental similarities which allow results on these to be extrapolated to the others (2).

NOAEL to use for MoS calculation (per substance)

INCI name	NOAEL (mg/kg bw/day)	NOAEC inhalation
Beheneth-25	400 mg/kg bw/day from the 90-day study in rats by analogy from PEG-3 Methyl ethers (2)	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 by analogy from a 90-day study in rats is assessed to be acceptable for use in the MoS calculation.

Behenth-25 is assessed to be safe for use as a cosmetic ingredient.

Reference list

1. CosIng, European Commission cosmetic database. Search: “Beheneth-25” Accessed March 10 2016.
2. CIR Expert panel meeting on Alkyl PEG Ether 2010 and Safety Assessment of Alkyl PEG/PPG Ethers as Used in Cosmetics
3. Safety Data Sheet according to (EC) No 1907/2006 SDS No: 39352 revised 2009. Cognis France.
4. HERA Risk assessment of Alcohol Ethoxylates 2009.

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
Disodium EDTA	Disodium salt of N,N'-1,2-Ethanediylbis[N-(carboxymethyl)glycine]; disodium dihydrogen ethylenediaminetetraacetate; disodium dihydrogen (ethylene-dinitrilo)-tetraacetate	>99 %	139-33-3	205-358-3

Impurities[H]

Impurities of significance not expected but heavy metals should be monitored. CIR notes a general level of <10 ppm heavy metals and less than <100 ppm of formaldehyde in disodium EDTA of cosmetic grade (2).

Function

Chelating agent (1).

Regulatory status

Not regulated in (EC) No 1223/2009.

Physical-chemical properties[I]

Property	Value	Reference
Molecular weight	372.24	(3)
Description	substituted diamine, white powder.	(2)
Log Pow	log Kow = -11.70 (est).	(6)
Water solubility	Soluble	(6)

Toxicological data

Acute toxicity: LD_{50} in rats 2800 mg/kg bw (4).

Corrosivity and irritation: Not a skin irritant (2). Not eye irritating (4).

Skin sensitisation: Not sensitising by analogy to Na_3EDTA (4).

Dermal absorption (per substance)

INCI name	Value in % or mg/cm2	Comments / reasoning	Reference
Disodium EDTA	0.001 %		(2,3)

Repeated toxicity: In a two-year study with rats, 0.5 % disodium EDTA caused no effects, NOAEL was 250 mg/kg b/day (3).

Mutagenicity/Genotoxicity: Weakly mutagenic in *in vitro* and *in vivo* studies in high doses probably due to secondary mechanisms (2). Not expected to be mutagenic in humans (5).

Carcinogenicity: Not carcinogenic by analogy to Na_3EDTA (2).

Reproductive toxicity: Oral exposures to EDTA produced reproductive/developmental toxicity in test animals at doses >1000 mg/kg bw/day presumably due to zinc depletion (2). Not likely to produce reprotoxic effects after dermal dosing (5).

Toxicokinetics: Not likely to be absorbed through the skin but might act as a penetration enhancer (2). Oral absorption in rats <3 % (3).

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

Human data: A maximum of 5 % is absorbed orally (2).

Others: An ADI of 0-2.5 mg/kg bw was established at the 17th JECFA (1973) (3).

NOAEL to use for MoS calculation (per substance)

INCI name	NOAEL (mg/kg bw/day)	NOAEC inhalation
Disodium EDTA	250 from a 2-year study in rats (3)	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 a 2-year study in rats is assessed to be acceptable for use in the MoS calculation.

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

Reference list

1. CosIng, European Commission cosmetic database. Search: “Disodium EDTA” Accessed 24 February 2016.
2. Final Report on the safety assessment of EDTA, Calcium Disodium EDTA, Diammonium EDTA, Dipotassium EDTA, Disodium EDTA, TEA-EDTA, Tetrasodium EDTA, Tripotassium EDTA, Trisodium EDTA, HEDTA, and Trisodium HEDTA. Int J Toxicol 21 (Suppl. 2), 2002.
3. Seventeenth Report of the Joint FAO/WHO Expert Committee on Food Additives, Wld Hlth Org. techn. Rep. Ser., 1974, No. 539; FAO Nutrition Meetings Report Series, 1974, No. 53. ETHYLENEDIAMINETETRAACETATE, DISODIUM AND CALCIUM DISODIUM SALTS.
4. REACH dossier http://echa.europa.eu/registration-dossier/-/registered-dossier/14817/7/3/2.
5. SCIENTIFIC COMMITTEE ON TOXICITY, ECOTOXICITY AND THE ENVIRONMENT (CSTEE) Opinion on the results of the Risk Assessment of: TETRASODIUM ETHYLENEDIAMINE TETRAACETATE (NA_4EDTA) CAS N° : 64-02-8 AND EDETIC ACID (EDTA) CAS NO. 60-00-4 HUMAN HEALTH PART (2003).
6. Pubchem Edetate disodium

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 (2)

Eye irritating in 100 % concentration (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 becoming sensitised 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 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 in 100 % concentration (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 (2).	

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.

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
Bisabolol	α,4-Dimethyl-α-(4-Methyl-3-Pentenyl)-3-Cyclohexene-1-Methanol	>93 % isolated from natural source	23089-26-1 / 515-69-5	208-205-9

Impurities[H]

<5 % impurities, <0.5 % of other compounds as bisabolene, bisabolol oxide, farnesol, chemazulene and nerolidol (2) and assessed as safe[K].

Function

Masking, skin conditioning, soothing (1).

Regulatory status

Not regulated in (EC) No 1223/2009.

Physical-chemical properties[I]

Property	Value	Reference
Molecular weight	222.72	(3)
Description	Unsaturated monocyclic sesquiterpene alcohol, clear to yellowish oily liquid with a characteristic odor	(2)

Toxicological data

Acute toxicity: Oral LD_{50} in rats: 14.9 ml/kg in males and 15.6 in female (2). Oral LD_{50} in mice: 15.1 ml/kg (2).

Corrosivity and irritation: Not irritant (2).

Skin sensitisation: Not sensitising (2).

Dermal absorption

INCI name	Value in % or mg/cm2	Comments / reasoning	Reference
Bisabolol	100 %	Default value	

[K] Tip: *For a detailed impurity profile, batch data from supplier needed. As this is a fictive product, these data are not available.*

Repeated toxicity: Subacute dermal toxicity (28d, rat), NOAEL 200 mg/kg/d (2). 6-week gavage study in Wistar rats NOAEL 850 mg/kg bw/day, no adverse effects highest dose tested (3).

Mutagenicity/Genotoxicity: Not mutagenicity/genotoxicity (2).

Carcinogenicity: No data. Acceptable as bisabolol is not mutagenic or genotoxic.

Reproductive toxicity: Teratogenicity study in rat, NOAEL 500 mg/kg/d (2).

Toxicokinetics: High dermal absorption, may enhance absorption of other substances (2).

Phototoxicity: Not phototoxic. Not photosensitising (2).

Human data: In a clinical study, a commercial product containing 0.1 % Bisabolol was negative in a test for sensitisation (2).

Others: No data.

NOAEL to use for MoS calculation (per substance)

INCI name	NOAEL (mg/kg bw/day)	NOAEC inhalation
Bisabolol	850 mg/kg/day, repeated dose study in rats (2)	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 a 6-week study in rats is assessed to be acceptable for use in the MoS calculation.

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

Reference list

1. CosIng, European Commission cosmetic database. Search: "*Bisabolol*" Accessed 24 February 2016.
2. CIR Final report on the Safety Assessment of Bisabolol as used in Cosmetics, 2015.
3. Bhatia SP, McGinty D, Letizia CS, Api AM. Fragrance material review on a-bisabolol. Food and Chemical Toxicology 46 (2008) S72–S76.

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
Polysorbate 80	Sorbitan, mono-9-octadecenoate, poly(oxy-1,2-ethanediyl) derivs., (Z)-	97 %	9005-65-6	500-019-9
Aqua		3 %	7732-18-5	231-791-2

Impurities[H]

The physicochemical behaviours of polysorbate vary markedly from batch to batch due to the inconsistency of the synthetic processes why it is important to have batch data for evaluation of this ingredient. 1.4-dioxane and ethylene oxide are possible impurities according to CIR (2). Both are CMR impurities and if several ingredients contain these impurities a MoS calculation of the sum in the product should be performed.

Function

Denaturant, emulsifying, surfactant (1).

Regulatory status

Not regulated in (EC) No 1223/2009.

Physical-chemical properties[I]

Property	Value	Reference
Molecular weight	6969 Da	(2)
Description	Polymer	(2)
Log Pow	4.51 (QSAR)	(4)
Water solubility	Poorly soluble	(4)

Toxicological data

Acute toxicity: LD_{50} rat >5000 mg/kg bw (2).

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

Skin sensitisation: Not sensitising (2).

Dermal absorption (per substance)

INCI name	Value in % or mg/cm2	Comments / reasoning	Reference
Polysorbate 80	1 %	Large molecule/polymer	(2)

Repeated toxicity: By analogy NOAEL 1000 mg/kg bw/day rat 13-week study with polysorbate 60 (3).

Mutagenicity/Genotoxicity: Not mutagenic in Ames test and in a mouse micronucleus test (2).

Carcinogenicity: Not carcinogenic (3).

Reproductive toxicity: Not reprotoxic or teratogenic (3).

Toxicokinetics: After oral administration the fat moiety hydrolyses in the gut and is fully absorbed as free fatty acid; the sorbitan moiety is excreted unchanged in faeces (2).

Phototoxicity: No data. Acceptable as clinical testing showed little potential for skin sensitisation or phototoxicity (2).

Human data: Clinical skin testing showed Polysorbates to have little potential for human skin irritation or evidence of skin sensitisation or phototoxicity (2).

Others: No data.

NOAEL to use for MoS calculation (per substance)

INCI name	NOAEL (mg/kg bw/day)	NOAEC inhalation
Polysorbate 80	1000, by analogy with polysorbate 60 from a rat 13-week study	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 a 13-week study in rats is assessed to be acceptable for use in the MoS calculation.

Polysorbate 80 is assessed to be safe for use as a cosmetic ingredient.

Reference list

1. CosIng, European Commission cosmetic database. Search: “Polysorbate 80” Accessed 21 March 2016.
2. CIR Final report on the Safety Assessment of Polysorbates as Used in Cosmetics, 2015.
3. Evaluation Report of Food Additives Polysorbates (Polysorbates 20, 60, 65 and 80) June 2007 Food Safety Commission Japan.
4. REACH dossier Sorbitan monooleate, ethoxylated.

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
Tocopherol	3,4-Dihydro-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)-2H-benzopyran-6-ol; .alpha.-tocopherol; Vitamin E	100 %, derived from non-GMO soybean	54-28-4 / 16698-35-4 / 10191-41-0 / 119-13-1 / 1406-18-4 / 1406-66-2 / 2074-53-5 / 59-02-9 /7616-22-0	215-798-8 / 606-803-8 / 604-195-9 / 233-466-0

Impurities[H]

Food grade quality, heavy metals generally monitored (2). Residues of hydroquinone to be controlled by GMP (2). Food grade quality impurity profile acceptable for cosmetic use.

Function

Antioxidant, masking, skin conditioning (1).

Regulatory status

Not regulated in (EC) No 1223/2009.

Physical-chemical properties[I]

Property	Value	Reference
Molecular weight	Approx. 400-430 Da	(2)
Description	Amphiphilic lipids	(2)
Low Pow	12.18 (Epiwin calc)	(5)
Water solubility	1.3 µg/L Insoluble	(4)

Toxicological data

Acute toxicity: Oral LD_{50} in rats >4 g/kg bw (2).

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

Skin sensitisation: Not sensitising (2).

Dermal absorption (per substance)

INCI name	Value in % or mg/cm2	Comments / reasoning	Reference
Tocopherol	100 %	Default	(2)

Repeated toxicity: A NOAEL of 125 mg/kg bw/day RRR-α-tocopheryl acetate from an oral 90-Day study with rats (3).

Mutagenicity/Genotoxicity: Generally not mutagenic or genotoxic (2, 3).

Carcinogenicity: Not carcinogenic (2).

Reproductive toxicity: Not reprotoxic (2).

Toxicokinetics: Oral absorption varies between 20 to 80 % depending on intake (3). Tocopherol is dermally absorbed (2).

Phototoxicity: Not phototoxic (2). Tocopherol, tocopheryl acetate, and tocopheryl succinate absorb in the ultraviolet B (UVB) range. Reported absorption maxima are 292-295 nm (in ethanol) for tocopherol, 284 nm (in ethanol) and 285.5 nm (in cyclohexane) for tocopheryl acetate, and 286 nm (in ethanol) for tocopheryl succinate (2).

Human data: Have photoprotective effect (2).

Others: No data.

NOAEL to use for MoS calculation (per substance)

INCI name	NOAEL (mg/kg bw/day)	NOAEC inhalation
Tocopherol	125 mg/kg bw/day from the 90-day rat study (3). Since the concentration of tocopherol in the product is low (0.004 %) it is not necessary to adjust the NOAEL for oral absorption.	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 a 90-day study in rats is assessed to be acceptable for use in the MoS calculation.

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

Reference list

1. CosIng, European Commission cosmetic database. Search: “Tocopherol” Accessed 10 March 2016.
2. CIR Final report on the Safety Assessment of Tocopherols and Tocotrienols as Used in Cosmetics, 2014.
3. Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of Vitamin E (expressed on 4 April 2003).
4. REACH dossier 3,4-Dihydro-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)-2H-benzopyran-6-ol.
5. REACH dossier Tocopherols.

Appendix F – User test

Product name:	**Dhiva baby body lotion**	**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 baby body lotion. 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 baby body lotion has been performed. The dermal tolerance of Dhiva baby body lotion was tested by a 4-week application test in accordance with international guidelines. The application test was carried out on 50 volunteers (20 adults and 30 babies/children aged between 6 months and 3 years). The lotion was used for skin care at least once daily. During the test and at the end of the test period none of the subjects showed any skin reaction to the test product or showed any skin disorders. The User Test on the Dhiva baby body lotion did not indicate any potential for dermal irritation.

Conducted in Sweden with 50 participants, Dec. 2015-Jan. 2016. See PIF for full study report (fictive study as Dhiva baby body lotion is a fictive product).

Document signed by R&D Team

Appendix G – Challenge test report No. 16/000000601

Challenge test report

Evaluating the antimicrobial efficacy of Dhiva Baby Body lotion

Report No. 16/000000601

Client:
Dhiva Cosmetics
Agern Allé 5
DK-2970 Hørsholm
Denmark

Contact:
Telephone:
Fax:
Email:

Testing Laboratory:
Cosmelab
Agern Allé 5
DK-2970 Hørsholm
Denmark

Contact:
Telephone:
Fax:
Email:

Objectives

The objective of the study is to evaluate the antimicrobial efficacy of a body lotion containing 0.4 % phenoxyethanol and 0.25 % sodium benzoate.

Test method

Anti-microbial preservation efficacy (challenge) test method ISO 11930 - Preservative Challenge Test

Samples

Samples labelled as detailed below was received at the laboratory on 4.04.16 and testing started on 5.04.16 for the product Baby Body lotion containing 0.4 % Phenoxyethanol and 0.25 % Sodium Benzoate

Conclusions

A water based body lotion containing 0.4 % phenoxyethanol and 0.25 % sodium benzoate was tested according to ISO 11930:2012 - Preservative Challenge Test – Antimicrobial preservation efficacy (challenge) test. The results of the test are summarised in the following table.

	Pass/Fail against				
Samples	**Mould**		**Yeast**	**Bacteria**	
	Aspergillus brasiliensis	***Candida albicans***	***Pseudomonas aeruginosa***	***Staphylococcus aureus***	***E. coli***
Baby Body Lotion 0.4 % Phenoxyethanol + 0.25 % Sodium Benzoate	Pass	Pass	Pass	Pass	Pass

Table 1 Challenge Test Results – Total Viable Count

Organism	Description	0 hour	7 days	14 days	28 days
A.brasiliensis	Baby Body Lotion 0.4 % phenoxyethanol + 0.25 % sodium benzoate	5.2×10^5		<20	<20
C.albicans	Baby Body Lotion 0.4 % phenoxyethanol + 0.25 % sodium benzoate	3.2×10^5		<20	<20
Ps.aeruginosa	Baby Body Lotion 0.4 % phenoxyethanol + 0.25 % sodium benzoate	5.1×10^6	<20		<20
S.aureus	Baby Body Lotion 0.4 % phenoxyethanol + 0.25 % sodium benzoate	4.3×10^6	<20		<20
E.coli	Baby Body Lotion 0.4 % phenoxyethanol + 0.25 % sodium benzoate	3.3×10^6	<20		<20

Report Review

The study has been carried out according to ISO 11930 - Preservative Challenge Test. All results have been checked by the responsible person and reviewed by the Laboratory Manager.

Signed by Lab