CONSUMER PRODUCTS SERVICES DIVISION

NANCHANG DENTAL BRIGHT TECHNOLOGY CO LTD

Technical Report: **(8522)077-0126(Revision)** May 31, 2022
Date Received: March 17, 2022

JUSTIN QIN

NANCHANG DENTAL BRIGHT TECHNOLOGY CO LTD
BUILDING 182,JIAHAI INDUSTRY PARK
NO.2799 TIANXIANG AVE
HI-TECH ZONE
NANCHANG, JIANGXI
CHINA

Sample Description:	COLOUR CORRECTOR / TEETH WHITENING COLOUR CORRECTOR / V34 COLOUR CORRECTOR	Vendor:	NANCHANG DENTAL BRIGHT TECHNOLOGY CO LTD
Sample Size:	1DOCUMENT	Manufacturer:	N/A
Style No(s):	N/A	Buyer:	N/A
SKN/SKU No.:	N/A	Labeled Age Grade:	NOT PRESENT
PO No.:	N/A	Appropriate Age Grade:	NOT REQUESTED
Ref #:	N/A	Client Specified Age Grade:	NOT SPECIFIED
Country of Origin:	NO INFORMATION	Tested Age Grade:	N/A
Assortment No.:	N/A	UPC Code:	N/A

EXECUTIVE SUMMARY:

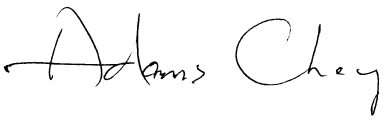
The sample(s) was tested to the following requirement(s) and the data provided is for informational purposes only:

- EC NO.1223/2009 Cosmetic Product Safety Report(CPSR)

Note: The cosmetic Product Safety Report was performed at a subcontract lab, the finding of result was presented in RESULT SECTION.

(*)Note: This report is amendment of and supersedes the previous (8522)077-0126 dated April 08, 2022.

BUREAU VERITAS SHENZHEN CO.,LTD



Choy Hon Kwong, Adams
Deputy Director
Analytical Department

AC/sz

DISCLAIMER OF REGULATORY LIABILITY:

Client fully acknowledges that any product testing performed by Company as part of the Services rendered for this Report is limited to non-release testing, and that Client or any third-party under its control will not under any circumstances use, describe, or represent to any other third party that the Company is performing finished product release, active ingredient release, or any other batch or release testing or final product acceptance testing, or that the Company's Services and/or Report relate in any way to product manufacturing or any quality control process required to be conducted by Client or any contractors of Client by law or regulation, including but not limited to any laws or regulations enforced under the jurisdiction of the U.S. Food and Drug Administration ("FDA")

Bureau Veritas Shenzhen Co., Ltd
1,2,3/F., Block A, 1,4,5/F., Block B, Minlida Industrial Building,
Honghualing Industrial Park, Xili, Nanshan District, Shenzhen,
Guangdong, China.
Tel: 86-755-86185200 Fax: 86-755-86185206
www.bureauveritas.com/cps

Cosmetic Product Safety Assessment

Colour Corrector /Teeth Whitening Colour Corrector /V34 Colour Corrector

PRODUCT DETAILS

Type of Product: Toothpaste - Child (Ficheux et al) | Rinse Off

Physical Form: Liquid, Paste

Client: Bureau Veritas Shenzhen Co., Ltd
1/F, Block A, Minlida Industrial Building, 4th Zone Of Honghualing Industrial Park, Xili Town, Nanshan District, Shenzhen, Guangdong, P.R.C.

Product Reference
BV Order No.: 85220770126

CONCLUSIONS & RECOMMENDATIONS

Required Safety Labelling

Do not swallow
Keep away from eyes. If material accidentally enters the eye, rinse well with plenty of clean water. Seek medical attention if irritation persists.

Overall Safety & Compliance

Under normal or reasonably foreseeable conditions of use, a product made to this formulation is unlikely to produce an abnormally high number of adverse reactions. Assuming the necessary warnings stated in the safety assessment are included on the product packaging it will give consumers the level of safety they can reasonably expect.

This product complies with the requirements of the EU Cosmetic Regulation (EC) No 1223/2009. The product must be manufactured according to Good Manufacturing Practice.

Delphic HSE Solutions (HK) Limited
210, 2/F, 16W, Science Park West Avenue, Hong Kong Science Park, Shatin, Hong Kong
Tel: +852 2657 8373 e-mail: tra-hk@delphichse.com

QUANTITATIVE & QUALITATIVE COMPOSITION

This formulation is an overview of the composition, listing only the chemical name and quantities added.
For full details on the ingredients, including INCI names for cosmetic products, please see Annex I - Raw Material Information.

The Assessment relates only to the formulation as described below. If this information is incorrect, please contact Delphic HSE with the correct information.

Ingredients	CAS Number	[Product]
Glycerin	56-81-5; 8013-25-0	33
Aqua	7732-18-5	27.7
Sorbitol	68425-17-2 (generic); 50-70-4; 98201-93-5; 1259528-21-6 (generic)	25
Hydrated Silica	63231-67-4; 10279-57-9; 1343-98-2; 7631-86-9; 112926-00-8	3
Xylitol	87-99-0	3
Polysorbate 80	9005-65-6	3
Cellulose Gum	9004-32-4; 99331-82-5; 9000-11-7	2.5
Mentha Piperita (Peppermint) Oil	84082-70-2; 8006-90-4	1
Phenoxyethanol	56257-90-0; 37220-49-8; 122-99-6	.5
Sucralose	56038-13-2	.5
Tetrasodium Pyrophosphate	7722-88-5	.5
CI 17200 (D&C Red 33)	3567-66-6	.1
Ethylhexylglycerin	70445-33-9	.1
CI 42090 (FD&C Blue No. 1)	71701-19-4 (K.Na salt); 71701-18-3 (K salt); 2650-18-2 (NH4 salt); 68921-42-6 (Al salt); 15792-67-3 (Al salt); 3844-45-9	.1

PHYSICAL / CHEMICAL CHARACTERISTICS AND STABILITY OF THE COSMETIC PRODUCT

Appearance:	Purple Paste	**Viscosity:**	Not Provided
Odour:	Characteristic	**Water Solubility:**	Not Provided
Melting Point:	Not Provided	**Log Kow:**	Not Provided
pH:	7 - 10	**Particle Size:**	Not Provided
Specific Gravity:	Not Provided		

The physical-chemical data supplied for review suggests it would be unlikely to significantly contribute to the toxicological profile of the product under normal conditions of use.

Product Stability:

A 12-week combined stability and compatibility test was carried out at -5±2℃ and 50±2℃. Any changes in appearance, odour, total bacterial count, pH and packaging appearance were observed. No significant changes were noted during the course of testing and the product has passed the test according to manufacturer criteria.

PHYSICAL / CHEMICAL CHARACTERISTICS OF THE SUBSTANCES OR MIXTURES

The physical-chemical characteristics of the substances and mixtures used within the formulation are continued in Annex I of this document. Such data provided are representative of publicly available data, and is provided for information purposes only.

MICROBIOLOGICAL QUALITY

TVC:	≤100 cfu/g (Under 3, Eye Area, Mucous Membrane)
	≤1000 cfu/g (All other products)
Specific Pathogens:	Absent in test sample
Yeasts & Moulds:	≤10 cfu/g

Based on the documentation provided for review this product meets the recommended microbiological specifications.

Manufacturer/responsible person must ensure that all batches are produced in line with these requirements.

Product underwent a 28-day challenge test in accordance with British Pharmacopoeia (2021), Appendix XVI C. Efficacy of Antimicrobial Preservation to determine the efficacy of its preservative system.

At the completion of testing the product was considered to fulfil the relevant criteria for an item of this nature, and can be considered to be adequately preserved.

Microbiological specifications of the substances and mixtures used within the product have not been reviewed, and will be subject to grade variation dependent upon manufacturer and batch. The Organisation responsible for placing the product on the market must ensure that all raw materials used in production are of a suitable cosmetic grade and would not contribute a microbial risk to consumers.

IMPURITIES, TRACES, INFORMATION ABOUT THE PACKAGING MATERIAL

The below information is a list of impurities & trace materials declared by the manufacturer / responsible person as being present within the product.
If no materials are identified it is understood that no impurities or trace materials have been disclosed to Delphic HSE Solutions at the time of review.

Substances	CAS Number	[Product]

Packaging Material: PET/PP

Details on the grades of material used in packaging manufacture have not been supplied for review, however materials of this nature have a generally good history of safe use. The manufacturer/responsible person must ensure that suitable grades of packaging material are used, and that they will not interact with the product in such a way as to pose a toxicological or microbiological risk to consumers.

Compatibility Testing: A 12-week combined stability and compatibility test was carried out at -5±2℃ and 50±2℃. Any changes in appearance, odour, total bacterial count, pH and packaging appearance were observed. No significant changes were noted during the course of testing and the product has passed the test according to manufacturer criteria.

Product Durability: PAO: 2 years

NORMAL & REASONABLY FORESEEABLE USE

Normal Use:

Toothpaste - Child (Ficheux et al) | Rinse Off

Reasonably Foreseeable Uses:

Manufacturers Instructions for Use:

After whitening teeth, use it every day, squeeze on the toothbrush, then brush on the teeth for two minutes, spit out after use, rinse with water. Keep your teeth bright and white.

EXPOSURE TO THE COSMETIC PRODUCT

Intended Consumer:	Children 12+	Minimum Expected Body Weight	41kg
Single Exposure:	1.647 g | 2 x per Day	Diluted in use:	No
Retention Factor:	0.05	Retained Exposure:	4.017 mg/kg/day

Exposure to Neat Product:

Body Site(s):	Lips; Mouth
Surface Area:	219.8 cm^2
Exposure Level:	0.749 mg/cm^2
Exposure Time:	Washed off after 2 - 3 minute delay

Exposure to Diluted Product: Product Not Diluted in Use

EXPOSURE TO THE SUBSTANCES & TOXICOLOGICAL PROFILE OF THE SUBSTANCES

The toxicological data of the substances and mixtures used within the formulation are continued in Annex II of this document. Such data provided are representative of publicly available data, and is provided for information purposes only.

UNDESIRABLE EFFECTS AND SERIOUS UNDESIRABLE EFFECTS

Details of previous sales and complaints data has not been supplied for review. This assessment is, therefore, completed on the assumption that no previous health-related complaints have been reported by consumers. If this is incorrect the manufacturer/responsible person must notify Delphic HSE of all such reported complaints so that the assessment can be updated.

Going forward the manufacturer/responsible person must ensure that details of any concerns or complaints relating to consumer safety and adverse health effects are provided to Delphic HSE so that the safety assessment can be updated accordingly.

INFORMATION ON THE COSMETIC PRODUCT

Details of user trials/additional product safety testing have not been supplied for review, and this assessment is conducted on the basis that no such testing has been undertaken. Should this be inaccurate, or additional testing be conducted in the future, Delphic HSE should be notified of the details of such testing so this safety assessment can be updated accordingly.

ASSESSMENT CONCLUSION

Under normal or reasonably foreseeable conditions of use, a product made to this formulation is unlikely to produce an abnormally high number of adverse reactions. Assuming the necessary warnings stated in the safety assessment are included on the product packaging it will give consumers the level of safety they can reasonably expect.

This product complies with the requirements of the EU Cosmetic Regulation (EC) No 1223/2009. The product must be manufactured according to Good Manufacturing Practice.

LABELLED WARNINGS & INSTRUCTIONS FOR USE

Do not swallow

Keep away from eyes. If material accidentally enters the eye, rinse well with plenty of clean water. Seek medical attention if irritation persists.

REASONING

A toothpaste product intended for use by children of 12 years old or above, for distribution to the EU market.

No Observed Adverse Effect Levels (NOAELs), or other suitable Points of Departure (PoD) were not available for review for some of the materials. For those materials where a Margin of Safety (MoS) was not derived this is due to either a history of safe use at similar levels in cosmetic products related to the product under review, lack of biological activity or for a reason explained in the individual ingredient toxicological summary in Annex II. For those substances where suitable PoDs were available, the resultant MoS are above the typical recommended values (see Preface to Annexes).

A number of materials have recommended safe levels in percentage terms, as established by bodies such as the Scientific Committee on Consumer Safety (SCCS) or Cosmetic Ingredients Review (CIR) expert panel, or legal limits that are described in percentage terms. All such materials are present at or below the recommended safe levels or legal maximums, as indicated by the relevant entries in Annex II.

Mentha Piperita (Peppermint) Oil is present at 0.05% in the product, according to International Fragrance Association (IFRA) analysis, the fragrance can be used at up to 40% in Toothpaste (class 6) under 48th amendment such as this and is therefore considered acceptable at this level.

Based on the harmonised CLP classifications for Tetrasodium Pyrophosphate, it has been classified as H318 for eye damage. However, as this is considered a cosmetic product and not a chemical or household product, CLP warnings relating to eye damage are not considered mandatory to be included on the label. Instructions to wash out eyes immediately incase of accidental contact has been included by the manufacturer, as well as recommendations to seek medical attention should such exposure occur.

Due the presence of ingredients such as sorbitol, which can exhibit a laxative effect if ingested at significant amounts, users should be instructed to not swallow the product.

Phenoxyethanol and Dichlorobenzyl alcohol are approved preservative in cosmetic products, its level is within the regulatory cosmetic limit. Hence, its presence is acceptable.

All the colorants and preservative are permitted for use in EU cosmetic. Therefore, they would not be expected to pose an undue risk of significant adverse effects in an item of this nature.

The manufacturer must ensure that all raw materials are of suitably safe EU cosmetic grade with the specification mentioned in the report and/or manufactured under GMP conditions as required by the regions to be sold, all polymers are fully polymerised.

Overall, assuming suitable grades of material are used during manufacture and the product is labelled appropriately, this item can be considered safe for the intended use. It would not be expected to pose a significant risk of adverse effects in a majority of individuals and would be expected to provide consumers with the level of safety they might reasonably expect from a product of this nature.

Skin Toxicity - Neat Product

Not expected to cause skin irritation following prolonged or repeated use.

Exposure to this product is unlikely to result in photo-toxic effects.

Unlikely to cause sensitisation following repeated skin contact.

Unlikely to produce systemic toxicity following skin contact.

Contact with the dilute solution is unlikely to cause skin irritation even if contact is prolonged or repeated.

Exposure to this product when diluted is unlikely to result in photo-toxic effects.

Repeated exposure to the diluted product is unlikely to produce allergy by skin contact.

When diluted in use, unlikely to cause systemic toxicity following skin contact.

Eye Toxicity - Neat Product

May irritate the eye.

When diluted in-use, the product may irritate the eye.

Oral Toxicity - Neat Product

All materials if swallowed in large amounts have the potential to cause injury. If incidentally swallowed in small amounts, the formulation as supplied may cause slight, transient irritation to the mouth and upper digestive tract.

Not expected to produce systemic toxicity following ingestion. All materials if swallowed in large amounts have the potential to cause injury.

If swallowed, the diluted product in-use is unlikely to cause any adverse effects.

Not expected to produce systemic toxicity following ingestion.

Inhalation Toxicity

It is unlikely that inhalation will be a route of exposure.

Toxicological & Regulatory Assessor

Hou Kin Lam, BSc (Hons), MSc, MRSB 23 May 2022

This report consists of 6 pages plus a Regulatory, Ingredient Data, Allergens, Exposure & Specifications Annex.
It is only valid as the original, complete document.

Preface to Annexes

Annex II - Ingredient Data

Physical/Chemical and Toxicological data presented within these reviews are representative of publicly available data and provided for informational purposes only. Sources of data are identified (typically in brackets) following each data point, and there may be multiple data points for any given toxicological endpoint.

Margins of Safety (MoS) are calculated where suitable data are available, and may related to mg/kg, µg/cm^2 or percentage-based indications of safety.

MoS based on systemic (mg/kg) effects are calculated as 'Point of Departure (PoD)' / 'Systemic Exposure Dose (SED)', where:

PoD = Data point considered to be indicative of a 'safe' level of exposure. This may be an animal-derived No Observed Adverse Effect Level (NOAEL) or a value indicated as being safe to humans. In the case of the latter this would typically be in the form of an ADI (Acceptable Daily Intake) or DNEL (Derived No Effect Level) established by a governmental or scientific committee / body.

SED = (Product Used (mg) x Retention Factor x Concentration of Material in Product x Dermal Absorption) / intended user body weight (kg)

In the absence of material specific data a dermal absorption of 100% is assumed.
Where an animal-derived NOAEL is used as the PoD an MoS greater than 100 is typically considered acceptable for indicating safety to consumers.
For PoD based on established safe levels in humans an MoS of greater than 1 is typically considered as acceptable for indicating safety to consumers.

MoS based on localised (µg/cm^2) effects are calculated as 'Point of Departure (PoD)' / 'Dermal Exposure', where:

PoD = Data point considered to be indicative of a 'safe' level of exposure. This would typically be a µg/cm^2 value identified from either a Local Lymph Node Assay (LLNA) or Human Repeat Insult Patch Test (HRIPT).

Dermal Exposure = (Product Used (µg) x Retention Factor x Concentration of Material in Product) / Surface Area of Application

MoS based on percentage data are calculated as 'Point of Departure PoD' / 'Ingredient Concentration in Product', where:

PoD = Data point considered to be indicative of a 'safe' level of exposure. Typically a percentage identified as safe for use within a leave-on consumer product, as established by legislation or by a governmental or scientific committee / body.

Ingredient Concentration in Product = Concentration of Material in Finished Product x Retention Factor
(As safe levels are typically identified for leave-on products the retention factor is included within the calculation to account for use in rinse-off products)
For PoD based on established safe levels in finished products an MoS of greater than 1 is typically considered as acceptable for indicating safety to consumers.

Retention Factor is an estimation of the amount of product in prolonged contact with the skin under normal conditions of use, and expressed as the decimal form of a percentage. A retention factor of 1 relates to 100% of the product staying in prolonged contact with the skin and is typically used for all leave-on products. All other products have retention factors as determined by typical conditions of use, and these are presented under 'Exposure Scenario'.

Annex III - Allergen Levels

This annex details the total levels of individuals allergens within the finished product, either from direct addition to the product or as part of fragrances and essential oils. Information is provided in both percentage and ug/cm^2 terms.

Indicative Toxicological Data is provided for each allergen where available and may include:

Research Institute for Fragrance Materials No Effect Level (RIFM NEL, indicated as a percentage)
Patch Test Concentration (percentage)
Buehler Test
Guinea Pig Maximisation Test
Human Repeat Insult Patch Test (HRIPT, in either percentage or ug/cm2)
Human Repeat Open Application Test (HROAT, in either percentage or ug/cm2)
Human Maximisation Test (HMT, in either percentage or ug/cm2)

Annex IV - Foreseeable Exposures

This annex details additional exposure scenarios identified during the safety assessment as being reasonably foreseeable under normal conditions of use.

For the purposes of the safety assessment all MoS are calculated based on the intended product use, and any comments or concerns relating particularly to additional exposure scenarios is detailed in the Reasoning or Toxicological & Regulatory Review portions the assessment.

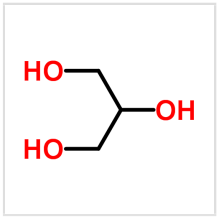
ANNEX I - REGULATORY CONTROLS

Substance: Glycerin

CAS: 56-81-5; 8013-25-0

Function: Denaturant; Humectant; Hair Conditioning; Oral Care; Perfuming; Skin Protecting; Viscosity Controlling

Concentration in Product: 33%



Regulatory Listings

Europe:

EINECS: 200-289-5

EU GHS Classification: Not Classified (self-classification)

REACh Annex XVII: Not Controlled

REACh SVHC: Not Controlled

EU Cosmetic Regulation: Not Controlled

EU INCI Name: Glycerin

EN71 Toy Standards: Special additive for liquid adhesives for paper and wood as per EN71-5. Ingredient used in the manufacture of finger paints per EN71 -7. Not listed in EN71-9.

EU Toy Directive: Not Controlled

EU Biocides Regulation: Not Registered for any Biocidal Uses

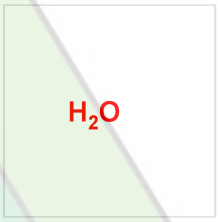
EU Detergents Regulation: Not Controlled

Substance: Aqua

CAS: 7732-18-5

Function: Solvent

Concentration in Product: 27.7%



Regulatory Listings

Europe:

EINECS: 231-791-2

EU GHS Classification: Unclassified

REACh Annex XVII: Not Controlled

REACh SVHC: Not Controlled

EU Cosmetic Regulation: Not Controlled

EU INCI Name: Aqua

EN71 Toy Standards: EN71 - 7 and EN71 - 9 Not Controlled

EU Toy Directive: Not Controlled

EU Biocides Regulation: Not Registered for any Biocidal Uses

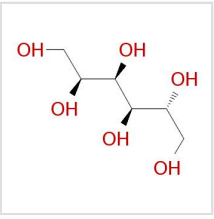
EU Detergents Regulation: Not Controlled

Substance: Sorbitol

CAS: 68425-17-2 (generic); 50-70-4; 98201-93-5; 1259528-21-6 (generic)

Function: Humectant; Plasticiser; Skin Conditioning

Concentration in Product: 25%



Regulatory Listings

Europe:

EINECS: 200-061-5

EU GHS Classification: Not Classified

REACh Annex XVII: Not Controlled

REACh SVHC: Not Controlled

EU Cosmetic Regulation: Not Controlled

EU INCI Name: Sorbitol

EN71 Toy Standards: Not Listed in EN71-7 or -9

EU Toy Directive: Not Controlled

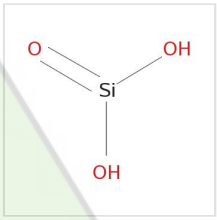
EU Detergents Regulation: Not controlled

Substance: Hydrated Silica

CAS: 63231-67-4; 10279-57-9; 1343-98-2; 7631-86-9; 112926-00-8

Function: Abrasive; Absorbent; Anticaking; Bulking; Opacifying; Viscosity controlling

Concentration in Product: 3%



Regulatory Listings

Europe:

EINECS: 215-683-2 ; 231-545-4

EU GHS Classification: Not Classified (self-classified)

REACh Annex XVII: Not Controlled

REACh SVHC: Not Controlled

EU Cosmetic Regulation: Not Controlled

EU INCI Name: Hydrated Silica

EN71 Toy Standards: Used as an extender in the manufacture of finger paints (EN71-7, Annex C)
Not listed in EN71-9

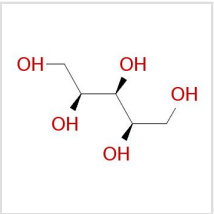
EU Toy Directive: Not Controlled

Substance: Xylitol

CAS: 87-99-0

Function: Humectant; Skin Conditioning

Concentration in Product: 3%



Regulatory Listings

Europe:

EINECS: 201-788-0

EU GHS Classification: Not Classified (self classified by 123 out of 123 notifiers)

REACh Annex XVII: Not Controlled

REACh SVHC: Not Controlled

EU Cosmetic Regulation: Not Controlled

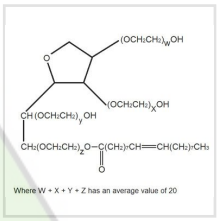
EU INCI Name: Xylitol

Substance: Polysorbate 80

CAS: 9005-65-6

Function: Denaturant; Emulsifying; Surfactant

Concentration in Product: 3%



Regulatory Listings

Europe:

EINECS: 500-019-9

EU GHS Classification: Not Classified (self-classified)

REACh Annex XVII: Not listed

REACh SVHC: Not listed

EU Cosmetic Regulation: Not controlled

EU INCI Name: Polysorbate 80

EN71 Toy Standards: Not listed in EN71 part 7 or 9

EU Toy Directive: Not controlled

EU Biocides Regulation: Not Controlled

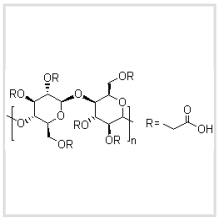
EU Detergents Regulation: Not Controlled

Substance: Cellulose Gum

CAS: 9004-32-4; 99331-82-5; 9000-11-7

Function: Emuslion Stabilising; Film Forming; Viscosity Controlling; Binding; Masking

Concentration in Product: 2.5%



Regulatory Listings

Europe:

EINECS: -

EU GHS Classification: Not Classified (self-classification)

REACh Annex XVII: Not Controlled

REACh SVHC: Not Controlled

EU Cosmetic Regulation: Not Controlled
EU INCI Name: Cellulose Gum
EN71 Toy Standards: Not listed in EN71-7 or 9
EU Toy Directive: Not Controlled
EU Biocides Regulation: Not Registered for any Biocidal uses.
EU Detergents Regulation: Not Controlled

Substance: Mentha Piperita (Peppermint) Oil

CAS: 84082-70-2; 8006-90-4

Function: Refreshing; Perfuming; Masking; Tonic

Concentration in Product: 1%



Regulatory Listings

Europe:

EINECS: - / 282-015-4

EU GHS Classification: H315, H317, H319, H412 (Self classified)

REACh Annex XVII: Not controlled

REACh SVHC: Not controlled

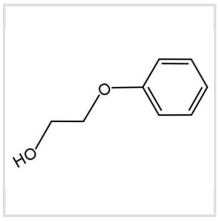
EU Cosmetic Regulation: Not controlled
EU INCI Name: Mentha Piperita Oil

Substance: Phenoxyethanol

CAS: 56257-90-0; 37220-49-8; 122-99-6

Function: Preservative

Concentration in Product: 0.5%



Regulatory Listings

Europe:

EINECS: 204-589-7

EU GHS Classification: H302 (Acute tox. 4); H318 (Eye Dam. 1); H335 (STOT SE 3) (harmonised classification)

REACh Annex XVII: Not Controlled

REACh SVHC: Not Controlled

EU Cosmetic Regulation: Approved Preservative - Annex V/29 - Maximum 1% all Products (SCCS considers 1% safe)

EU INCI Name: Phenoxyethanol

EN71 Toy Standards: EN71-5: Permitted in Embedding Sets, Adhesives, paints, lacquers, varnishes, thinners and cleaning agents (solvents) supplied or recommended in model sets ; EN71-7 Annex B Item 23: Approved Preservative, 1% in finger paints.

EU Toy Directive: Not controlled

EU Biocides Regulation: PT01, 02, 04 (Approval in progress)
PT03 (Not approved)
PT06,13 (Cancelled application)

EU Detergents Regulation: Preservation agents shall be labelled, irrespective of their concentration

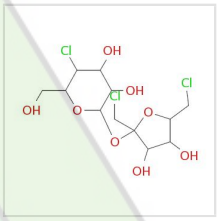
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Substance: Sucralose

CAS: 56038-13-2

Function: Skin Conditioning

Concentration in Product: 0.5%



Regulatory Listings

Europe:

EINECS: 259-952-2

EU GHS Classification: Not classified (145 notifiers)
(self classification according to ECHA C&L Inventory)

REACh Annex XVII: Not Controlled

REACh SVHC: Not Controlled

EU Cosmetic Regulation: Not Controlled

EU INCI Name: Sucralose

Substance: Tetrasodium Pyrophosphate

CAS: 7722-88-5

Function: Anticaking; Chelating; Oral care; Buffering

Concentration in Product: 0.5%

Regulatory Listings

Europe:

EINECS: 231-767-1

EU GHS Classification: Self classified:
H302 (Harmful if swallowed, Category 4); H318 (Cause serious eye damage, Category 1); H315 Causes skin irritation.(Category 2); H319 Causes serious eye irritation.(Category 2); H335 May cause respiratory irritation.(Category 3)

REACh Annex XVII: Not Controlled

REACh SVHC: Not Controlled

EU Cosmetic Regulation: Not Controlled

EU INCI Name: Tetrasodium Pyrophosphate

EN71 Toy Standards: Not listed in EN71 part 7 or 9

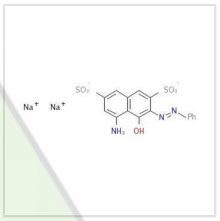
EU Toy Directive: Not Controlled

Substance: CI 17200 (D&C Red 33)

CAS: 3567-66-6

Function: Pigment

Concentration in Product: 0.1%



Regulatory Listings

Europe:

EINECS: 222-656-9

EU GHS Classification: Not Classified (self-classified, 123 notifiers with experimental data support)
H319 (self-classified, 262 notifiers)
* Not an eye irritant based on experimental data

REACh Annex XVII: Not Controlled

REACh SVHC: Not Controlled

EU Cosmetic Regulation: Permitted pigment: Annex IV item 37 - All Cosmetic Products; Hair dye substance in non-oxidative hair dye products, Maximum concentration in ready for use preparation 0.5%

EU INCI Name: CI 17200

EN71 Toy Standards: Not listed in EN71 Part 7 & 9

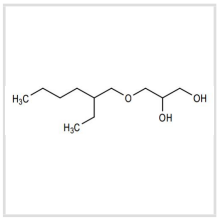
EU Toy Directive: Not Controlled

Substance: Ethylhexylglycerin

CAS: 70445-33-9

Function: Skin Conditioning; Deodorant

Concentration in Product: 0.1%



Regulatory Listings

Europe:

EINECS: 408-080-2

EU GHS Classification: H318 (Causes serious eye damage)
H412 (Harmful to aquatic life with long-lasting effects)

REACh Annex XVII: Not Controlled

REACh SVHC: Not Controlled

EU Cosmetic Regulation: Not Controlled

EU INCI Name: Ethylhexylglycerin

EN71 Toy Standards: Not listed in EN71 Part 7 or 9

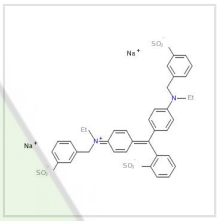
EU Toy Directive: Not Controlled

Substance: CI 42090 (FD&C Blue No. 1)

CAS: 71701-19-4 (K.Na salt); 71701-18-3 (K salt); 2650-18-2 (NH4 salt); 68921-42-6 (Al salt); 15792-67-3 (Al salt); 3844-45-9

Function: Pigment

Concentration in Product: 0.1%



Regulatory Listings

Europe:

EINECS: 220-168-0 / 223-339-8 / 272-939-6 / 239-897-0 / 275-866-8 / 275-867-3

EU GHS Classification: Not classified (by 1496 / 1633 Notifiers under REACH)
H315, H319 (Self-classified by 81 / 1633 Notifiers under REACH)

REACh Annex XVII: Not Controlled

REACh SVHC: Not Controlled

EU Cosmetic Regulation: Permitted pigment: Annex IV item 63 - All Cosmetic Products, Purity criteria as set out in Commission Directive 231/2012/EC (E133)
Restricted Pigment: Annex III item 190 - Permitted in Hair dye substance in non-oxidative hair dye products at up to 0.5%. The free base and salts of this hair colouring ingredient, unless prohibited under Annex II, are permitted for use.

EU INCI Name: CI 42090

EN71 Toy Standards: Not listed in EN71-7 or 9

EU Toy Directive: Not Controlled

EU Biocides Regulation: Not controlled

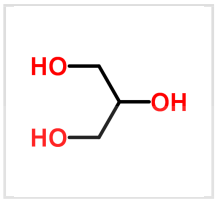
EU Detergents Regulation: Not controlled

ANNEX II - INGREDIENT DATA

Substance: Glycerin
CAS: 56-81-5; 8013-25-0
Function: Denaturant; Humectant; Hair Conditioning; Oral Care; Perfuming; Skin Protecting; Viscosity Controlling

Concentration in Product: 33%
Dermal Exposure Level: 0.247274795 mg/cm^2
Daily Body Burden: 1.3256341463mg/kg

Chemical Structure



Physical/Chemical Characteristics

Appearance	Colourless syrup
Boiling Point	290˚C
Explosive Properties	Non-explosive
Flammability	400C
Flash Point	177˚C (Open Cup)

Log Kow	1.76
Molecular Mass	92.11
Melting Point	18.2˚C
Odour	Sweet

Toxicological Summary

The below information is a summary of the toxicological profile for this raw material, including a description of general hazards associated with the material as well as discussion of the most critical studies relating to the overall safety in use of this substance/mixture in consumer products. Details of the available toxicological data can be found overleaf.

Overall Toxicity Review:

Glycerin is a trihydroxy sugar alcohol that is commonly used as a solvent, emollient, as well as cosmetic functions of denaturant, hair conditioning, humectant, oral care, perfuming, skin protecting and viscosity controlling (SDA, 1990). Glycerin constitutes around 10% of the Fat found in a typical Human Diet and is readily metabolised on ingestion, and has generally recognised as safe (GRAS) status in the US. (FDA, 21CFR§182.1320).

Test results in rabbits shows the substance has minimal irritancy properties in both the skin and eye. Clinical evaluations have also concluded the substance has no dermal irritation and sensitising potentials. The compound's structure does not contain conjugated double bonds, therefore, it will not absorb UV light which is a prerequisite for phototoxicity.

When given orally at 20% in the diet over 2 years showed no adverse effects in rats. Has a high Oral LD50 (>10g/kg in Rats). However ingestion of large amounts of this material can cause an osmotic effect in the gastrointestinal tract leading to dehydration, nausea and headaches. Glycerine has also been determined to be non-toxic via dermal application (LD50 >10g/kg in Rabbits) and inhalation of saturated vapours (4h LC50 >2.75 mg/L).

Systemic toxicity via ingestion is considered, and moreover, a no-observed-adverse-effect-level (NOAEL) of 8000-10000 mg/kg bw was determined based on the absence of treatment-related effects in rats from the 2-year diet study. The lower of these values of 8000 mg/kg bw is conservatively chosen as the point of departure.

A NOAEC of 167mg/m3 was reported from a nose-only aerosol exposure 90-day repeated dose toxicity study in rats; this was due to local lung irritation effects seen at higher concentrations.

Glycerine was not mutagenic in an Ames assay, and a 2 year dietary study in rats found no increase in the rates of tumour formation compared to control animals. There was no effect noted on growth, fertility and reproductive performance in rats through two generations, and no developmental toxicity of offspring was observed.

As dermal absorption is dependent on the molecular properties, concentration, exposure time and vehicle simultaneously, in the absence of relevant experimental data it is difficult to assess an exact value. If not stated otherwise within the risk assessment, we assume 100% dermal absorption, however it must be noted that for the majority of compounds, even low molecular weight, lipophilic compounds, dermal absorption is expected to be significantly lower than 100%.

Given the low toxicity profile of this substance, and the fact it is a constituent of a typical human diet, its use in Consumer Products is not expected to produce significant localised or systemic toxicity. The Cosmetic Ingredients Review (CIR Expert Panel on glycerine reports that glycerine is used in leave-on products at up to 79.2% and in baby products in the range of 0.23-21% (CIR, 2019).

References:

CIR, 2019. Safety Assessment of Glycerin as Used in Cosmetics .IJT 38(Suppl. 3):6-22, 2019

GRAS Listing, [Glycerin]. FDA, 21 CFR. §182.1320 (Last accessed 21/03/2019).

The Soap and Detergent Association (SDA), 1990. Glycerine: an overview. Glycerine & Oleochemical Division. New York.

ECHA registration dossier, Glycerol, CAS: 56-81-5.

Margin(s) of Safety

Point of Departure - Animal Study: 8000.0000mg/kg
Exposure from Product 1.32563415mg/kg
Margin of Safety 6034.84756

Physical/Chemical and Toxicological data used in generating these review are representative of publicly available data, and is provided for information purposes only.
For further information on any of the data or conclusions reported here, or for information Margins of Safety and how they are Calculated, please contact Delphic HSE.

ANNEX II - INGREDIENT DATA

Glycerin

Acute Toxicity Acute Toxicity, Lethality [Other]		LD50 = 27.2g/kg
Rat	Oral, Gavage	
Acute Toxicity Acute Toxicity, Non-Lethal [Other]		TDLo oral 1428mg/kg Behavioural: headache Gastrointestinal: nausea or vomiting
Human	Oral, NOS	
Acute Toxicity Acute Toxicity, Lethality [Other]		LD50 = 56.75g/kg [Occlusive bandage in contact with skin for 4 days.]
Guinea Pig	Dermal	
Acute Toxicity Acute Toxicity, Lethality [Other]		A calculated 4 hour LC50 value based on nominal concentration would be >2.75 mg/L The L(Ct)50 for Glycerine was 4655 mg minute/litre.
Rat	Inhalation	
Carcinogenicity Carcinogenicity studies [Other]		Non-carcinogenic Doses: 5, 10 and 20% in diet (males: 2000, 4000 and 8000 mg/kg bw/day; females: 2500, 5000 and 10000 mg/kg bw/day) [Dietary exposure over 2 years.]
Rat	Oral, Feed	
Eye Irritation In vivo Eye Irritation [Other]		Glycerin was considered to be non irritating in 19 laboratories and of questionable irritation in one laboratory.
Rabbit	Instillation	
Genotoxicity Bacterial reverse mutation test (Ames) [OECD 471]		Negative with and without metabolic activation [S. typhimurium TA1535, TA1537, TA98, TA100. Up to 10,000µg/plate.]
Bacteria	In vitro exposure	
Repeated Dose Chronic Toxicity Studies in Rodents [OECD 452]		NOAEL = 8000-10,000 mg/kg bw/day Doses:5, 10, 20% in diet (males 2000, 4000 and 8000 mg/kg bw, females 2500, 5000 and 10000 mg/kg bw); 2-year exposure.
Rat	Oral, Feed	
Repeated Dose 90-day Inhalation Toxicity Study [OECD 413]		The NOAEC was 167 mg/m3 based on local irritant effects on the upper respiratory tract, from a viscous liquid aerosol generator by nose-only exposure.
Rat	Inhalation	
Repeated Dose Repeat Dose Dermal Toxicity Study [Other]		There were no effects noted in rabbits dosed 8 hours/day, 5 days/week for 45 weeks with dose levels as high as 4.0 ml/kg.
Rabbit	Dermal	
Reproductive Toxicity Two-Generation Reproduction Toxicity [OECD 416]		Glycerin was administered by oral gavage to groups of male and female rats through two generations. There was no effect noted on growth, fertility and reproductive performance through two generations at a dose level of ~2000 mg/kg/day.
Rat	Oral, Gavage	
Reproductive Toxicity Prenatal Development Toxicity Study [OECD 414]		No Effects Up To 1,310 mg/kg/day (highest tested dose) [Dosing on days 6 to 15 of gestation.]
Rat	Oral, Gavage	
Skin Irritation In vivo skin irritation [Other]		Glycerin was considered to be non irritating to the skin in rabbit irritation studies in 14 testing laboratories.
Rabbit	Dermal	
Skin Irritation In vivo skin irritation [Other]		The dermal irritation potential was examined in 33 humans, 30 female and 3 male. Under the conditions of the study, Glycerine USP (25% concentration) exhibited no clinical irritation when tested in humans.
Human	Dermal	
Skin Sensitisation Repeat Insult Patch Test (RIPT) [Other]		In a study of 420 patients with eczema, 419 showed no irritation or sensitization when tested with a 50% solution in water. A result from one patient was questionable.
Human	Dermal	

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ANNEX II - INGREDIENT DATA

Substance: Aqua
CAS: 7732-18-5
Function: Solvent

Concentration in Product: 27.7%
Dermal Exposure Level: 0.207560965 mg/cm^2
Daily Body Burden: 1.1127292683mg/kg

Chemical Structure

H_2O

Physical/Chemical Characteristics

Boiling Point	100°C
Appearance	Clear colourless liquid
Flammability	Not flammable
Flash Point	not flammable
Molecular Mass	18
Melting Point	0°C
Odour	none
pH	7
Specific Gravity	1

Toxicological Summary

The below information is a summary of the toxicological profile for this raw material, including a description of general hazards associated with the material as well as discussion of the most critical studies relating to the overall safety in use of this substance/mixture in consumer products. Details of the available toxicological data can be found overleaf.

Overall Toxicity Review:

A ubiquitous chemical substance that is the basis for all known forms of life. Use in consumer products is not expected to result in any Acute or Chronic Toxicity following typical exposures.

Margin(s) of Safety

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ANNEX II - INGREDIENT DATA

Aqua

Details on specific toxicological studies related to endpoints of concern are not available for Aqua, please see the previous page for a justification of safety based on history of use &/or weight of evidence.

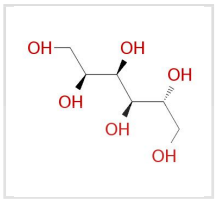
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ANNEX II - INGREDIENT DATA

Substance: Sorbitol
CAS: 68425-17-2 (generic); 50-70-4; 98201-93-5; 1259528-21-6 (generic)
Function: Humectant; Plasticiser; Skin Conditioning

Concentration in Product: 25%
Dermal Exposure Level: 0.187329390 mg/cm^2
Daily Body Burden: 1.0042682927mg/kg

Chemical Structure



Physical/Chemical Characteristics

Appearance	Solid / Syrupy liquid
Boiling Point	Decomposes
Molecular Mass	182.17
Melting Point	111.5°C
pH	5 to 7 (50% Aq)
Specific Gravity	1.489
Viscosity	400 mPa.s @ 20°C
Water Solubility	Soluble

Toxicological Summary

The below information is a summary of the toxicological profile for this raw material, including a description of general hazards associated with the material as well as discussion of the most critical studies relating to the overall safety in use of this substance/mixture in consumer products. Details of the available toxicological data can be found overleaf.

Overall Toxicity Review:

Polyhydric alcohol with about half the sweetness of sucrose. Occurs naturally and also produced synthetically from glucose. It is used as a humectant, plasticiser and skin conditioning material in cosmetics. Non-active ingredient in drugs in the US. Food additive (E420) with the generally recognized as safe (GRAS) status in the US (21CFR184.1835) and non-specified acceptable daily intake (ADI) as established by The Joint FAO/WHO Expert Committee on Food Additives (JECFA) in 1982.

It is not acutely toxic, with an LD50 > 2000 mg/kg via the oral, intravenous, subcutaneous and intraperitoneal routes in experimental animals. A TDLo of 1.7g/kg was reported in women, though this is in relation to effects on the GI tract. Given that ingestion would not be a significant route of exposure in typical Consumer Chemicals this value is not considered relevant under the majority of circumstances.

Based on available in-vivo data, not expected to be a skin or eye irritant and no evidence of genotoxicity or developmental and reproductive toxicity. Based upon history of use, not expected to be a skin sensitiser.

Rat feed with 10% or 15% Sorbitol for 17 months showed no evidence of deleterious effects. The only difference with the controls was slight diarrhoea. In supplement, a reproduction study was conducted and extended over four generations did not reveal any abnormalities. In amounts of 40 g daily, spread throughout the day's intake of food, Sorbitol was well tolerated for a long period by human subjects.

Sorbitol has been used for many years in the diet, especially of diabetics. There have been no indications of significant harmful effects. Considering the biochemical and toxicological data obtained on animals and man and the known facts about the nutritional properties of Sorbitol, JECFA considered there is no need for the limitation of Sorbitol as a food additive on toxicological grounds (JECFA 1973)

As dermal absorption is dependent on the molecular properties, concentration, exposure time and vehicle simultaneously, in the absence of relevant experimental data it is difficult to assess an exact value. If not stated otherwise within the risk assessment, we assume 100% dermal absorption, however it must be noted that for the majority of compounds, even low molecular weight, lipophilic compounds, dermal absorption is expected to be significantly lower than 100%.

Overall the use of this material at typical levels within a Consumer Product would not be expected to pose an undue risk of significant adverse effects.

References:
JECFA, 1982. FNP 25-JECFA 26/181. R

JECFA, 1978. WHO FOOD ADDITIVES SERIES NO. 13. Twenty-second Report of the Joint FAO/WHO Expert Committee on Food Additives, Geneva, 1978, WHO Technical Report Series No. 631

JECFA. FAS 5/NMRS 53A-JECFA 17/498 (1973). Available at: http://www.inchem.org/documents/jecfa/jecmono/v05je91.htm (Accessed 20 May 2019)

Margin(s) of Safety

Physical/Chemical and Toxicological data used in generating these review are representative of publicly available data, and is provided for information purposes only.
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ANNEX II - INGREDIENT DATA

Sorbitol

Acute Toxicity Acute Toxicity, Lethality [Other]		LD50 = 15000 mg/kg
Mouse [NOS]	Intraperitoneal	
Acute Toxicity Acute Toxicity, Non-Lethal [Other]		TDLo oral in women; 1700 mg/kg (gastrointestinal, hypermotility, diarrhea).
Human	Oral, NOS	
Acute Toxicity Acute Toxicity, Lethality [Other]		LD50 = 9480 mg/kg
Mouse	Intravenous	
Acute Toxicity Acute Toxicity, Lethality [Other]		LD50 = 24000 mg/kg
Mouse	Subcutaneous	
Acute Toxicity Acute Oral Toxicity, Lethality [OECD 401, OECD 423, OECD 425]		LD50 = 15900 mg/kg
Rat	Oral, NOS	
ADME Toxicokinetic study [OECD 417]		57.4% of the activity was excreted as CO2, 17.3% in the urine, 4.2% was found as liver glycogen and 0.6% as liver fatty acids.
Rat	Intraperitoneal	
Eye Irritation Bovine Corneal Opacity & Permeability (BCOP) Test [OECD 437]		Unable to classify, not occular corrosive Read-across form "glucose syrups, wheat hydrolised".
Ex-vivo Tissue	In vitro exposure	
Genotoxicity Bacterial reverse mutation test (Ames) [OECD 471]		Negative Read across from Syrups, corn hydrogenated. Tested material: Lycasin 80/55 (Sorbitol 7.6%; maltitol 53.6%; triitols 16.4%)
Bacteria	In vitro exposure	
Genotoxicity Mammalian erythrocyte micronucleus test [OECD 474]		Negative Read across from Syrups, corn hydrogenated. Tested material: Lycasin 80/55 (Sorbitol 7.6%; maltitol 53.6%; triitols 16.4%)
Mouse	Oral, Gavage	
Repeated Dose Chronic Toxicity Studies in Rodents [OECD 452]		10% and 15% Sorbitol in diet was given to rats for 17 months showed no evidence of deleterious effect on weight gain, reproduction, lactation or histopathological appearances of the main organs. The only difference with the control was slight diarrhoea.
Rat	Oral, Feed	
Repeated Dose Repeat Dose Oral Toxicity Study [Other]		In amounts of 40 g daily, spread throughout the day's intake of food, sorbitol was well tolerated for a long period by human subjects
Human	Oral, Feed	
Reproductive Toxicity In vivo reproductive toxicity study [Other]		Rats was given sorbitol at levels of 10% or 15% in the diet for 17 months showed no evidence of deleterious effects. In supplement, a reproduction study made on male and female rats and extended over four generations did not reveal any abnormalities.
Rat	Oral, Feed	
Skin Irritation Reconstructed Human Epidermis (RHE) Test [OECD 431, OECD 439]		Non-irritant Read-across from glucose syrups wheat hydrogenated.
Ex-vivo Tissue	In vitro exposure	

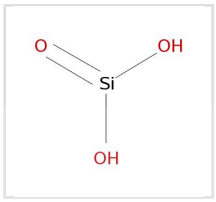
Physical/Chemical and Toxicological data used in generating these review are representative of publicly available data, and is provided for information purposes only.
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ANNEX II - INGREDIENT DATA

Substance: Hydrated Silica
CAS: 63231-67-4; 10279-57-9; 1343-98-2; 7631-86-9; 112926-00-8
Function: Abrasive; Absorbent; Anticaking; Bulking; Opacifying; Viscosity controlling

Concentration in Product: 3%
Dermal Exposure Level: 0.022479527 mg/cm^2
Daily Body Burden: 0.1205121951mg/kg

Chemical Structure



Physical/Chemical Characteristics

Appearance	White Granular solid / powder
Boiling Point	2 230 °C
Molecular Mass	60.09 + xH2O molecules
Melting Point	1700 C
Odour	None
Particle Size	60 to 200 microns
pH	6.5 (50% suspension @ 20 C)
Specific Gravity	0,430 – 0,490
Water Solubility	insoluble

Toxicological Summary

The below information is a summary of the toxicological profile for this raw material, including a description of general hazards associated with the material as well as discussion of the most critical studies relating to the overall safety in use of this substance/mixture in consumer products. Details of the available toxicological data can be found overleaf.

Overall Toxicity Review:

Hydrated Silica is the inorganic oxide that conforms generally to the formula: SiO2.xH2O where x varies with the method of precipitation or gelation and extent of drying performed on the material, also known as hydrated silicon dioxide. There are 2 categories of silica, crystalline and amorphous. Only the amorphous forms of silica, and more specifically, synthetic amorphous silica and silicates, are used in cosmetics. Hydrated silica functions as an abrasive, absorbent, anti-caking agent, bulking agent, opacifying agent, oral care agent and a skin-conditioning agent. Silica has been permitted as a food additive for direct addition to food for human consumption (21CFR172.480).

Undiluted hydrated silica was not irritating to the skin in a dermal study on human volunteers and was mildly irritating to the abraded and shaved skin of rabbits. It was mildly irritating to the eyes of rabbits in an ocular study. Hydrated silica showed little to no allergenic potential in skin sensitisation studies with human volunteers. No sensitisation reaction was observed when hydrated silica (20% in distilled water) was administered to guinea pigs.

The acute oral, dermal and inhalation toxicity of hydrated silica is low. The acute oral LD50 value in rats and the acute dermal LD50 value in rabbits was greater than 2000 mg/kg.

A NOAEL of 8980 mg/kg/d was determined in a dietary study in which rats received up to 8980 mg/kg/day hydrated silica for 6 months. No treatment related findings were observed in this study. 8980 mg/kg/d (highest dose tested) is the point of departure and is conservatively chosen. The true NOAEL could be higher.

Hydrated silica is not genotoxic, carcinogenic or toxic to the reproductive system.

As dermal absorption is dependent on the molecular properties, concentration, exposure time and vehicle simultaneously, in the absence of relevant experimental data it is difficult to assess an exact value. If not stated otherwise within the risk assessment, we assume 100% dermal absorption, however it must be noted that for the majority of compounds, even low molecular weight, lipophilic compounds, dermal absorption is expected to be significantly lower than 100%.

The Cosmetic Ingredient Review (CIR) Expert Panel has assessed the safety of hydrated silica as used in cosmetics and concluded it is safe at the present uses and concentrations in cosmetic products (CIR 2009). Latterly some questions have been raised about safety in products which would result in significant inhalation exposure due to a lack of toxicological data. Use in products without significant levels of inhalation exposure do, however, have an extensive history of safe use and none of the available data indicates a significant safety concern. Use in Powder products should be more carefully considered, with likelihood of inhalation of particulates the major concern from a systemic point of view.

References

CIR, 2009. Safety Assessment of Silica and Related Cosmetic Ingredients

21 CFR , part 172 -- food additives permitted for direct addition to food for human consumption. US FDA. Available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?FR=172.480&CFRPart=&FRSearch=

Margin(s) of Safety

Point of Departure - Animal Study: 8980.0000mg/kg
Exposure from Product 0.12051220mg/kg
Margin of Safety 74515.2803

Physical/Chemical and Toxicological data used in generating these review are representative of publicly available data, and is provided for information purposes only.
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ANNEX II - INGREDIENT DATA

Hydrated Silica

Acute Toxicity Acute Toxicity, Non-Lethal [Other]		LD50 > 3.16 g/kg
Rabbit	Oral, NOS	
Acute Toxicity Acute Dermal Toxicity, Lethality [OECD 402]		LD50 > 2000 mg/kg bw.
Rabbit	Dermal	
ADME In vivo absorption study [Other]		When silica is inhaled by rats, it accumulates in the lungs and lymph nodes initially. When treatment ceases, the silica decreases.
Rat	Inhalation	
Carcinogenicity Carcinogenicity studies [Other]		No carcinogenic effects. -Pyrogenic silica was orally administered to rats (20 males, 20 females) in their feed (100 mg/kg) for 24 months.
Rat	Oral, Feed	
Eye Irritation In vivo Eye Irritation [Other]		Mild ocular irritation. - a single dose of an aqueous solution of pyrogenic silica (3 mg) was instilled in to the eyes of albino rabbits (n = 3).
Rabbit	Instillation	
Genotoxicity Bacterial reverse mutation test (Ames) [OECD 471]		Negative [Fumed silica.; up to 10,000 µg/ml.; With and without metabolic activation.; Strain tested: S. typhimurium (TA98, TA100, TA1535, TA1537, TA1538).]
Bacteria	In vitro exposure	
Genotoxicity Mammalian cell micronucleus test [OECD 487]		No clastogenicity observed. Test substance: Pyrogenic silica. Test concentration: up to 0.93mg/ml.
In-vitro culture	In vitro exposure	
Genotoxicity Mammalian bone marrow chromosome aberration test [OECD 475]		Negative. Test substance: silical gel. Dose tested: up to 5 x 1.4-5,000 mg/kg. Exposure duration : 6 hours.
Rat	Oral, NOS	
Repeated Dose Repeat Dose Oral Toxicity Study [Other]		NOAEL: 8980 mg/kg/d. (There were no treatment-related findings.) [12/sex/dose.; doses were 2170 and 7950 mg/kg/d for males and 2420 and 8980 mg/kg/d hydrated silica for females for 6 months.]
Rat	Oral, Feed	
Repeated Dose Repeat Dose Inhalation Toxicity Study [Other]		NOEL: 1.3 mg/m3. -rats, 50/sex/dose. -exposed to 1.3, 5.9, 31 mg/m3 silica for 6 h/d, 5 d/week, for 13 weeks.
Rat	Inhalation	
Repeated Dose Repeat Dose Inhalation Toxicity Study [Other]		No signs of silicosis. -workers (n=215) were exposed to silica between 1947 and 1959 using chest x-rays. Exposure ranged from 15 to 100 mg/m3, 2 to 6 mg/m3 , and 3 to 7 mg/m3. - Slight interlobar pleuritis seen.
Human	Inhalation	
Reproductive Toxicity Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test		NOEL was >500 mg/kg for developmental and reproductive toxicity. -Rats were fed 500 mg/kg/day pyrogenic silica for up to 6 months. There was no treatment related effects in offspring's and parental animals.
Rat	Oral, Feed	
Skin Irritation In vivo skin irritation [Other]		Non-irritating and non-toxic. -dusting powder that included micronized silica gel (amount not provided) on patients (n = 300).
Human	Dermal	
Skin Irritation In vivo skin irritation [Other]		Mild dermal irritation. -pyrogenic silica (5 or 10 g as a paste in water) was applied to the intact and abraded skin of albino rabbits (n = 4) daily, 5 d/week, for 15 applications.
Rabbit	Dermal	
Skin Sensitisation Repeat Insult Patch Test (RIPT) [Other]		little or no sensitising properties. -dusting powder that included micronized silica gel (amount not provided) on patients (n = 300).
Human	Dermal	
Skin Sensitisation Maximisation Test [OECD 406]		No reaction observed. - hydrated silica (20% in distilled water) was administered to 10 guinea pigs.
Guinea Pig	Dermal	

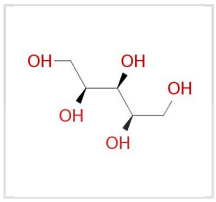
Physical/Chemical and Toxicological data used in generating these review are representative of publicly available data, and is provided for information purposes only.
For further information on any of the data or conclusions reported here, or for information Margins of Safety and how they are Calculated, please contact Delphic HSE.

ANNEX II - INGREDIENT DATA

Substance: Xylitol
CAS: 87-99-0
Function: Humectant; Skin Conditioning

Concentration in Product: 3%
Dermal Exposure Level: 0.022479527 mg/cm^2
Daily Body Burden: 0.1205121951mg/kg

Chemical Structure



Physical/Chemical Characteristics

Appearance	White Crystalline powder
Boiling Point	216 °C
Molecular Mass	152.15 g mol−1
Melting Point	92-96 °C
Specific Gravity	1.52 g/cm³

Toxicological Summary

The below information is a summary of the toxicological profile for this raw material, including a description of general hazards associated with the material as well as discussion of the most critical studies relating to the overall safety in use of this substance/mixture in consumer products. Details of the available toxicological data can be found overleaf.

Overall Toxicity Review:

A monosaccharide sugar added to improve the palatability of toothpaste in cosmetics. It also functions as a Humectant and Skin Conditioning agent in cosmetic products, and finds extensive usage within the human food chain; within the EU it is listed as E967 as a food additive.

Xylitol was non-irritant to rabbit skin, and would not be expected to possess significant ocular irritation potential. Although specific data on skin sensitisation potential was not available for review, the material is not known to be associated with allergenicity following skin contact or ingestion. The widespead use within the food and cosmetic industry evidences safety in this regard.

The material shows low oral acute toxicity, with a LD50 higher than 4000 mg/kg. It is not mutagenic under in vitro study conditions, and there was no evidence of reproductive toxicity or carcinogenicity in animal studies.

A NOAEL of 5000 mg/kg bw/day is selected from a rat carcinogenicity study. This value is protective of the NOAELs identified in a repeat dose study (20,000 mg/kg bw/day) and a reproductive toxicity studiy (6,770 mg/kg bw/day).

As dermal absorption is dependent on the molecular properties, concentration, exposure time and vehicle simultaneously, in the absence of relevant experimental data it is difficult to assess an exact value. If not stated otherwise within the risk assessment, we assume 100% dermal absorption, however it must be noted that for the majority of compounds, even low molecular weight, lipophilic compounds, dermal absorption is expected to be significantly lower than 100%.

Xylitol is authorised as a carrier at quantum satis in most type of food within the EU (EC 1333/2008, E967) and is considered safe for the whole population in a life perspective. In 1983, the JECFA confirmed a "not specified" ADI for the material - indicating it to be safe in diet without limit.

Based on the available toxicological data, and considering its widespread use in the food chain, Xylitol is considered unlikely to pose a risk of significant localised or systemic toxicity under normal conditions of use.

References

JECFA (1983). Summary of Evaluations Performed by the Joint FAO/WHO Expert Committee on Food Additives. Available at http://www.inchem.org/documents/jecfa/jeceval/jec_2404.htm (accessed 22 Jul 2020)

Margin(s) of Safety

Point of Departure - Animal Study: 5000.0000mg/kg
Exposure from Product 0.12051220mg/kg
Margin of Safety 41489.577

Physical/Chemical and Toxicological data used in generating these review are representative of publicly available data, and is provided for information purposes only.
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ANNEX II - INGREDIENT DATA

Xylitol

Acute Toxicity		LD50 > 4000 mg/kg
Acute Oral Toxicity, Lethality [OECD 401, OECD 423, OECD 425]		
Rat	Oral, Gavage	
Carcinogenicity		Non-carcinogenic. NOAEL = 10% (approx. 5000 mg/kg bw/day) 2-year study; 0, 2, 5, 10 and 20%. The LOAEL of 20% was due to enlargement of the cecum. No other adverse effects were observed.
Carcinogenicity studies [OECD 451]		
Rat	Oral, Feed	
Genotoxicity		Not mutagenic
Bacterial reverse mutation test (Ames) [OECD 471]		
Bacteria	In vitro exposure	
Genotoxicity		Negative
Mammalian chromosome aberration test [OECD 473]		
In-vitro culture	In vitro exposure	
Repeated Dose		NOAEL = 20 g/kg bw/day 0, 5, 10, 20 g/kg bw/day; 8/sex/dose
90-Day Oral Toxicity Study [OECD 408, OECD 409]		
Rat	Oral, Feed	
Reproductive Toxicity		NOAEL: 6770 mg/kg bw/day Exposure: 0%, 2%, 5%, 10% and 20% from Gestation Days 7 to 19 There was no indication of any embryotoxic or teratogenic effect in the young; weight development during the treatment period was retarded in the does.
In vivo reproductive toxicity study [Other]		
Rabbit	Oral, Feed	
Skin Irritation		Non-irritant.
In vivo skin irritation [Other]		
Rabbit	Dermal	

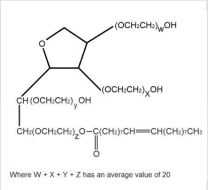
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ANNEX II - INGREDIENT DATA

Substance: Polysorbate 80
CAS: 9005-65-6
Function: Denaturant; Emulsifying; Surfactant

Concentration in Product: 3%
Dermal Exposure Level: 0.022479527 mg/cm^2
Daily Body Burden: 0.1205121951mg/kg

Chemical Structure



Physical/Chemical Characteristics

Appearance	yellow oily liquid
Boiling Point	>100 C
Flash Point	280C
Melting Point	-20.5 C
Odour	Slight fatty

pH	6.5 (3% aqu.)
Specific Gravity	1.06 - 1.10
Vapour Pressure	<0.1 kPa (@ 20°C)
Water Solubility	Soluble

Toxicological Summary

The below information is a summary of the toxicological profile for this raw material, including a description of general hazards associated with the material as well as discussion of the most critical studies relating to the overall safety in use of this substance/mixture in consumer products. Details of the available toxicological data can be found overleaf.

Overall Toxicity Review:

A highly ethoxylated oleate ester of sorbitol. Low potential to cause skin and eye irritation. Various grades are available with different degrees of ethoxylation, however the toxicological properties are similar. Materials have an extensive history of safe use in cosmetics and food.

Polysorbate 80 has low acute toxicity (oral LD50 > 38.0 g/kg) and is not or mildly irritating to skin, not irritating to the eyes, not sensitising. Polysorbate 80 was non-genotoxic in an Ames Assay.

A 28-day Oral Gavage study in rats identified a NOAEL of 3,700mg/kg/day, the highest tested dose. Whilst not likely to represent a true NOAEL.

A NOAEL of 5% in diet (equivalent to 2500 mg/kg bw/day) of polyoxyethylene (20) sorbitan monostearate (polysorbate 60) was found in life-span studies in rats. Based on it, JECFA set the group ADI of 0-25 mg/kg bw/day for polyoxyethylene (20) sorbitan monoesters of lauric, oleic, palimitic and stearic acid and triester of steatic acid (Polysorbates 20, 40, 60, 65 and 80) using a safety factor of 100 (JECFA 1973).

The EFSA panel re-evaluated the polyoxyethylene sorbitans (E432-E436). The Panel concluded that based on the NOAEL of 2500 mg/kg bw/day, identified from an oral carcinogenicity study with polysorbate 80 in rats and applying an uncertainty factor of 100, a group ADI of 25 mg/kg bw/day for polysorbates 20, 80, 40, 60 and 65 (E432, E433, E434, E435 and E436, respectively) can be established (EFSA 2015).

The molecular weight of Polysorbate 80 is 604.8 Da, that is over 500 Da, thus it is expected that a very low dermal absorption and a skin absorption rate of 10% is assumed for safety assessment according to SCCS (SCCS/1602/18) guidance.

CIR (Moore, 2015) reported that Polysorbate 80 was used in 932 products at a range of 0.00031-11.9% in leave-on products and 0.0038-18.1% in rinse-off products and concluded that it is safe in cosmetic when formulated to be non-irritating.

Overall, based on the available data and history of safe use in cosmetics and food, the inclusion of Polysorbate 80 at typical levels within consumer products is considered most unlikely to pose an undue risk of significant adverse effects.

References:

JECFA, Polyethylene (20) sorbitan Monooleate (Synonyms: Polysorbate 80). CAS no. 9005-65-6. Available at: http://apps.who.int/food-additives-contaminants-jecfa-database/chemical.aspx?chemID=2507. Report: NMRS 53/TRS 539-JECFA 17/20. Tox Monograph: FAS 5/NMRS 53A-JECFA 17/254.

EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS). (2015). 'Scientific Opinion on the re-evaluation of polyoxyethylene sorbitan monolaurate (E 432), polyoxyethylene sorbitan monooleate (E 433), polyoxyethylene sorbitan monopalmitate (E 434), polyoxyethylene sorbitan monostearate (E 435) and polyoxyethylene sorbitan tristearate (E 436) as food additives'. *EFSA Journal*, 13(7), 4152.

Moore, J. (1984). 'Final report on the safety assessment of polysorbates 20, 21, 40, 60, 61, 65, 80, 81, and 85'. J Am Coll Toxicol, 3, 1-82.

CIR (2015). Safety Assessment of Polysorbates as Used in Cosmetics.

Margin(s) of Safety

Point of Departure - Animal Study:	2500.0000mg/kg	**Exposure from Product**	0.12051220mg/kg	**Margin of Safety**	20744.7885
Point of Departure - Human Data:	25.0000mg/kg	**Exposure from Product**	0.12051220mg/kg	**Margin of Safety**	207.447885

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ANNEX II - INGREDIENT DATA

Polysorbate 80

Acute Toxicity		Oral LD50 > 38.0 g/kg
Acute Toxicity, Lethality [Other]		
Rat	Oral, NOS	
Carcinogenicity		NOAEL = 5% in diet (2500 mg/kg bw/day), Polysorbate 80, 2 years feed study.
Carcinogenicity studies [OECD 451]		
Rat	Oral, Feed	
Eye Irritation		Non-irritant 100% Polysorbate 80 applied, 6 unwashed and 3 washed with water after 2 seconds. No irritation.
Draize [Other]		
Rabbit	Instillation	
Genotoxicity		Non-genotoxic, with and without metabolic activation. (S. typhimurium TA1535, TA1537, TA98 and TA100 | E. coli strain WP2 uvr A)
Bacterial reverse mutation test (Ames) [OECD 471]		
Bacteria	In vitro exposure	
Repeated Dose		NOAEL = 3,700mg/kg/day (6 rats/dose, 148, 740 and 3,700mg/kg/day. 28-day dosing following 28 days of high-fat diet. No adverse effects at any dose.)
Repeat Dose Oral Toxicity Study [Other]		
Rat	Oral, Gavage	
Repeated Dose		NOEL = 5% (equivalent to 2500 mg/kg bw) Doses: 2%, 5%, 10% and 25% of Polysorbate 80. The whole life-span study. No effect at 2% and 5% levels.
Chronic Toxicity Studies in Rodents [OECD 452]		
Rat	Oral, Feed	
Reproductive Toxicity		NOAEL = 5% (equivalent to 2500 mg/kg bw) Doses: 5%, 10%, 20% in diet. The whole life-span study. Observations were also made on three successive generations. This extensive study included tests on gestation and fertility, mortality, blood and urine constituents, and histopathology. No abnormalities were found at the 5% level.
In vivo reproductive toxicity study [Other]		
Rat	Oral, Feed	
Skin Irritation		Not irritating (100% Polysorbate 80 applied under occlusion from 15mins to 4hrs to human volunteers. 1 positive reaction from 29 volunteers.)
In vivo skin irritation [Other]		
Human	Dermal	
Skin Irritation		Non to minimal irritating 100% Polysorbate 80 applied. 6 rabbits: PII: 0.0, no signs of irritation. 9 rabbits: PII 0.17 (max = 4.0), minimal irritation
In vivo skin irritation [Other]		
Rabbit	Dermal	
Skin Sensitisation		Not sensitising. Polysorbate 80 tested in guinea pigs by repeated intradermal infections of a 0.1% in saline followed by a challenge dose after 2 weeks. There was no indication of sensitisation reported.
Maximisation Test [Other]		
Guinea Pig	Dermal	
Skin Sensitisation		Minimal irritation; no sensitisation. 2.5% Polysorbate 80 in cream. 210 subjects.
Repeat Insult Patch Test (RIPT) [Other]		
Human	Dermal	

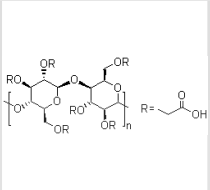
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ANNEX II - INGREDIENT DATA

Substance: Cellulose Gum
CAS: 9004-32-4; 99331-82-5; 9000-11-7
Function: Emuslion Stabilising; Film Forming; Viscosity Controlling; Binding; Masking

Concentration in Product: 2.5%
Dermal Exposure Level: 0.018732939 mg/cm^2
Daily Body Burden: 0.1004268293mg/kg

Chemical Structure



Physical/Chemical Characteristics

Appearance	White powdered solid
Flammability	Auto-Ignition Temperature: 370°C
Water Solubility	Readily soluble
Odour	Odourless

Toxicological Summary

The below information is a summary of the toxicological profile for this raw material, including a description of general hazards associated with the material as well as discussion of the most critical studies relating to the overall safety in use of this substance/mixture in consumer products. Details of the available toxicological data can be found overleaf.

Overall Toxicity Review:

A sodium salt of carboxymethylcellulose, which is essentially an inert thickening agent with a long history of safe use in consumer products. It is an approved food additive in EU (E 466) and given the generally recognized as safe (GRAS) status by US FDA Select Committee on GRAS Substances (SCOGS) as a multiple purpose food substance upon fulfilling required specifications (21CFR182.1745). In cosmetics it is commonly used as a binding, emulsion stabilising, film forming, masking and viscosity controlling agent.

It is not expected to be irritating to skin and eyes, nor be associated with significant allergenic potential. Being practically non-toxic from acute oral exposures.

Repeated dose oral and dermal studies also found no systemic toxic effects in treated animals. Rats feeding at up to 1.0 g/kg Cellulose Gum for 25 months showed no significant differences were noted between the controls and test animals in urinalyses, haematological values, fertility, or findings at necropsy. No neoplasms were found in the test rats. Although it may not be the true NOAEL as the highest tested dose in the study, 1.0 g/kg bw/day is chosen as a conservative point of departure for safety assessment.

In a three-generation feeding study in rats at up to 1.0 g/kg feed found no significant adverse effects in fertility, and the Cosmetic Ingredients Review (CIR) Expert panel reported the ingredient being used as negative control in multiple reproductive studies at up to 2% (CIR, 2009).

It is demonstrated to be negative in an Ames test as well as in a mammalian chromosomal aberration test. Although there are no carcinogenicity data, the long history of safe use in cosmetics, food, pharmaceuticals, and consumer products suggests such potential is unlikely.

As dermal absorption is dependent on the molecular properties, concentration, exposure time and vehicle simultaneously, in the absence of relevant experimental data it is difficult to assess an exact value. If not stated otherwise within the risk assessment, we assume 100% dermal absorption, however it must be noted that for the majority of compounds, even low molecular weight, lipophilic compounds, dermal absorption is expected to be significantly lower than 100%.

In 2009, the CIR Expert Panel reported the use of up to 20% in cosmetic products, and the Panel concluded it is safe in the practices of use and concentration described in the assessment (CIR, 2009).

Overall, this material is not expected to produce significant localised or systemic toxicity at typical levels found within cosmetic and consumer products.

References:

FDA GRAS. https://www.fda.gov/food/ingredientspackaginglabeling/foodadditivesingredients/ucm091048.htm (last accessed15:54:47 25/03/2019)

CIR (2009). Amended Safety Assessment of Cellulose and Related Polymers as used in Cosmetics, *Cosmetic Ingredient Review,*

Margin(s) of Safety

Point of Departure - Animal Study: 1000.0000mg/kg **Exposure from Product** 0.10042683mg/kg **Margin of Safety** 9957.49848

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ANNEX II - INGREDIENT DATA

Cellulose Gum

Acute Toxicity		LD50 = 27000 mg/kg bw
Acute Toxicity, Lethality [Other]		
Rat	Oral, NOS	
Eye Irritation		Non-irritating (score of 0 out of 110) [0.1 mg in water or 0.01g as solid, no rinse, exposure and observation up to 7 days]
Draize [Other]		
Rabbit	Oral, Feed	
Genotoxicity		Negative with and without metabolic activation.
Bacterial reverse mutation test (Ames) [OECD 471]		
Bacteria	In vitro exposure	
Genotoxicity		Negative with and without metabolic activation.
In vitro genotoxicity assay [Other]		
In-vitro culture	In vitro exposure	
Phototoxicity		Minimally irritating but not phototoxic [0.5% in liquid eyeliner formulation]
In vivo phototoxicity		
Rabbit	Dermal	
Repeated Dose		No toxic effects (slight decrease in growth was attributed to a decrease in nutrient food intake resulting from the bulkiness of the diet) [20% in diet, 63 day exposure]
Repeat Dose Oral Toxicity Study [Other]		
Rat	Oral, Feed	
Repeated Dose		Not systemically toxic (No significant adverse effects were noted) [3% in wrinkle smoother product or 1.1% in lotion, 13 week exposure]
Repeat Dose Dermal Toxicity Study [Other]		
Rat	Dermal	
Repeated Dose		NOAEL = 1.0 g/kg No significant differences were noted between the controls and test animals in urinalyses, hematological values, fertility (through three generations), or findings at necropsy. No neoplasms were found in the test rats [0, 0.1, 0.5, 1.0 g/kg feed of Cellulose Gum, 25 months]
Repeat Dose Oral Toxicity Study [Other]		
Rat	Oral, Feed	
Reproductive Toxicity		No significant adverse effects were noted in fertility, gross or microscopic lesions, urinalyses, and hematological values [0, 0.1, 0.5, and 1.0 g/kg feed, 3-generation study]
In vivo reproductive toxicity study [Other]		
Rat	Oral, Feed	
Skin Irritation		No signs of skin irritation [Undiluted, application on shaved abdominal area, 5 times per week, 4-week exposure]
In vivo skin irritation [Other]		
Rabbit	Dermal	
Skin Sensitisation		Non-irritating and non-sensitizing [Undiluted, SIPT, 200 subjects]
Maximisation Test [Other]		
Human	Dermal	

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ANNEX II - INGREDIENT DATA

Substance: Mentha Piperita (Peppermint) Oil
CAS: 84082-70-2; 8006-90-4
Function: Refreshing; Perfuming; Masking; Tonic

Concentration in Product: 1%
Dermal Exposure Level: 0.007493176 mg/cm^2
Daily Body Burden: 0.0401707317mg/kg

Chemical Structure



Physical/Chemical Characteristics

Toxicological Summary

The below information is a summary of the toxicological profile for this raw material, including a description of general hazards associated with the material as well as discussion of the most critical studies relating to the overall safety in use of this substance/mixture in consumer products. Details of the available toxicological data can be found overleaf.

Overall Toxicity Review:

An Essential Oil that finds widespread use in Foodstuffs and in Traditional Medicine.

According to the Cosmetic Ingredient Review (CIR), "European and American peppermint oil is distilled with steam from the fresh, above-ground parts of the flowering plant Mentha piperita Linne, rectified by distillation and not dementholized" (CIR 2018). The CIR also reported the major constituents to include the terpenes: (-)-menthol (30 - 55%),(-)-menthone (14 - 32%), (+)-isomenthone (1.5 - 10%), (-)-menthyl acetate (2.8-10%), (+)-menthofuran (1.0 -9.0%), and 1,8-cineol (3.5 - 14%).

In the neat form the material is not irritating, however, it may provoke an allergic reaction due to the presence of up to 3% Limonene (CIR, 2018). Also reported to contain high concentrations of Menthol, which is reported to be a rare allergen, with reactions typically only being seen in those who frequently handle the neat oil (i.e. occupational exposure). Skin sensitisation data on menthol indicates it is not a skin sensitiser. Data on the oil itself indicated it is not sensitising. Overall, the risk of skin sensitisation is considered to be low in consumer settings when formulated to be not sensitising. The oil is also considered to be unlikely to be phototoxic based on in-vivo tests.

The oil is expected to be well tolerated following acute dermal and oral exposure with LD50 values larger than 5000 and 2000 mg/kg bw/day, respectively.

The compound is unlikely to be genotoxic based on negative results obtained from in-vitro tests.

A NOAEL of 40 mg/kg bw/day was reported from a 90-day repeated dose toxicity study on rats. Another NOAEL of 400 mg/kg bw/day from a 28-day repeated dose toxicity study. As a conservative approach the lowest NOAEL can be selected as a point of departure for risk assessment. However, it must be noted that the levels of the constituents of peppermint oil can vary significantly depending on a variety of factors.

In the US, peppermint oil is generally recognised as safe (GRAS) for food use by the FDA (21 CFR 182.20, 172.230). It is also an inactive component of drug products that have been approved by the FDA (UNII AV092KU4JH). Peppermint oil also has a history of safe use in cosmetic products, and was concluded as safe in the current concentrations and practices of use by the CIR (up to 5% in leave on products and up to 2.9% in products with incidental ingestion possibilities).

At typical levels within a Leave-on Consumer Product it would not be expected to pose an undue risk of adverse reactions. However particular care should be taken in products applied to the Lips (due to the particularly thin and sensitive nature of the skin on the lips) along with Massage Oils (due to the high exposure levels). It must be noted that appropriate grades of material must be used to ensure safety.

References:

CIR 2018. Amended Safety Assessment of Mentha piperita (Peppermint)-Derived Ingredients as Used in Cosmetics.

US FDA Inactive Ingredient for Approved Drug Products. Peppermint oil, 8006-90-4. Available at: https://www.accessdata.fda.gov/scripts/cder/iig/index.cfm?event=BasicSearch.page (Accessed 13th Mar. 2019)

US FDA Substances Added to Food (formerly EAFUS), Peppermint oil, 8006-90-4. Available at: https://www.accessdata.fda.gov/scripts/fdcc/index.cfm?set=FoodSubstances&id=PEPPERMINTOILMENTHAPIPERITA (Accessed 13th Mar. 2019)

Margin(s) of Safety

Point of Departure - Animal Study: 40.0000mg/kg
Exposure from Product 0.04017073mg/kg
Margin of Safety 995.749848

Physical/Chemical and Toxicological data used in generating these review are representative of publicly available data, and is provided for information purposes only.
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ANNEX II - INGREDIENT DATA

Mentha Piperita (Peppermint) Oil

Acute Toxicity Acute Oral Toxicity, Lethality [OECD 401, OECD 423, OECD 425]		Peppermint oil diluted in olive oil. LD 50 = 2410 mg/kg bw
Mouse	Oral, NOS	
Acute Toxicity Acute Oral Toxicity, Lethality [OECD 401, OECD 423, OECD 425]		Peppermint oil LD50 = 2650 mg/kg bw (>= 2 300 - <= 3 000 mg/kg bw)
Rat	Oral, Gavage	
Acute Toxicity Acute Dermal Toxicity, Lethality [OECD 402]		Peppermint oil LD50 > 5000 mg/kg bw
Rabbit	Dermal	
Genotoxicity Bacterial reverse mutation test (Ames) [OECD 471]		Negative with and without metabolic activation.
Bacteria	In vitro exposure	
Genotoxicity Genetic Toxicology: In Vitro Sister Chromatid Exchange Assay in Mammalian Cells [OECD 479]		Essential oil extracted from peppermint (Menthaxpiperita L.) Negative without metabolic activation
In-vitro culture	In vitro exposure	
Phototoxicity In vivo phototoxicity		Non-phototoxic at 100%.
Mouse	Dermal	
Repeated Dose Repeat Dose Oral Toxicity Study [Other]		Peppermint oil was given to groups of 28 wistar rats at doses of 10, 40, and 100 mg/kg bw for 90 days. The sample was diluted in soybean oil. The NOAEL was determined to be 40 mg/kg bw/day.
Rat	Oral, NOS	
Repeated Dose 28-day Oral Toxicity Study [OECD 407]		Peppermint oil, 0, 100, 200, and 400 mg/kg bw/day. No toxicologically relevant effects were observed in females. In male rats, alpha-2-microglobulin-associated hydrocarbon nephropathy was observed, which is not relevant to humans as it is a male rat-specific effect. A NOAEL of 400 mg/kg bw/day (highest tested dose) was established for peppermint oil.
Rat	Oral, Gavage	
Skin Irritation Draize Test [OECD 404]		Peppermint Flavour – Brazilian, not irritating The mean scores calculated from the numerical values given to the skin irritation observed at the 24, 48, and 72 hour examinations were 1.6, 1.6, and 1.8 resp., for erythema and also for oedema
Rabbit	Dermal	
Skin Sensitisation Repeat Insult Patch Test (RIPT) [Other]		In a HRIPT with 104 male and female subjects, 20% peppermint oil was non irritating and non-sensitising.
Human	Dermal	
Skin Sensitisation Buehler [OECD 406]		Menthol: Not sensitising Test material: L-menthol Dose level: 25% in ethanol:DEP (for induction and challenge)
Guinea Pig	Dermal	
Skin Sensitisation Maximisation Test [Other]		Menthol: Not sensitising, no positive reactions 25 volunteers, 8 % D/L-menthol in petrolatum
Human	Dermal	
Skin Sensitisation Local Lymph Node Assay [OECD 429, OECD 442A, OECD 442B]		Menthol: L-Menthol was not sensitising in the mouse local lymph node assay. The increase in isotope incorporation was less than 3 -fold at 1, 10 and 30 %. Also the response was not consistent with a biological dose-response.
Mouse	Dermal	

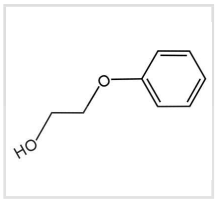
Physical/Chemical and Toxicological data used in generating these review are representative of publicly available data, and is provided for information purposes only.
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ANNEX II - INGREDIENT DATA

Substance: Phenoxyethanol
CAS: 56257-90-0; 37220-49-8; 122-99-6
Function: Preservative

Concentration in Product: 0.5%
Dermal Exposure Level: 0.003746588 mg/cm^2
Daily Body Burden: 0.0200853659mg/kg

Chemical Structure



Physical/Chemical Characteristics

Appearance	Viscous liquid - colourless
Odour	Faint aromatic (Rose aroma)
Specific Gravity	1.123
pH	7.0
Melting Point	14°C
Boiling Point	245°C
Water Solubility	2.67E+04 mg/L @ 20°C (2.6%)
Log Kow	1.16
Vapour Pressure	0.007 mm HG @ 25°C

Toxicological Summary

The below information is a summary of the toxicological profile for this raw material, including a description of general hazards associated with the material as well as discussion of the most critical studies relating to the overall safety in use of this substance/mixture in consumer products. Details of the available toxicological data can be found overleaf.

Overall Toxicity Review:

A preservative material that finds widespread use in consumer products.

The neat material is a mild skin irritant and an eye irritant. No evidence of allergenic potential in common animal assays or human patch testing. Undiluted phenoxyethanol under occlusion and with UVA exposure was not photoirritating to 28 panelists (CIR 1990).

Phenoxyethanol displays moderate acute toxicity by the oral route. The available data suggests low acute toxicity by the dermal and inhalation routes.

The French National Agency for Medicines and Health Products Safety (ANSM) have previously recommended to prohibit the use of phenoxyethanol in cosmetic products for the nappy zone and to reduce the allowed phenoxyethanol concentration to 0.4 % in other types of products for children under the age of three. A review by the Scientific Committee for Consumer Safety (SCCS) in 2016 indicated they believed current levels of use (up to 1% in all products) were acceptable based on a corrected NOAEL of 357 mg/kg bw/day from a 90-day repeat-dose dermal study in rabbits (Dow unpublished report, 1986). As part of this process they indicated that a Margin of Safety (MoS) of 25 or more would be acceptable as opposed to the standard 100-fold; a conclusion based on the known toxicokinetic data.

Negative in the Ames Assay with and without metabolic activation, and no evidence of significant carcinogenic effects. Has a history of safe use in Cosmetics within the EU at up to 1% and the Cosmetic Ingredient Review (CIR, 1990) panel has previously concluded that it can be considered safe at up to 5%.

As dermal absorption is dependent on the molecular properties, concentration, exposure time and vehicle simultaneously, in the absence of relevant experimental data it is difficult to assess an exact value. If not stated otherwise within the risk assessment, we assume 100% dermal absorption, however it must be noted that for the majority of compounds, even low molecular weight, lipophilic compounds, dermal absorption is expected to be significantly lower than 100%.

Based on the available data it is considered that the use of phenoxyethanol at typical levels within a consumer product would be unlikely to produce significant localised or systemic toxicity.

References:
CIR (1990). Final Report on the Safety Assessment of Phenoxyethanol. JACT, 9(2).

SCCS (2016). Opinion on phenoxyethanol SCCS/1575/16.

Margin(s) of Safety

Maximum Recommended Exposure	1.0000%	**Exposure from Product**	0.50000000%	**Margin of Exposure**	2.00
Point of Departure - Animal Study:	357.0000mg/kg	**Exposure from Product**	0.02008537mg/kg	**Margin of Safety**	17774.1348

Physical/Chemical and Toxicological data used in generating these review are representative of publicly available data, and is provided for information purposes only.
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ANNEX II - INGREDIENT DATA

Phenoxyethanol

Acute Toxicity Acute Oral Toxicity, Lethality [OECD 401, OECD 423, OECD 425]		Combined LD50 = 2740 mg/kg bw Female LD50 = 1840 mg/kg bw Male LD50 = 4070 mg/kg bw
Rat	Oral, Gavage	
Acute Toxicity Acute Toxicity, Lethality [Other]		LD50 > 2,214 mg/kg bw [Limit dose of 2 mL/kg bw, corresponding to 2214 mg/kg bw. Protocol: Draft IRLG (Interagency Regulatory Liaison Group) Guidelines for Selected Acute Toxicity Tests (August. 1979).]
Rabbit	Dermal	
Acute Toxicity Acute Toxicity, Lethality [Other]		LC50 > 1000 mg/m³ air (nominal) [Based on OECD 412 sub-acute inhalation toxicity. Exposure: 6 hours per day, 5 days per week for 14 days (10 exposures)]
Rat	Inhalation	
ADME In vitro skin absorption [OECD 428]		37% + 10% dermal absorption in rinse-off formulations. 78% + 7% in leave-on formulations
Ex-vivo Tissue	In vitro exposure	
Carcinogenicity Carcinogenicity studies [OECD 451]		NOAEL = 5000 ppm (468 mg/kg bw/day in males and 586 mg/kg bw/day in females.). [No evidence of carcinogenic activity of phenoxyethanol in male or female mice. NOAEL related to a decreases in cholesterol, phospholipids and triglycerides.]
Mouse	Oral, Water	
Eye Irritation Draize, Standard [OECD 405]		Irritating [0.1ml of undiluted test substance was placed into the conjunctival sac of the right eye of rabbits. Clear signs of eye irritation were observed in all three animals.]
Rabbit	Instillation	
Genotoxicity Bacterial reverse mutation test (Ames) [OECD 471]		Negative with and without metabolic activation.
Bacteria	In vitro exposure	
Genotoxicity Mammalian erythrocyte micronucleus test [OECD 474]		Phenoxyethanol did not induce an increase in number of cells with micronuclei in erythrocytes of treated mice.
Mouse	Intraperitoneal	
Genotoxicity Mammalian bone marrow chromosome aberration test [OECD 475]		Phenoxyethanol did not induce an increase in number of cells with chromosomal aberrations in erythrocytes of treated rats.
Rat	Oral, Gavage	
Repeated Dose 90-day Dermal Toxicity Study [OECD 411]		NOAEL = 500 mg/kg bw/day. Corrected NOAEL with multiplying factor of 5/7 = 357mg/kg/day. [Concentrations: 0, 50, 150, 500 mg/kg bw/day. 6 hours per day, 5 days/week for 13 consecutive weeks.]
Rabbit	Dermal	
Repeated Dose 90-Day Oral Toxicity Study [OECD 408, OECD 409]		NOAEL 369 mg/kg bw/day (actual dose received) [0, 1250, 2500, 5000, 10000, and 20000 mg/L dose in water.]
Rat	Oral, Water	
Repeated Dose 28-day Inhalation Toxicity Study [OECD 412]		NOAEC = 48.2 mg/m³ air (analytical) [Concentrations: 0, 40, 200, 1000 mg/m³ (nominal conc.)]
Rat	Inhalation	
Reproductive Toxicity In vivo reproductive toxicity study [Other]		NOAEL for Male mice (F0) was 2.5% in diet, corresponding to 4000 mg/kg bw/day. NOAEL for parental males was 400 mg/kg bw/day and females was 950 mg/kg bw/day
Mouse	Oral, Gavage	
Reproductive Toxicity Prenatal Development Toxicity Study [OECD 414]		Maternal Toxicity NOAEL = 300 mg/kg bw/day Developmental NOAEL = 1000 mg/kg bw/day.
Rat	Oral, Gavage	
Skin Irritation Draize Test [OECD 404]		Non-irritating (neat material)
Rabbit	Dermal	
Skin Sensitisation Maximisation Test [OECD 406]		Non-sensitising [10 animals per treatment group]
Guinea Pig	Dermal	

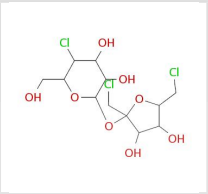
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ANNEX II - INGREDIENT DATA

Substance: Sucralose
CAS: 56038-13-2
Function: Skin Conditioning

Concentration in Product: 0.5%
Dermal Exposure Level: 0.003746588 mg/cm^2
Daily Body Burden: 0.0200853659mg/kg

Chemical Structure



Physical/Chemical Characteristics

Appearance	Off-White Amorphous Solid
Boiling Point	669.4 °C at 760 mmHg
Flash Point	358.7 °C
Molecular Mass	397.63 g/mol
pH	Neutral in aqueous solution
Specific Gravity	1.69 g/cm3
Water Solubility	Soluble

Toxicological Summary

The below information is a summary of the toxicological profile for this raw material, including a description of general hazards associated with the material as well as discussion of the most critical studies relating to the overall safety in use of this substance/mixture in consumer products. Details of the available toxicological data can be found overleaf.

Overall Toxicity Review:

A selectively tri-chlorinated analog of sucrose (1,6-fructo- and 4-galacto-chlorinated), sucralose is a direct food additive as a multipurpose additive that meets the specifications of the Foods Chemical Codex; it is used as a sweetener in foods generally, in accordance with current GMP in an amount not to exceed that reasonably required to accomplish the intended effect (21CFR172.831). It is also listed in the USP/NF as an inactive ingredient or sweetening agent in pharmaceuticals. In cosmetics, it functions as a skin conditioning agent.

It is not absorbed in the human gut, and has a very high oral LD50 (> 10 g/kg). Non-animal models demonstrated low order of irritating potential to skin and eyes, and no sensitising effects observed in guinea pigs. A lip balm formulation containing 0.6% sucralose is also not an irritant or sensitiser in human patch testing.

The ingredient is not genotoxic in both in-vitro and in-vivo models. Repeated dose and reproductive toxicity studies mostly identified reduced body weight gain as the major systemic outcome. However, this is mostly secondary to reduced food intake because of impalatability of the diet. To date there are adequate evidence to believe that there are no concerns about mutagenicity, carcinogenicity, developmental or reproductive toxicity.

The CIR Expert Panel reported usage of up to 0.6% in leave-on and up to 1.2% in rinse-off cosmetic formulations, and concluded the ingredient is safe in present practices of use. The EU Scientific Committee on Food (SCF) concludes that sucralose is acceptable as a sweetener for general food use and that a full ADI of 0-15 mg/kg bw can be established (SCF/CS/ADDS/EDUL/190). U.S. Food and Drug Administration (USFDA) approved sucralose as a general-purpose sweetener. The acceptable daily intake (ADI) for sucralose in US is 5mg/kg body weight/day. Use in a non-powdered form in a consumer product at a low level is unlikely to result in a serious risk of adverse effects.

References

CIR report (2013), Safety Assessment of Monosaccharides and Disaccharides as Used in Cosmetics

SCF/CS/ADDS/EDUL/190 Final (2000), Opinion of the Scientific Committee on Food on sucralose, https://ec.europa.eu/food/sites/food/files/safety/docs/sci-com_scf_out68_en.pdf

USFDA (2018) Additional information about high-intensity sweeteners perfmittes for use in food in the United States, https://www.fda.gov/food/food-additives-petitions/additional-information-about-high-intensity-sweeteners-permitted-use-food-united-states

Margin(s) of Safety

Maximum Recommended Exposure	1.2000%	**Exposure from Product**	0.50000000%	**Margin of Exposure**	2.40
Point of Departure - Human Data:	5.0000mg/kg	**Exposure from Product**	0.02008537mg/kg	**Margin of Safety**	248.937462

Physical/Chemical and Toxicological data used in generating these review are representative of publicly available data, and is provided for information purposes only.
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ANNEX II - INGREDIENT DATA

Sucralose

Acute Toxicity		LD50 > 10000 mg/kg
Acute Oral Toxicity, Lethality [OECD 401, OECD 423, OECD 425]		
Rat	Oral, Gavage	
Eye Irritation		IVIS score of -0.04 and does not require classification for eye irritation
Bovine Corneal Opacity & Permeability (BCOP) Test [OECD 437]		
Ex-vivo Tissue	Instillation	
Genotoxicity		Not mutagenic in the absence and presence of metabolic activation up to 10000 ug/plate
Bacterial reverse mutation test (Ames) [OECD 471]		
Bacteria	In vitro exposure	
Genotoxicity		No treatment induced damage to chromosomes or other damage leading to micronucleus formation in polychromatic erythrocytes of treated mice after 24, 48, or 72 hours of exposure to sucralose at up to 5000 mg/kg bw/day.
Mammalian erythrocyte micronucleus test [OECD 474]		
Mouse	Oral, Gavage	
Repeated Dose		NOAEL > 3000 mg/kg bw/day Dosages of up to 3000 mg/kg/day for 26 weeks
Repeat Dose Oral Toxicity Study [Other]		
Rat	Oral, Gavage	
Reproductive Toxicity		NOAEL - Reproductive endpoints = 3% in diet - General toxicity = 1% in diet
Two-Generation Reproduction Toxicity [OECD 416]		
Rat	Oral, Feed	
Reproductive Toxicity		Maternal effects NOEL = 350 mg/kg bw/day Fetal effects NOAEL > 1000 mg/kg bw/day
In vivo reproductive toxicity study [Other]		
Rabbit	Oral, Gavage	
Skin Irritation		Not considered to be irritant in the in vitro skin model EpiDerm SIT (EPI-200)
Reconstructed Human Epidermis (RHE) Test [OECD 431, OECD 439]		
Human	In vitro exposure	
Skin Sensitisation		Determined to not elicit delayed contact hypersensitivity in guinea pigs
Maximisation Test [OECD 406]		
Guinea Pig	Dermal	
Skin Sensitisation		Non-sensitizing and non-irritating (0.6% in lip balm product)
Repeat Insult Patch Test (RIPT) [Other]		
Human	Dermal	

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ANNEX II - INGREDIENT DATA

Substance: Tetrasodium Pyrophosphate
CAS: 7722-88-5
Function: Anticaking; Chelating; Oral care; Buffering

Concentration in Product: 0.5%
Dermal Exposure Level: 0.003746588 mg/cm^2
Daily Body Burden: 0.0200853659mg/kg

Chemical Structure

Physical/Chemical Characteristics

Appearance	White Crystalline Solid
Molecular Mass	265.91
Melting Point	622 - 985C
pH	10.3
Specific Gravity	2.53
Water Solubility	Soluble

Toxicological Summary

The below information is a summary of the toxicological profile for this raw material, including a description of general hazards associated with the material as well as discussion of the most critical studies relating to the overall safety in use of this substance/mixture in consumer products. Details of the available toxicological data can be found overleaf.

Overall Toxicity Review:

Tetrasodium pyrophosphate is an alkaline salt of phosphoric acid. It was self-classified as H302 Harmful if swallowed, Category 4.

In the neat form and at 10 %, Tetrasodium pyrophosphate irritating the occular tissues of the Rabbit on the Draize test. No evidence of skin irritation. Not a skin sensitiser; negative at concentrations up to 10 % in the Mouse Local Lymph Node Assay.

Low acute systemic toxicity evident by oral and dermal LD50 values equal to or greater than 2 g/kg bw.

A no-observed adverse-effect level (NOAEL) of 500 mg/kg bw was reported from a repeated dose 90-day oral toxicity study using rat. This value is considered as an appropriate Point of Departure.

No evidence of genotoxicity was reported from the S. typhimurium bacterial reverse mutation test, micronueus test using human peripheral blood culture and in the cell gene mutation test with mouse lymphoma cells. Furthermore the material was not found carcinogenic in 3-generation oral study using rats. Reproductive and developmental toxicity was tested in the prenatal studies in which mice were administered Tetrasodium Pyrophosphate from day 6 to 16 of gestation. No effects on fetuses or the mother were noted at up to 130 mg/kg bw per day.

As dermal absorption is dependent on the molecular properties, concentration, exposure time and vehicle simultaneously, in the absence of relevant experimental data it is difficult to assess an exact value. If not stated otherwise within the risk assessment, we assume 100% dermal absorption, however it must be noted that for the majority of compounds, even low molecular weight, lipophilic compounds, dermal absorption is expected to be significantly lower than 100%.

In 2016, The Cosmetic Ingredient Committee (CIR) expert panel report the use of Tetrasodium pyrophosphate in a total of 118 cosmetics, at concentrations ranging from 0.03% to 3% and 0.0000014% to 6% in leave-on and rinse-off products, respectively. They concluded that this material is safe in the present practices of use and concentration in cosmetics, when formulated to be non-irritating.

In conclusion, at typical levels of use where ingestion and eye contact are minimal, the material would not be expected to pose an undue risk of significant adverse effects.

References:

CIR (2016). Safety Assessment of Phosphoric Acid and Its Salts as Used in Cosmetics. Final report released on November, 16 2016. Available at https://online.personalcarecouncil.org/ctfa-static/online/lists/cir-pdfs/FR710.pdf.

Margin(s) of Safety

Point of Departure - Animal Study: 500.0000mg/kg
Exposure from Product 0.02008537mg/kg
Margin of Safety 24893.7462

Physical/Chemical and Toxicological data used in generating these review are representative of publicly available data, and is provided for information purposes only.
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ANNEX II - INGREDIENT DATA

Tetrasodium Pyrophosphate

Acute Toxicity Acute Oral Toxicity, Lethality [OECD 401, OECD 423, OECD 425]		LD50 = 3770 mg/kg
Rat	Oral, Gavage	
Acute Toxicity Acute Toxicity, Lethality [Other]		LD50 > 2 000 mg/kg bw
Rabbit	Dermal	
Carcinogenicity Carcinogenicity studies [Other]		[3-generation study in which rats were fed diet containing up to 1.7% Potassium Metaphosphate and up to 5% Tetrasodium Pyrophosphate] Not carcinogenic
Rat	Oral, Feed	
Eye Irritation Draize, Standard [OECD 405]		Mild eye irritant (insuffuicient information provided for CLP classification)
Rabbit	Instillation	
Eye Irritation Draize [Other]		Irritation at 10 %
Rabbit	Instillation	
Genotoxicity Mammalian cell micronucleus test [OECD 487]		No evidence of structural of numerical aberrations of chromosomes up to a concentration of 2000 µg/mL +/- S9 metabolic activation
In-vitro culture	In vitro exposure	
Genotoxicity Mammalian cell gene mutation test (TK gene) [OECD 490]		Not mutagenic at up to 2000 µg/mL +/- S9 metabolic activation
In-vitro culture	In vitro exposure	
Genotoxicity Bacterial reverse mutation test (Ames) [OECD 471]		Not mutagenic at up to 4820 µg/plate on Salmonella typhimurium strains TA98, TA100, TA1535, and TA1537, and Escherichia coli strain WP2uvrA +/- metabolic activation.
In-vitro culture	In vitro exposure	
Repeated Dose 90-Day Oral Toxicity Study [OECD 408, OECD 409]		250, 500, 1000 mg/kg/day; 10/sex/dose NOAEL = 500 mg/kg (kidney effects at 1000)
Rat	Oral, Gavage	
Repeated Dose Repeat Dose Oral Toxicity Study [Other]		39 weeks study LOEL = 495 mg/kg/day (highest dose tested) based on slight growth retardation during the first part of the experiment and slight renal calcification after 39 weeks.
Rat	Oral, Feed	
Reproductive Toxicity Prenatal Development Toxicity Study [OECD 414]		exposure from GD6 to GD15 1.3, 6, 28, 130 mg/kg bw/day NOAEL = 130 mg/kg bw/day
Mouse	Oral, Gavage	
Skin Irritation Draize Test [OECD 404]		Not irritating
Rabbit	Dermal	
Skin Sensitisation Local Lymph Node Assay [OECD 429, OECD 442A, OECD 442B]		2.5, 5, 10% Not sensitising
Mouse	Dermal	

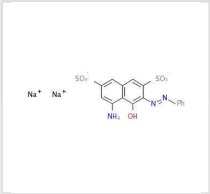
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ANNEX II - INGREDIENT DATA

Substance: CI 17200 (D&C Red 33)
CAS: 3567-66-6
Function: Pigment

Concentration in Product: 0.1%
Dermal Exposure Level: 0.000749318 mg/cm^2
Daily Body Burden: 0.0040170732mg/kg

Chemical Structure



Physical/Chemical Characteristics

Appearance	Red solid/powder
Melting Point	Decomposes at 240C
Specific Gravity	469.42 g/mole
Water Solubility	Soluble

Toxicological Summary

The below information is a summary of the toxicological profile for this raw material, including a description of general hazards associated with the material as well as discussion of the most critical studies relating to the overall safety in use of this substance/mixture in consumer products. Details of the available toxicological data can be found overleaf.

Overall Toxicity Review:

CI 17200 is a pigment used in cosmetics, which is permitted for use in all product types in the EU, and in the US for externally applied Cosmetics, Mouthwashes and Dentifrices, in lip products at a maximum of 3%, but not permitted for use in the Eye area.

CI 17200 was not a skin or eye irritant, and did not demonstrate potential for skin sensitisation.

It has reasonably low acute toxicity, with an oral LD50 of greater than 3160 mg/kg bw in rats, and greater than 1000 mg/kg bw in dogs.

The no-observed-adverse-effect-level (NOAEL) in a long-term feeding toxicity study in rats was set at 102 mg/kg bw/day. Another study reports a lowest-observed-adverse-effect-level (LOAEL) of 150 mg/kg bw/d for increased levels of leukocytes and reticulocytes in mice. This effect has been described in several long term studies and there is no consensus for the biological explanation.

CI 17200 produced no maternal and reprotoxic effects at up to 25 mg/kg bw/d. This value was identified as the critical point of departure (PoD) for risk assessment purposes by the Scientific Committee on Consumer Products (SCCP), however, as the highest tested dose, it is considered conservative.

CI 17200 was negative for mutagenicity in the Ames test, mammalian cell gene mutation test and the mammalian erythrocyte micronucleus test. There was no evidence of reproductive toxicity in a multi-generation study.

The maximum dermal absorption was 0.17% (15.2µg/cm²) and is considered appropriate for safety assessment by the SCCP.

SCCP (2007) reports that maximum authorised concentration in non-oxidative hair dye formulations is 0.5%. For other types of cosmetic products the exposure have not been considered.

Based on the long history of safe use in a variety of Consumer Products the incorporation of this material within a formulation is considered unlikely to pose a risk of significant adverse effects.

References:

SCCP (2007). Opinion on Acid Red 33. Colipa No C22. SCCP/1102/07

Margin(s) of Safety

Point of Departure - Animal Study: 25.0000mg/kg
Exposure from Product 0.00401707mg/kg
Margin of Safety 6223.43655

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ANNEX II - INGREDIENT DATA

CI 17200 (D&C Red 33)

Acute Toxicity Acute Toxicity, Lethality [Other]		LD50 > 3160 mg/kg
Rat	Oral, NOS	
Acute Toxicity Acute Toxicity, Lethality [Other]		LD50 > 1000 mg/kg
Dog	Oral, NOS	
ADME In vitro skin absorption [OECD 428]		Dermal absorption: 0.17% Max absorption: 15.2µg/cm² (draft OECD 428)
Pig	In vitro exposure	
Carcinogenicity Carcinogenicity studies [Other]		Dose: 150, 1502, and 8764 mg/kg bw/d for males and 181, 1809, and 10,362 mg/kg bw/d for females Exposure period: 24 months Result: not oncogenic
Mouse	Oral, Feed	
Eye Irritation In vivo Eye Irritation [Other]		0.2 mL of 10% aqueous solution. Applied twice daily, 5 x /week for 4 weeks. Not irritating
Rabbit	Instillation	
Genotoxicity Bacterial reverse mutation test (Ames) [OECD 471]		Negative in S. typhimurium TA 98, TA 100, TA 1535, TA 1537 and E. coli WP2 uvrA with and without metabolic activation
Bacteria	In vitro exposure	
Genotoxicity Mammalian cell gene mutation test [OECD 476]		Negative at the tk Locus of mouse lymphoma cells with and without metabolic activation.
Mouse	In vitro exposure	
Genotoxicity Mammalian erythrocyte micronucleus test [OECD 474]		Negative when tested in doses up to 2000 mg/kg bw
Mouse	Oral, NOS	
Repeated Dose Repeat Dose Oral Toxicity Study [Other]		NOAEL = 102 mg/kg bw/d (long term feeding study, > 12 months)
Rat	Oral, Feed	
Repeated Dose Repeat Dose Oral Toxicity Study [Other]		[24 month study] In all groups including the lowest dose an increase in the leucocytes/reticulocytes number was observed. This lowest dose of 150 mg/kg bw/d is considered as LOAEL.
Mouse	Oral, Feed	
Reproductive Toxicity In vivo reproductive toxicity study [Other]		NOAEL = 25 mg/kg/day (highest tested dose) Multi-generation study. 0.25, 2.5, 7.5, 25 mg/kg/day, up to F3 generation (110 days)
Rat	Oral, NOS	
Skin Irritation In vivo skin irritation [Other]		Not irritating to rabbit skin. 0.5 g/kg of 0, 0.1, 1% formulation in white petrolatum or a hydrophilic cream; 65 applications, or 15 applications on damage skin. Not irritant
Rabbit	Dermal	
Skin Sensitisation Maximisation Test [OECD 406]		Not sensitising in a guinea pig maximisation test. intradermal induction: 5% dilution; epidermal induction and challenge: 25% dilution
Guinea Pig	Dermal	

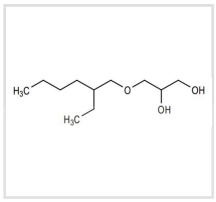
Physical/Chemical and Toxicological data used in generating these review are representative of publicly available data, and is provided for information purposes only.
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ANNEX II - INGREDIENT DATA

Substance: Ethylhexylglycerin
CAS: 70445-33-9
Function: Skin Conditioning; Deodorant

Concentration in Product: 0.1%
Dermal Exposure Level: 0.000749318 mg/cm^2
Daily Body Burden: 0.0040170732mg/kg

Chemical Structure



Physical/Chemical Characteristics

Appearance	Colourless liquid
Boiling Point	145°C
Flammability	Autoignition 250°C
Flash Point	152°C
Log Kow	2.53
Melting Point	< - 76°C
Odour	Almost odourless
pH	6 to 8 (1.8 g/L @ 22°C)
Specific Gravity	0.95 @ 20°C

Toxicological Summary

The below information is a summary of the toxicological profile for this raw material, including a description of general hazards associated with the material as well as discussion of the most critical studies relating to the overall safety in use of this substance/mixture in consumer products. Details of the available toxicological data can be found overleaf.

Overall Toxicity Review:

Ethylhexylglycerin is a synthetic alkyl glyceryl ether. It has been reported as being used in cosmetic products for its skin conditioning and deodorant properties.

It is only a mild skin irritant, but a significant eye irritant as supplied. Further testing identified that a 5% aqueous solution of ethylhexylglycerin was only a mild ocular irritant.

No evidence of significant allergenic activity was identified in the Guinea Pig Maximisation Test. The compound's structure does not contain conjugated double bonds, therefore, it will not absorb UV light which is a prerequisite for phototoxicity.

The material displays low acute toxicity by the Oral, Dermal and Inhalation routes. A 28-day oral repeat dose study in rats identified a no observed adverse-effect level (NOAEL) of 100 mg/kg/day. A NOAEL of 50 mg/kg bw/day was identified in rats in a 13-week oral repeated dose toxicity study.

No evidence of mutagenic or genotoxic activity either in-vitro or in-vivo in the mammalian erythrocyte micronucleus test. Amongst two repeated dose and one reproductive toxicity studies the lowest NOAEL of 50 mg/kg bw/day was identified as Point of Departure.

The Cosmetic Ingredient Review (CIR) expert panel concluded that current practices of use and concentration (up to 2% in leave-on products and up to 8% in rinse off products; up to 8% in dermal contact cosmetics and up to 0.5% in cosmetics that come into contact with mucous membranes) could be considered safe.

In an in-vitro study using human skin, the dermal absorption ranged from 44.65% to 54.94% when tested at different concentrations. Overall, based on the information available for review, use of this material at typical levels within a consumer product would not be expected to pose an undue risk of significant adverse effects in a majority of individuals.

References

CIR, (2013). Safety assessment of alkyl glyceryl ethers as used in cosmetics. International Journal of Toxicology 32(suppl 3):5S-21S

ECHA registration dossier: 3-(2-ethylhexyloxy)propan-1,2-diol. CAS number 70445-33-9.

Margin(s) of Safety

Point of Departure - Animal Study: 50.0000mg/kg
Exposure from Product 0.00401707mg/kg
Margin of Safety 12446.8731

Physical/Chemical and Toxicological data used in generating these review are representative of publicly available data, and is provided for information purposes only.
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ANNEX II - INGREDIENT DATA

Ethylhexylglycerin

Acute Toxicity Acute Oral Toxicity, Lethality [OECD 401, OECD 423, OECD 425]		LD50 > 2000 mg/kg bw (2000mg/kg bw was the highest tested dose)
Rat	Oral, Gavage	
Acute Toxicity Acute Dermal Toxicity, Lethality [OECD 402]		LD50 > 2000 mg/kg bw Under semi-occlusive conditions.
Rat	Dermal	
Acute Toxicity Acute Inhalation Toxicity, Lethality [OECD 403, OECD 436]		LC50 2.83mg/L air based on effect level in male rats
Rat	Inhalation	
ADME In vitro absorption study [Other]		3 concentration tested in ethanol- water 10:90 v/v. lowest concentration was 2%. The mean absorption values were 44.65% (at 31 µg/cm2), 47.15% (at 60 µg/cm2) and 54.94 (at 151 µg/cm2).
Human	Dermal	
Eye Irritation Draize, Standard [OECD 405]		0.1 ml of undiluted ethylhexylglycerin caused severe eye damage, whilst following the same procedure a 5% aqueous solution resulted in conjunctival erythema, but no signs of irritation to the iris or cornea, and was thus considered as mildly irritating to the eyes.
Rabbit	Instillation	
Genotoxicity Bacterial reverse mutation test (Ames) [OECD 471]		Negative in the Ames bacterial reverse mutation assay in S.typhimurium with or without metabolic activation.
Bacteria	In vitro exposure	
Genotoxicity Mammalian erythrocyte micronucleus test [OECD 474]		Negative in the mouse micronucleus test.
Mouse	Oral, NOS	
Repeated Dose 28-day Oral Toxicity Study [OECD 407]		A 28-day study on 10 rat at doses of 100, 500, and1,500 mg/kg. Slight to moderate hypertrophy (rats from all dose groups), fatty infiltration of hepatocytes (high –dose males), and necrosis of hepatocytes were observed for high-dose rats, especially females. The NOAEL was defined as 100 mg/kg.
Rat	Oral, Gavage	
Repeated Dose 90-Day Oral Toxicity Study [OECD 408, OECD 409]		A 13-week rat study at doses of 0, 50, 200, and 800 mg/kg bw/day demonstrated a significant increase in absolute and relative to body weight liver weights. This was the only toxicologically significant finding in the low dose group. The study authors considered 50 mg/kg/day to be an NOAEL, however this was considered by NICNAS to be a LOAEL.
Rat	Oral, Gavage	
Reproductive Toxicity Prenatal Development Toxicity Study [OECD 414]		In a male and female rat study administered 50, 200 and 800 mg/kg bw/day, the NOAEL for 1-generation developmental toxicity in both sexes was 50 mg/kg bw/day, based on treatment related findings of the males in the mid and high dose groups.
Rat	Oral, Gavage	
Skin Irritation Draize Test [OECD 404]		Not classified: Not irritating to mildly irritating. The mean erythema score was 0.56 and the mean oedema score was 0, when tested undiluted.
Rabbit	Dermal	
Skin Sensitisation Maximisation Test [OECD 406]		Not sensitising following a 50% challenge patch for 24 or 48 hours, 2 weeks after induction test.
Guinea Pig	Dermal	

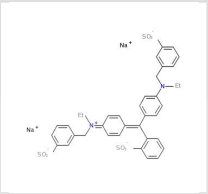
Physical/Chemical and Toxicological data used in generating these review are representative of publicly available data, and is provided for information purposes only.
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ANNEX II - INGREDIENT DATA

Substance: CI 42090 (FD&C Blue No. 1)
CAS: 71701-19-4 (K.Na salt); 71701-18-3 (K salt); 2650-18-2 (NH4 salt); 68921-42-6 (Al salt); 15792-67-3 (Al salt); 3844
Function: Pigment

Concentration in Product: 0.1%
Dermal Exposure Level: 0.000749318 mg/cm^2
Daily Body Burden: 0.0040170732mg/kg

Chemical Structure



Physical/Chemical Characteristics

Appearance	Solid
Melting Point	283°C
Appearance	Blue Powder
Log Kow	-0.32
Molecular Mass	792

Melting Point	283
Odour	None
pH	5 to 6 @ 1%
Specific Gravity	0.8 to 1.0

Toxicological Summary

The below information is a summary of the toxicological profile for this raw material, including a description of general hazards associated with the material as well as discussion of the most critical studies relating to the overall safety in use of this substance/mixture in consumer products. Details of the available toxicological data can be found overleaf.

Overall Toxicity Review:

CI 42090 (FD&C Blue 1) is a dye thoroughly tested for use as a food additive (FD&C Colour in the USA, E133 in the EU) and as cosmetic dye and with a long history of use.

Not irritating to skin, and only mild transient irritation to eyes. There was no evidence of skin sensitisation in the mouse local lymph node assay.

The dye has low acute toxicity, with high oral LD50 of > 1,900 mg/kg and a subcutaneous LD50 of 4,600 mg/kg. Not acutely sensitising or irritating effects are known.

The no-observed-effect-level (NOEL) from an extended one generation reproductive feeding study in rats was determined to be 631mg/kg bw/day for the F1 females. There is growing evidence of some adverse reactions to the material, mainly attributed to its inhibitory effects on mitochondrial respiration of human cells. It has been shown that oral administration of the material may be unsafe particularly during an illness associated with enhanced gut permeability. However, this is mainly observed in clinical settings where blue dye 1 is used as a way to detect pulmonary aspiration of gastric contents in enterally fed patients (Maloney et al., 2002). It must be noted that this review is not in accordance with EFSA, however, the clinical use settings are considered to be extreme (continuous feeding in already compromised patients) compared to use as a food. Moreover, this would be unlikely to pose a risk of adverse effects via the dermal route, considering the information mentioned above.

The compound is unlikely to be genotoxic based on negative results from an Ames test and a mammalian erythrocyte micronucleus test. It also showed no evidence of carcinogenicity in a 24 month feeding study in mice at 5% in the diet (7,000 mg/kg bw).

The high molecular weight and octanol-water partition coefficient indicate that dermal absorption is expected to be negligible.

European Food Safety Authority (EFSA) established an acceptable daily intake (ADI) of 6 mg/kg bw/day.

Is not expected to pose an undue risk of significant adverse effects in a consumer product under typical conditions of use.

References:
ECHA Registration Dossier. Dihydrogen (ethyl)[4-[4-[ethyl(3-sulphonatobenzyl)]amino]-2'-sulphonatobenzhydrylidene]cyclohexa-2,5-dien-1-ylidene](3-sulphonatobenzyl)ammonium, disodium salt Cas: 3844 -45-9.

EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS). (2010). Scientific Opinion on the re-evaluation of Brilliant Blue FCF (E 133) as a food additive. EFSA Journal, 8(11), 1853.

Maloney, J. P., Ryan, T. A., Brasel, K. J., Binion, D. G., Johnson, D. R., Halbower, A. C., ... & Moss, M. (2002). Food dye use in enteral feedings: a review and a call for a moratorium. Nutrition in Clinical Practice, 17(3), 169-181.

Margin(s) of Safety

Point of Departure - Human Data: 6.0000mg/kg
Exposure from Product 0.00401707mg/kg
Margin of Safety 1493.62477

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ANNEX II - INGREDIENT DATA

CI 42090 (FD&C Blue No. 1)

Acute Toxicity Acute Toxicity, Lethality [Other]		LD50: 4,600 mg/kg bw
Mouse	Subcutaneous	
Acute Toxicity Acute Oral Toxicity, Lethality [OECD 401, OECD 423, OECD 425]		LD50: > 1,900 mg/kg bw
Rat	Oral, Gavage	
ADME In vitro absorption study [Other]		No measurable permeation through skin was detected.
Ex-vivo Tissue	In vitro exposure	
ADME In vivo metabolism study [Other]		Very low intestinal absorption based on several studies in rats
Rat [NOS]	Oral, Gavage	
Carcinogenicity Combined chronic toxicity/carcinogenicity studies [OECD 453]		NOAEL: >7000 mg/kg bw corresponding to 5% in the diet for 24 months. Absence of carcinogenic effects at the highest tested dose
Mouse	Oral, Feed	
Eye Irritation Draize, Standard [OECD 405]		Transient irritation in rabbits [aqueous formulation containing 38% CI42090, 47% water and 7% oxalic acid]
Rabbit	Instillation	
Genotoxicity Bacterial reverse mutation test (Ames) [OECD 471]		Negative with or without activation in S. typhimurium TA 1535, TA 1537, TA 98, TA 100 and TA 102 and in E. coli WP2 uvr A.
Bacteria	In vitro exposure	
Genotoxicity Mammalian erythrocyte micronucleus test [OECD 474]		Negative in the micronucleus study in mice at up to 1010 mg/kg bw/day
Mouse	Intraperitoneal	
Reproductive Toxicity Extended One-Generation Reproductive Toxicity Study [OECD 443]		NOEL: F1 Female 631 mg/kg bw/day; F1 male >= 1072 mg/kg bw/day. No adverse effects on reproductive organs in both dose.
Rat	Oral, Feed	
Skin Irritation Draize Test [OECD 404]		Not irritating to skin. oedema score 0 out of 4, erythema score not determinable due to staining of skin. [aqueous formulation containing 38% CI42090, 47% water and 7% oxalic acid]
Rabbit	Dermal	
Skin Sensitisation Local Lymph Node Assay [OECD 429, OECD 442A, OECD 442B]		Not sensitising in the mouse local lymph node assay at up to 25%
Mouse	Dermal	

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ANNEX IV - ADDITIONAL REASONABLY FORESEEABLE EXPOSURES

ANNEX V - RAW MATERIAL SPECIFICATIONS

Substance: Glycerin
CAS: 56-81-5; 8013-25-0

Specification

Glycerin does not have minimum purity specifications set within the EU Cosmetic (or related) Regulations. Manufacturer should ensure that a suitably safe grade is used, including:

≤ 10ppm Heavy Metals (total sum of)

< 0.1% substances classified as H317 (May cause an allergic skin reaction) in accordance with the EU Classification, Labelling & Packaging Regulation (1272/2008)

< 1ppm substances classified as Carcinogenic, Mutagenic or Reproductive Toxins in accordance with the EU Classification, Labelling & Packaging Regulation (1272/2008)

< 10ppm substances Prohibited or Restricted for use under Annex II or Annex III of the EU Cosmetic Regulation (1223/2009)

< 0.1% Substances of Very High Concern (SVHC), as defined under EU REACH Regulation (1907/2006)

Microbiological Specification: TVC ≤ 1,000 cfu/g, absence of specific pathogens

Substance: Aqua
CAS: 7732-18-5

Specification

There are no minimum legal purity specifications for water used in the manufacture of cosmetics.

It should ensure that the grade of water used in the manufacture of this product is of a suitably safe specification, following criteria such as those of laid out in GMP standards like ISO 22716.

Substance: Sorbitol
CAS: 68425-17-2 (generic); 50-70-4; 98201-93-5; 1259528-21-6 (generic)

Specification

Sorbitol does not have minimum purity specifications set within the EU Cosmetic (or related) Regulations. Manufacturer should ensure that a suitably safe grade is used, including:

≤ 10 ppm Heavy Metals (sum of)

< 0.1% substances classified as H317 (May cause an allergic skin reaction) in accordance with the EU Classification, Labelling & Packaging Regulation (1272/2008)

< 1ppm substances classified as Carcinogenic, Mutagenic or Reproductive Toxins in accordance with the EU Classification, Labelling & Packaging Regulation (1272/2008)

< 10ppm substances Prohibited or Restricted for use under Annex II or Annex III of the EU Cosmetic Regulation (1223/2009)

< 0.1% Substances of Very High Concern (SVHC), as defined under EU REACH Regulation (1907/2006)

Microbiological Specification: TVC ≤ 1,000 cfu/g, absence of specific pathogens

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Substance: Hydrated Silica
CAS: 63231-67-4; 10279-57-9; 1343-98-2; 7631-86-9; 112926-00-8

Specification

Hydrated Silica does not have minimum purity specifications set within the EU Cosmetic (or related) Regulations. Manufacturer should ensure that a suitably safe grade is used, including:

≤ 10 ppm Heavy Metals (sum of)

< 0.1% substances classified as H317 (May cause an allergic skin reaction) in accordance with the EU Classification, Labelling & Packaging Regulation (1272/2008)

< 1ppm substances classified as Carcinogenic, Mutagenic or Reproductive Toxins in accordance with the EU Classification, Labelling & Packaging Regulation (1272/2008)

< 10ppm substances Prohibited or Restricted for use under Annex II or Annex III of the EU Cosmetic Regulation (1223/2009)

< 0.1% Substances of Very High Concern (SVHC), as defined under EU REACH Regulation (1907/2006)

Microbiological Specification: TVC ≤ 1,000 cfu/g, absence of specific pathogens

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Substance: Xylitol
CAS: 87-99-0

Specification

Xylitol does not have minimum purity specifications set within the EU Cosmetic (or related) Regulations. Manufacturer should ensure that a suitably safe grade is used, including:

≤ 10 ppm Heavy Metals (sum of)

< 0.1% substances classified as H317 (May cause an allergic skin reaction) in accordance with the EU Classification, Labelling & Packaging Regulation (1272/2008)

< 1ppm substances classified as Carcinogenic, Mutagenic or Reproductive Toxins in accordance with the EU Classification, Labelling & Packaging Regulation (1272/2008)

< 10ppm substances Prohibited or Restricted for use under Annex II or Annex III of the EU Cosmetic Regulation (1223/2009)

< 0.1% Substances of Very High Concern (SVHC), as defined under EU REACH Regulation (1907/2006)

Microbiological Specification: TVC ≤ 1,000 cfu/g, absence of specific pathogens

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Substance: Polysorbate 80
CAS: 9005-65-6

Specification

Polysorbate 80 does not have minimum purity specifications set within the EU Cosmetic (or related) Regulations. Manufacturer should ensure that a suitably safe grade is used, including:

≤ 10ppm Heavy Metals (sum of)

< 0.1% substances classified as H317 (May cause an allergic skin reaction) in accordance with the EU Classification, Labelling & Packaging Regulation (1272/2008)

< 1ppm substances classified as Carcinogenic, Mutagenic or Reproductive Toxins in accordance with the EU Classification, Labelling & Packaging Regulation (1272/2008)

< 10ppm substances Prohibited or Restricted for use under Annex II or Annex III of the EU Cosmetic Regulation (1223/2009)

< 0.1% Substances of Very High Concern (SVHC), as defined under EU REACH Regulation (1907/2006)

Microbiological Specification: TVC ≤ 1,000 cfu/g, absence of specific pathogens

Substance: Cellulose Gum
CAS: 9004-32-4; 99331-82-5; 9000-11-7

Specification

Cellulose Gum does not have minimum purity specifications set within the EU Cosmetic (or related) Regulations. Manufacturer should ensure that a suitably safe grade is used, including:

≤ 10 ppm Heavy Metals (sum of)

< 0.1% substances classified as H317 (May cause an allergic skin reaction) in accordance with the EU Classification, Labelling & Packaging Regulation (1272/2008)

< 1ppm substances classified as Carcinogenic, Mutagenic or Reproductive Toxins in accordance with the EU Classification, Labelling & Packaging Regulation (1272/2008)

< 10ppm substances Prohibited or Restricted for use under Annex II or Annex III of the EU Cosmetic Regulation (1223/2009)

< 0.1% Substances of Very High Concern (SVHC), as defined under EU REACH Regulation (1907/2006)

Microbiological Specification: TVC ≤ 1,000 cfu/g, absence of specific pathogens

Substance: Mentha Piperita (Peppermint) Oil
CAS: 84082-70-2; 8006-90-4

Specification

As a botanical extract, must be extracted and processed in such a way as to remove any hazardous biological contaminants or plant protection / pesticide substances.

Maximum levels of declared allergens (identified as such by either the EU Cosmetic Regulation or the EU CLP Regulation) as outlined in Annex I as part of the fragrance safety assessment.

<1% Pulegone

≤ 10 ppm Heavy Metals (sum of)

< 0.1% substances classified as H317 (May cause an allergic skin reaction) in accordance with the EU Classification, Labelling & Packaging Regulation (1272/2008)

< 1ppm substances classified as Carcinogenic, Mutagenic or Reproductive Toxins in accordance with the EU Classification, Labelling & Packaging Regulation (1272/2008)

< 10ppm substances Prohibited or Restricted for use under Annex II or Annex III of the EU Cosmetic Regulation (1223/2009)

< 0.1% Substances of Very High Concern (SVHC), as defined under EU REACH Regulation (1907/2006)

Microbiological Specification: TVC ≤ 1,000 cfu/g, absence of specific pathogens

Substance: Phenoxyethanol
CAS: 56257-90-0; 37220-49-8; 122-99-6

Specification

Phenoxyethanol does not have minimum purity specifications set within the EU Cosmetic (or related) Regulations. It should ensure that a suitably safe grade is used, including:

Minimum Purity 99%

Phenol <10 ppm

Ethylene oxide <2 ppm

≤ 10 ppm Heavy Metals (sum of)

< 0.1% substances classified as H317 (May cause an allergic skin reaction) in accordance with the EU Classification, Labelling & Packaging Regulation (1272/2008)

< 1ppm substances classified as Carcinogenic, Mutagenic or Reproductive Toxins in accordance with the EU Classification, Labelling & Packaging Regulation (1272/2008)

< 10ppm substances Prohibited or Restricted for use under Annex II or Annex III of the EU Cosmetic Regulation (1223/2009)

< 0.1% Substances of Very High Concern (SVHC), as defined under EU REACH Regulation (1907/2006)

Microbiological Specification: TVC ≤ 1,000 cfu/g, absence of specific pathogens

It should ensure that each batch of material is checked against specification before inclusion within the manufacturing process of a finished cosmetic product.

Substance: Sucralose
CAS: 56038-13-2

Specification

Sucralose does not have minimum purity specifications set within the EU Cosmetic (or related) Regulations. Manufacturer should ensure that a suitably safe grade is used, including:

≤ 10 ppm Heavy Metals (sum of)

< 0.1% substances classified as H317 (May cause an allergic skin reaction) in accordance with the EU Classification, Labelling & Packaging Regulation (1272/2008)

< 1ppm substances classified as Carcinogenic, Mutagenic or Reproductive Toxins in accordance with the EU Classification, Labelling & Packaging Regulation (1272/2008)

< 10ppm substances Prohibited or Restricted for use under Annex II or Annex III of the EU Cosmetic Regulation (1223/2009)

< 0.1% Substances of Very High Concern (SVHC), as defined under EU REACH Regulation (1907/2006)

Microbiological Specification: TVC ≤ 1,000 cfu/g, absence of specific pathogens

Substance: Tetrasodium Pyrophosphate
CAS: 7722-88-5

Specification

Tetrasodium Pyrophosphate does not have minimum purity specifications set within the EU Cosmetic (or related) Regulations. Manufacturer should ensure that a suitably safe grade is used, including:

< 0.1% substances classified as H317 (May cause an allergic skin reaction) in accordance with the EU Classification, Labelling & Packaging Regulation (1272/2008)

< 1ppm substances classified as Carcinogenic, Mutagenic or Reproductive Toxins in accordance with the EU Classification, Labelling & Packaging Regulation (1272/2008)

< 10ppm substances Prohibited or Restricted for use under Annex II or Annex III of the EU Cosmetic Regulation (1223/2009)

< 0.1% Substances of Very High Concern (SVHC), as defined under EU REACH Regulation (1907/2006)

Microbiological Specification: TVC ≤ 1,000 cfu/g, absence of specific pathogens

Substance: CI 17200 (D&C Red 33)
CAS: 3567-66-6

Specification

Not less than 90% Total colour

≤ 10% Sum of volatile matter (at 135 deg. C), chlorides and sulfates (calculated as sodium salts)
≤ 0.2% Aniline
≤ 0.4% 3-Hydroxy-2-naphthoic acid, calcium salt
≤ 1% Subsidiary colours
≤ 20ppm Lead (as Pb)
≤ 3ppm Arsenic (as As)
≤ 1ppm Mercury (as Hg)

< 0.1% substances classified as H317 (May cause an allergic skin reaction) in accordance with the EU Classification, Labelling & Packaging Regulation (1272/2008)

< 1ppm substances classified as Carcinogenic, Mutagenic or Reproductive Toxins in accordance with the EU Classification, Labelling & Packaging Regulation (1272/2008)

< 10ppm substances Prohibited or Restricted for use under Annex II or Annex III of the EU Cosmetic Regulation (1223/2009)

< 0.1% Substances of Very High Concern (SVHC), as defined under EU REACH Regulation (1907/2006)

Substance: Ethylhexylglycerin
CAS: 70445-33-9

Specification

Ethylhexylglycerin does not have minimum purity specifications set within the EU Cosmetic (or related) Regulations. It must be ensured that a suitably safe grade is used, including:

≥ 99% of ethylhexylglycerin

≤ 1% water
≤ 100ppm a-tocopherol
≤ 100ppm 2-ethylhexylglycidylether

≤ 10 ppm Heavy Metals (sum of)

< 0.1% substances classified as H317 (May cause an allergic skin reaction) in accordance with the EU Classification, Labelling & Packaging Regulation (1272/2008)

< 1ppm substances classified as Carcinogenic, Mutagenic or Reproductive Toxins in accordance with the EU Classification, Labelling & Packaging Regulation (1272/2008)

< 10ppm substances Prohibited or Restricted for use under Annex II or Annex III of the EU Cosmetic Regulation (1223/2009)

< 0.1% Substances of Very High Concern (SVHC), as defined under EU REACH Regulation (1907/2006)

Microbiological Specification: TVC ≤ 1,000 cfu/g, absence of specific pathogens

Substance: CI 42090 (FD&C Blue No. 1)
CAS: 71701-19-4 (K.Na salt); 71701-18-3 (K salt); 2650-18-2 (NH4 salt); 68921-42-6 (Al salt);

Specification

For cosmetic products sold within the EU the manufacturer must ensure that the grade of material used complies with the purity criteria as set out in Commission Directive 231/2012/EC (E133). This includes:

Water insoluble matter: Not more than 0,2 %
Subsidiary colouring matters: Not more than 6,0 %
Organic compounds other than colouring matters:
Sum of 2-, 3- and 4-formyl benzene sulfonic acids: Not more than 1,5 %
3-((ethyl)(4-sulfophenyl) amino) methyl benzene sulfonic acid: Not more than 0,3 %
Leuco base: Not more than 5,0 %
Unsulfonated primary aromatic amines: Not more than 0,01 % (calculated as aniline)
Ether extractable matter: Not more than 0,2 % at pH 7

Arsenic: Not more than 3 mg/kg
Lead: Not more than 2 mg/kg
Mercury: Not more than 1 mg/kg
Cadmium: Not more than 1 mg/kg

≤ 10 ppm Heavy Metals (sum of)

< 0.1% substances classified as H317 (May cause an allergic skin reaction) in accordance with the EU Classification, Labelling & Packaging Regulation (1272/2008)

< 1ppm substances classified as Carcinogenic, Mutagenic or Reproductive Toxins in accordance with the EU Classification, Labelling & Packaging Regulation (1272/2008)

< 10ppm substances Prohibited or Restricted for use under Annex II or Annex III of the EU Cosmetic Regulation (1223/2009)

< 0.1% Substances of Very High Concern (SVHC), as defined under EU REACH Regulation (1907/2006)

Microbiological Specification: TVC ≤ 1,000 cfu/g, absence of specific pathogens

-END OF REPORT-