Cosmetic Product Safety Assessment of

Make-up : P6DH.Pearl Purple/ P3WH.Pearl Blue/ P42H.Gold/ P5C.Pearl Green/ P8G.Pearl Black/ P9E.Pearl White

This safety assessment relates to the formulation described below. If the information below is incorrect, please amend and resubmit for reassessment.

Intertek Taiwan

Formulation Ref: FS-16RP

PRODUCT FORMULATION

The chemical names shown below refer to the raw materials used to formulate this product. The identity of the raw materials is not necessarily based on the International Nomenclature of Cosmetic Ingredients (INCI) and does not represent the INCI listing that must be shown on the product label and is for assessment purposes only. An outline INCI label can be prepared on request.

Chemical Name	Conc	% Active	Active in Product	CAS No	Einecs No
PARAFFIN WAXES	20.00	100	20	64742-43-4/ 64742-51-4 (8002-74-2)	265-145-6/ 265-154-5 (232-315-6)
PETROLATUM	18.00	100	18	8009-03-8 / 8063-27-2	232-373-2
GLYCERIN	10.00	100	10	56-81-5 / 8013-25-0	200-289-5
CALCIUM CARBONATE	23.80	100	23.8	471-34-1 / 1317-65-3	207-439-9
ETHOXYLATED ALCOHOL	4.40	100	4.4	68439-49-6/ 68439-50-9/ 78330-21-9	POLYMER
ETHYLHEXYLGLYCERIN & PHENOXYETHANOL	0.40	100	.4	70445-33-9 & 122-99-6	408-080-2 & 204-584-7
DISODIUM EDTA	0.20	100	.2	139-33-3 / 6381-92-6	205-358-3
SODIUM BENZOATE	0.20	100	.2	532-32-1	208-534-8
ACACIA SENEGAL GUM	0.80	100	.8	9000-01-5	232-519-5
DEXTRIN	14.20	100	14.2	9004-53-9	232-675-4
AQUA	1.00	100	1		
MICA (CI 77019)	7.00	100	7	12001-26-2	310-127-6
MAY CONTAIN (+/-)				----------	----------
CI 15850:1 (D&C RED NO.7 CALCIUM LAKE)	0.413	100	.413	5858-81-1/ 5281-04-9	226-109-5
CI 77891 (TITANIUM DIOXIDE)	1.82	100	1.82	13463-67-7/1317-70-0/1317-80-2	236-675-5/205-280-1/215-282-2
CI 19140 (FD&C YELLOW 5)	0.84	100	.84		
CI 77510 (FERRIC FERROCYANIDE)	1.701	100	1.701	14038-43-8	237-875-5
CI 77499 (BLACK IRON OXIDE)	2.45	100	2.45	12227-89-3	235-442-9
CI 77163 (BISMUTH OXYCHLORIDE)	0.35	100	.35	7787-59-9	232-122-7
ZINC OXIDE (CI 77947)	0.63	100	.63	1314-13-2	215-222-5

LABELLED WARNINGS & INSTRUCTIONS OF USE

Keep away from eyes.

Discontinue use if irritation or rash develops

CONSUMER EXPOSURE

Product Class: Face paint
IFRA Product type: Face Paint
IFRA Category: Category 5
Targeted Population: Children 16.7kg (Mean)

Amount per application/g:	1.4	Number of applications per day:	Once per day
Skin Surface Area of Application/cm^2:	475.000	Physical form:	Solid
Total Amount applied per day/g:	1.4	Part of body exposed to undiluted	Face and hands
Estimated Daily Exposure mg/kg/day:	-		
Amount Per Unit Area of Skin per day mg/cm^2/day:	3.000		
Retention factor:	1.00		
Exposure Time Neat:	480 minutes		
Exposure Time Dilute:	Not Applicable		
Exposure time Solvent Inhalation:	Not Applicable		
Exposure time Aerosol Inhalation:	Not Applicable		

This product has been assessed taking into account that it will be used by children above three years of age.

STABILITY OF COSMETIC PRODUCT

It is assumed that the responsible person has selected all pertinent criteria required to evaluate the stability of this cosmetic product during reasonable foreseeable conditions of storage. The stability report provided by the supplier and based upon the conclusions made therein, this cosmetic product appears to be stable under reasonably foreseeable storage conditions.
The Stability Test Report in which the parameters: exterior, colour, taste and microbial limits were investigated at the storage conditions of the following temperatures: 45 °C, 23 °C and -10 °C,were supplied and recorded to be stable, and the microbial limits < 100 cfu/ml complied with the requirements (Luck Art Industrial, dated 2nd August 2013

MICROBIOLOGICAL QUALITY

To comply with the Guidelines on the Microbiological Quality (SCCNFP/0004/98), the following maximum limits apply:
Category 1: Products specifically intended for children under 3 years, eye area and mucous membranes.
TVC:- 100 cfu/g or ml in 0.5 g or ml of the product.
Pseudomonas aeruginosa, Staphylococcus aureus and Candida albicans must not be detectable in 0.5 g or ml of the cosmetic product
Category 2: Other cosmetic products.
TVC:- 1000 cfu/g or ml in 0.1 g or ml of the product
Pseudomonas aeruginosa, Staphylococcus aureus and Candida albicans must not be detectable in 0.1 g or ml of the cosmetic product
The microbiological specifications for the product have been supplied and based upon the conclusions therein, meet the Industry requirements specified in the Guidelines on the Microbiological Quality of the Cosmetic Product, 1999 Edition.
The preservative challenge test results for this product have been supplied and based upon the conclusions made therein appear to meet the industry requirements specified in the Notes of guidance for testing of cosmetic ingredients for their safety evaluation, Annex 8 - Guidelines on the Microbiological Quality of the Cosmetic Product, 1999 Edition.
Total Aerobic Microbial Count test report were supplied and the bacterial, yeast and mould counts were reported to be < 10 cfu/g (ref. of test method used: *USP XXXIV <61>.and ASTM F963-08 Section 4.3.6.3.* The specific pathogens using the micro-organisms, Bile-Tolerant Gram-Negative Bacteria, *Escherichia Coli*, *Salmonella*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Clostridia*, and *Candida albicans*, were found to be absent following the test methods, *Specified Microorganisms As per USP XXXIV <62>.and ASTM F963-08 Section 4.3.6.3* (Report No. Number : TWNC00252943S1, Item A (Face Paints), Lucky Art Industrial Co., Ltd.).

PACKAGING INFORMATION/COMPATIBILITY

It is assumed that the responsible person has identified the most applicable testing required to determine the packaging stability and its interaction with the cosmetic product contained within it. Taking into consideration the information supplied to the assessor, there appears to be no immediate health concern due to the characteristics of packaging materials in direct contact with the final product.

A Packing Attestation supplied indicated that the Make-up (Water-based Face Paint - Pearl Colour) is packaged in a primary packaging in a blister pack made of PVC and PS plastics with paper cartond used as a secondary packaging (Luck Art Industrial Co., Ltd., dated 04/25/2012). The packaging is described as of virgin grade, does not contain CMRs, no colorants, no SVHC and is not known to leach or migration of chemicals from the packaging into the product. Heavy metals contents report were supplied and found to be within limits (ref. Lucky Art Industrial Co., Ltd., Report No. TWNC00251059S1, dated Apr 26, 2012).

SERIOUS / UNDESIRABLE EFFECTS

On request, the supplier has not supplied information of any reports known to him of serious undesirable effect or undesirable effects on the cosmetic product, or where relevant, other similar cosmetic products and this cannot be commented upon. If the supplier is aware of an abnormally high level of customer complaints the supplier must bring this to the attention of the safety assessor and submit this formulation for reassessment and notify the competent authorities of corrective actions taken.

HUMAN STUDIES

No existing studies from human volunteers were provided at the time of assessment.

FRAGRANCE COMPOSITIONS

This formulation does not contain a synthetic fragrance and therefore a fragrance safety evalution as per IFRA code of practice is not applicable to this product.

PRESENCE OF NANOMATERIALS

The supplier has confirmed that this cosmetic product does not contain any nanomaterials that are known to them within the meaning of the definition as stated in Cosmetic Product Regulation (EC) No 1223/2009.

IMPURITIES /TRACES/ PROHIBITED SUBSTANCES

Where the specification is provided it is noted that this product does not contain any impurities at levels likely to cause harm to the user

TOXICOLOGICAL & REGULATORY REASONING

This is a preserved and emulsified mixture of predominantly antioxidant stabilised waxy / oily ingredients with bulking, thickening / viscosity controlling, skin conditioning, chelating agents and colour pigments dispersed. The product is intended to be used for painting the face by consumers of target age group from over three years old. The most relevant route for systemic exposure is therefore the skin and less so the eyes; ingestion and inhalation may occur with the younger age group bearing in mind the behaviour of children (e.g. direct and indirect hand-to-mouth contact, hand-to-eye contact) which can result in misuse or abuse of a product (*Bremmer, H.J and van Veen, M.P. 2002. RIVM report 612810012/200 - To assess the risks for the consumer. Table 2: Relationship between exposure category and type of toys - face paints)*. Application on the skin of the face can also be accompanied by application near the eyes, and hand-to-eyes contact being also a route of exposure. Vapour generated from this product would be expected to be low and so inhalation would be an unlikely route of exposure. The MSDS supplied for the predominant ingredients, petroleum derived waxes indicated that they are both of food, cosmetic and pharmaceutical grades. Ingestion of them is therefore likely to pose a negligible risk to health (LD50: species not specified > 5000 mg/kg, MSDS information for Petroleum Wax, CAS # 64742-43-4). Note that this CAS # 8002-74-2 (Synthetic Wax) given in the compositional form differs from that supplied in the MSDS. The MSDS also stated that prolonged or repeated inhalation of the vapour or mist may cause irritation of the respiratory tract and deposits of the oil droplets in the lungs may cause fibrosis and reduced pulmonary function. Inhalation however is not a major route of exposure of this product. The viscosity controlling / skin conditioning agent, Glycerin, has a minimum potential to irritate the skin and the eye. Data obtained from animal and human exposure have indicated that Glycerin is not a skin sensitiser and structural and long-term studies do not suggest potential for mutagenicity and/or carcinogenicity. Acacia Senegal gum is a thickening / viscosity controlling / stabilising ingredient commonly used in food. It is equated to Gum Arabic and thus the safety data obtained from the toxicological evaluation of the latter was used here (CIR, 2011). The powder has been associated with severe eye irritation and a respiratory allergen noted particularly in printing workers. It may also cause skin sensitisation in susceptible individuals. In US products, its use is recommended to be restricted to 9% (CIR, 2010); the concentration in this product is thus within the maximum recommended level. The low absorption rate observed due to its large molecular weight and water solubility suggested that when used at a low concentration in a formulation, its irritancy potential may be considerably reduced. There is a concern with regards to PCB/pesticide contamination (not to exceed 40 ppm) and impurities from certain heavy metals advised to have the following appropriate limits: Arsenic (3 mg/kg maximum), heavy metals (0.002% maximum), and Lead (5 mg/kg maximum) (CIR, 2011). The presence of the chelating agent in the formulation may minimise the heavy metals effect. The bulking agents are Mica, Calcium carbonate and Dextrin. Calcium carbonate has little or no acute or chronic irritant or allergenic potential in contact with the skin. However, the powder may cause a foreign body reaction in contact with the eye and it may irritate the nose and respiratory system upon inhalation. In this product therefore, it poses a low to negligible risk of skin irritation. The nature of the formulation makes its inhalation impractical. Mica is not classified as an eye or skin irritant nor a skin sensitiser. As well as a bulking agent, it also imparts opaqueness to the product. It is practically inert and the form supplied for this formulation is described a "may cause delayed respiratory disease if dust is inhaled over a prolonged period" (Product name: MICA325/ MICA1000/ MICA2000 from Goodwill Chemical Corporation, not dated). However in this formulation, the amount used is low and is dedusted by its blending into an oily / waxy medium thus reducing any potential for inhalation that would result in 'delayed respiratory disease'. Consequently, it is of a low toxicological concern. Mica is permitted for use in cosmetic products in the EU and U.S. Dextrin, a high molecular weight glucose polymer has a low potential to cause irritancy or allergy. Its presence in this product is therefore expected to pose a negligible risk to the user of this product. The emulsifying agent, Ethoxylated Alcohol, as supplied is classified as harmful if swallowed, irritating to skin and can cause risk of serious damage to eyes. It is not known as a skin sensitiser. However at a low concentration in a formulation, it is expected to pose a reduced irritancy risk. The preservatives are EU approved and are within the maximum permitted concentrations for this type of leave-on product. The mixture, Ethylhexylglycerin & Phenoxyethanol, has the potential to cause severe eye irritation but not at the concentration present in this product. The Certificate of Analysis supplied for the other preservative, Sodium Benzoate, indicated that its minimum purity to be 99% and maximum to be 100.5% and was stated to meet all USP-National Formulary (NF), Food Chemicals Codex (FCC), EP and BP specifications (Emerald Performance Materials LLC, 2010). The colour pigments are all EU approved but in the USA, the following pigment (called color additive in the USA) is not approved near the eye area (CI 15850 (D&C Red 6) along with its Calcium Lake, D&C Red 7). Consequently in the USA, the Face Paints containing this colour additive should be labelled 'Keep away from the eyes' and the use of this product by children age 3 - 11 years old should be accompanied by adult supervision. The MSDS supplied for the colour pigment, CI 19140 (FD & C Yellow 5), indicated adverse acute effects such as contact with eyes may cause slight mechanical eye irritation, skin exposure may cause slight skin irritation in sensitive people, it may be harmful if swallowed and may cause respiratory irritation if inhaled (Sensient Colors Inc., October 2008). Repeated exposure may result in allergic reactions in very susceptible individuals. Subsequently, the product containing this colour should be labelled to warn sensitive individuals to discontinue use if this product disagrees with them. Consequently, this product complies to the EU Directive 76/768/EEC and U.S. regulatory requirements.

Thus, review of the toxicology of the ingredients for this product indicated the potential for low to negligible risk from irritation, allergy, ingestion, inhalation, corrosivity, phototoxicity, photosensitization, if used as directed, either for a prolonged period or repeatedly. Also, there are no known or documented carcinogenic, mutagenic or reprotoxic effects of the ingredients to cause adverse effects when used as directed. However, the possibility cannot be discounted that a small number of consumers may experience an allergic reaction or other idiosyncratic reaction to an ingredient in the formulation if they have been previously sensitised to the ingredient to the health of the majority of consumers.

Where the NOAEL value has been derived, the margin of safety calculated at even 100% dermal absorption supported the safe use of this product for the targeted age group.

A Declaration was supplied indicating that the Face Paint products contained no nanomaterials (Luck Art Industrial Co., Ltd., not dated).

A Non-Animal Testing Declaration was supplied stating that Luck Art Industrial Co., Ltd., does not commission nor perform any animal testing on any of its products (not dated).

A test report for the heavy metal contents were supplied and found to be compliant (Report No. TWNC00251059S1, Item A - Face Paints, Toxic Elements Analysis In Substrate, dated Apr 26, 2012, Lucky Art Industrial Co., Ltd.).

A Preservative (Antimicrobial) Efficiacy Test provided indicated that the bacteria were reduced by equal or > 2 log by day 14 with no further increase on day 28; for the yeast and mould no further increase were observed from day 14 (Test Report No. TWNC00310031, Lucky Art Industrial Co., Ltd., dated Jun 13, 2013).

Where a NOAEL is available for a chemical ingredient that is considered as a toxicological concern, the Margin of Safety (MoS) has been calculated as greater than 100 taking into consideration any known data on dermal absorption and bioavailability. It is generally accepted that the MoS should be a least 100 to declare a substance safe for use in a finished product and the safety of this formulation is further supported by this uncertainty factor.

The raw materials used to formulate this product are all well known ingredients. They are present at typical concentrations where they are unlikely to cause irritation or allergy.

If used as directed, use of this product should be uneventful.

Health effects of the product as supplied on the skin

The formulation as supplied may cause only minimal skin irritation even if exposure is prolonged and/or repeated.

There are low concentrations of substances present in this product which have allergenic activity. The concentrations present are sufficiently low for the level of use to ensure that people do not become sensitised. However, people who are already sensitised to a substance may react adversely to any product containing that substance even when present at

Exposure to this product is unlikely to result in phototoxic effects.

Unlikely to cause damage to internal organs following absorption through the skin.

Health effects of the product as supplied on the eye

The particulate matter within the product may cause a foreign body reaction should it accidentally enter the eye.

Accidental exposure of the eye to the formulation as supplied may result in slight eye irritation.

Health effects following ingestion of the product as supplied

The neat product if swallowed is unlikely to cause harm.

Health effects of inhaling the product

Inhalation is an unlikely route of exposure

Overall Assessment Conclusion

The ingredients are legally permitted as per Cosmetic Regulation (EC) No 1223/2009 and its amendments and the safety assessment has been carried out in accordance to Article 3 of this regulation. They must comply with the relevant purity standards for cosmetic ingredients. It is assumed that these ingredients do not contain any undisclosed impurities/contaminants that would affect the conclusions reached. The product must be manufactured in accordance with EU Guidance on Good Manufacturing Practice.

The ingredients are legally permitted as per the Federal Food, Drug, and Cosmetic Act (FD&C Act - CFR21) and its amendments. They must comply with the relevant purity standards. The product must be manufactured in accordance with FD&C guidance on Good Manufacturing Practice.

Keep away from eyes.

Discontinue use if irritation or rash develops

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. The product will give users the level of safety they can reasonably expect when used as directed.

Cosmetic Regulations Product Safety Assessor

M U Iwobi BSc, MSc, PhD, C Biol, MSB, EurProBiol
Centre Court, Meridian Business Park, Leicester. LE19 1WD

Date: 28 Nov 2013

Make-up : P6DH.Pearl Purple/ P3WH.Pearl Blue/ P42H.Gold/ P5C.Pearl Green/ P8G.Pearl Black/ P9E.Pearl White

TOXICOLOGICAL PROFILE OF SUBSTANCES

Chemical Substance: PARAFFIN WAXES

EU INCI NAME: PARAFFIN

CAS: 64742-43-4/ 64742-51-4 (8002-74-2)

EINECS 265-145-6/ 265-154-5 (232-315-6)

Cosmetic Regulatory Summary:

EU Cosmetics Status: Controlled

Systemic Exposure Dosage / Margin of Safety:

SED Adult mg/kg bw/day: 4.666 No NOAEL Available NO(A)EL mg/kg bw day: -

SED Child mg/kg bw/day: 16.766 No NOAEL Available

SED Baby mg/kg bw/day: 47.457 No NOAEL Available

Toxicological Summary:

Cosmetic Functions : Emollient / Fragrance Ingredient / Skin Conditioning / Viscosity Controlling / Viscosity Increasing-Nonaqueous. A paraffin wax with minimal skin and eye irritancy potential. Unlikely to cause allergy. Must not contain >0.1% Butadiene. Paraffin waxes (petroleum), hydrotreated or clay-treated. A complex combination of hydrocarbons obtained by treating a petroleum wax with hydrogen in the presence of a catalyst. It consists predominantly of straight chain paraffinic hydrocarbons having carbon numbers predominantly in the range of about C20 through C50. CIR expert panel concludes this is safe at the present uses and concentrations in a cosmetic product (up to 99%).

Chemical Substance: PETROLATUM

EU INCI NAME: PETROLATUM

CAS: 8009-03-8 / 8063-27-2 Function: Antistatic/Emollient

EINECS 232-373-2

Appearance: solid or semi-solid

Log Kow: > 6

Cosmetic Regulatory Summary:

EU Cosmetics Status: Controlled

Saudi Cosmetics Status: Not controlled by Saudi legislation

US Cosmetics Status: up to 82% typically (CIR 2009)

Regulatory Summary:

EU Classification: unclassified

GHS Classification: unclassified

REACh Annex XVII controlled: Not Controlled

REACh SVHC Candidate List: Not Controlled

Systemic Exposure Dosage / Margin of Safety:

SED Adult mg/kg bw/day: 4.200 MoS - Adult 60kg: 595.2 NO(A)EL mg/kg bw day: 2500

SED Child mg/kg bw/day: 15.089 MoS - Child 16.7kg: 165.6 NOAEL test method: oral chronic toxicity study

SED Baby mg/kg bw/day: 42.711 MoS - Baby 5.9kg: 58.5

Toxicological Summary:

Cosmetic Functions : Antistatic / Emollient / Hair & Skin Conditioning Agent / Skin Protectant. A highly refined very soft waxy jelly / oil with low potential to cause irritation of the skin or eye. It has been documented that repeated oral intake (ingestion) have resulted in absorption and transport to and accumulation the live, lymph nodes and spleen (Brown, BE *et al*. 1995. Fate of topical hydrocrbons in the skin *J. Soc. Cosmet. Chem., 46*, 1 - 9; von Wright, A. A review: Oral Toxicity Of Mineral Oils And Related Compounds, MO/064/11). Commonly used in skin application products, face and body and in colour cosmetics including around the eye area and lipsticks. The grade used should have low levels of polynuclear hydrocarbons and should be free of carcinogenic potential. US or European Pharmacopoeia-standard white petroleum jelly must be used. No known allergenic potential. Absorption studies of topical applications of hydrocarbon-containing compounds such as petroleum jelly and mineral oil under both *in vitro* and *in vivo* conditions using fluorescent and ultrastructural methods, found skin penetration to be limited largely to the stratum corneum interstices and did not enter nucleated cell layers of the epidermis (Brown, BE *et al*. 1995). In either intact or damaged skin (acetone-treated), the distribution of petrolatum was restricted mainly to the stratum corneum and outer the epidermis of the skin (Brown, BE *et al*. 1995). It was concluded that it was extremely unlikely following intermittent topical application that relevant quantity of white mineral hydrocarbons of a level of toxicological concern should enter the general circulation from an intact or damaged skin (Brown, BE *et al*. 1995).

Chemical Substance: GLYCERIN

EU INCI NAME: GLYCERIN

CAS: 56-81-5 / 8013-25-0
EINECS 200-289-5
Appearance: Liquid (Syrup)
Log Kow: 1.76
Water Solubility: miscible with water (1000 g/L)

Function: Denaturant / Humectant / Perfuming / Solvent / Fragrance Ingredient / Hair & Skin Conditioning Agent / Oral Care Agent / Skin Protectant / Viscosity Decreasing Agent

Melting Point: ~18^{0}C
Boiling Point: 290^{0}C
Vapour Pressure: <0.01 mm Hg @ 20

Cosmetic Regulatory Summary:

EU Cosmetics Status: Not controlled
ASEAN Cosmetics Status: Not controlled
Saudi Cosmetics Status: Not controlled by Saudi legislation
US Cosmetics Status: Not controlled
Canadian Cosmetics Status: Controlled

Regulatory Summary:

EU Classification: Not classified
GHS Classification: Not classified
REACh Annex XVII controlled: Not Controlled
REACh SVHC Candidate List: Not Controlled

Systemic Exposure Dosage / Margin of Safety:

SED Adult mg/kg bw/day: 2.333
SED Child mg/kg bw/day: 8.383
SED Baby mg/kg bw/day: 23.728

MoS - Adult 60kg: 2142.8
MoS - Child 16.7kg: 596.4
MoS - Baby 5.9kg: 210.7

NO(A)EL mg/kg bw day: 5000
NOAEL test method: 90-day oral study, rat (REACH Dossier, 2012).

Toxicological Summary:

Function: Denaturant / Humectant / Solvent /Conditioner, Viscosity Decreasing Agent. Glycerin is a sweet- tasting simple polyol compound with three hydrophilic hydroxyl groups that are responsible for its solubility in water and its hygroscopic nature. The glycerol backbone is central to all lipids known as triglycerides. Used extensively in cosmetics, toiletries and pharmaceutical products for over 100 years and is generally recognised for its low risk health effects. Consumer exposure to glycerin will occur principally through dermal and oral exposure. Upon contact, skin may feel warm due to the absorption of moisture from the skin. The majority of the toxicological information on this material is from human data. Toxic doses of glycerol, as with all chemicals, can be obtained when administered in sufficient quantities. However, health individuals can easily tolerate doses of up to 1.5g/kg or less with only slight diuresis occurring. Glycerol is absorbed from the intestinal tract and is metabolised to carbon dioxide and glycogen in the liver.

Acute toxicity: Low acute toxicity (oral and dermal LD50> 4g/kg; Inhalation LC50 (rat)> 570 mg/m3/hr). Adverse effects in humans following oral administration of glycerol include mild headache, dizziness, nausea, vomiting, thirst, and diarrhoea. A single prolonged exposure to glycerin is not likely to be absorbed in significant amounts through the skin and so is not likely to cause toxicity.

Irritation: Non-irritant on skin in the Draize test. Very low eye irritation potential. 0.1 mL undiluted glycerol was instilled in the eyes of 6 rabbit) caused no evidence of irritation after 1, 24 and 72 hours and after 7 days. The overall irritation score using the Draize system was 0-2. Causes slight irritation on topical application to the eyes. Regularly used as ophthalmic solution; repeated application of 100% glycerol to the surface of human eye has been shown on microscopic examination to cause reversible changes in the appearance of the endothelium.

Sensitisation: Non-sensitising. No reported evidence of skin sensitisation potential in human and in animal testing.

Mutagenicity/Genotoxicity: Non mutagenic or genotoxic in bacterial assay and in vitro chromosome aberration studies with or without metabolic activation.

Repeat dose toxicity: Repeated oral exposure to glycerol did not induce adverse effects other than local irritation of the gastro-intestinal tract. No toxicity effects observed in a 2-year study in rats orally administered ~ 10 g/kg bw/d (i.e. 20%) in the diet and in a 90-day study in rats administered 50000 or 200000 ppm in the diet. The NOEL in the 90-day study was concluded as 50000 ppm (~ 5000 mg/kg bw/d). For inhalation exposure to aerosols, the NOAEC for local irritant effects to the upper respiratory tract is 165 mg/m3 and 662 mg/m3 for systemic effects. Effects on fertility and reproductive performance were not observed in a 2-generation study with glycerol administered by gavage (NOAEL 2000 mg/kg bw/day). No maternal toxicity or teratogenic effects were seen in the rat, mouse or rabbit at the highest dose levels tested in a guideline comparable teratogenicity study (NOEL >1180 mg/kg bw/day). No evidence for carcinogenicity seen in the lifetime study in the rat.

Photo-induced toxicity: No data available which indicates phototoxicity including irritation or sensitisation potential.

Other data (human): Ingestion of 30 ml of glycerol thrice daily for a period of 50 days by normal human subjects was found to be harmless. However, a few cases of reactions such as lowered blood sugar and unconsciousness, following intravenous or oral doses have been reported in susceptible individuals.

Dermal / percutaneous absorption: When applied to unbroken skin, pure glycerine apparently is not appreciably absorbed. However, glycerin may be absorbed in potentially harmful amounts when applied in large quantities to severe burns (second or third degree) over large areas of the body as part of a cream or other topical application. Absorption under such circumstances can elevate serum osmolality and may result in osmotic shock (DOW, 2009). Worst case dermal absorption of 100% is assumed.

Margin of Safety: NOEL: 5000 mg/kg bw/d; Dermal Absorption (Dap) = 100%

References:

Dow 2009: OPTIM Glycerine Safety and Handling. Dow Perf. Materials and Basic Chem Answer Centre. Assessed on 26/02/2013 at:: https://dow-answer.custhelp.com/app/answers/detail/a_id/3491/~/optim-glycerine-safety-and-handling

OECD SIDS Initial Assessment Report for SIAM 14, 2002.

REACH Dossier for Glycerin (CAS No. 56-81-5; EINECS No. 200-285-9). Accessed at: http://echa.europa.eu

Chemical Substance: CALCIUM CARBONATE

EU INCI NAME: CALCIUM CARBONATE

CAS: 471-34-1 / 1317-65-3

EINECS 207-439-9

Appearance: Brilliant white solid reduced in amorphous powder

Melting Point: 1339°C under 1025 atm

Boiling Point: N/A

Water Solubility: < 0.1% at 23°C DIN ISO 787 -20°C 0,3%)

Vapour Pressure: N/A

Cosmetic Regulatory Summary:

EU Cosmetics Status: Approved colour all products

Saudi Cosmetics Status: Permitted colour field 1 All products

US Cosmetics Status: Not controlled

Canadian Cosmetics Status: Not controlled

Regulatory Summary:

EU Classification: unclassified

GHS Classification: Unclassified

REACh Annex XVII controlled: Not Controlled

Systemic Exposure Dosage / Margin of Safety:

SED Adult mg/kg bw/day: 5.553 No NOAEL Available

SED Child mg/kg bw/day: 19.952 No NOAEL Available

SED Baby mg/kg bw/day: 56.474 No NOAEL Available

NO(A)EL mg/kg bw day: -

NOAEL test method: -

Toxicological Summary:

Cosmetic Functions : Abrasive / Buffering / Bulking / Opacifying / Oral Care. A mineral also considered as an approved colouring agent-CI 77220. An inorganic salt with little or no irritant or allergenic potential in contact with the skin. As supplied, no acute toxic effect was observed locally from either inhalation, skin or eye contact, nor by ingestion (MSDS information, PROVENCALE S.A., 2010). It has a very low acute oral toxicity (LD50: rat, 6450 mg/kg), it was moderately irritating to skin (500 mg/24h in rabbit) and eyes (50 mg/24h in rabbit) (MSDS information, PROVENCALE S.A., 2010). The powder may cause a foreign body reaction in contact with the eye and irritate the nose and respiratory system. Unlikely to cause adverse effects at the typical concentrations used in cosmetics.

No free silica (MSDS information, PROVENCALE S.A., 2010).

Chemical Substance: ETHOXYLATED ALCOHOL

CAS: 68439-49-6/ 68439-50-9/ 78330-21-9

EINECS polymer

Log Kow: not known

Melting Point: 47.5

Vapour Pressure: 133.322368

Water Solubility: n/a

Cosmetic Regulatory Summary:

Saudi Cosmetics Status: Not controlled by Saudi legislation

Regulatory Summary:

EU Classification: R22-38-41

Systemic Exposure Dosage / Margin of Safety:

SED Adult mg/kg bw/day: 1.026 No NOAEL Available

SED Child mg/kg bw/day: 3.688 No NOAEL Available

SED Baby mg/kg bw/day: 10.440 No NOAEL Available

NO(A)EL mg/kg bw day: -

Toxicological Summary:

Cosmetic Function : Surfactant. An ethoxylated fatty alcohol which are usually harmful if swallowed so ingestion will cause irritation of the GI tract. Also irritating to skin and eyes when supplied but when diluted in a formulation unlikely to make a major contribution to irritancy. Will interact with other surfactants to give reduced overall irritancy. Not a known sensitiser. When used in a formulation the concentration will be reduced and the irritant properties reduced but effects on the eye will still be noted. Widely used in household and personal products with good acceptance in the marketplace.

Chemical Substance: ETHYLHEXYLGLYCERIN & PHENOXYETHANOL

EU INCI NAME: ETHYLHEXYLGLYCERIN & PHENOXYETHANOL

CAS: 70445-33-9 & 122-99-6 Function: Preservative
EINECS 408-080-2 & 204-584-7

Cosmetic Regulatory Summary:

EU Cosmetics Status: Approved preservative (phenoxyethanol 1%)
ASEAN Cosmetics Status: Approved preservative (phenoxyethanol 1%)
Saudi Cosmetics Status: Approved preservative (phenoxyethanol 1%)
US Cosmetics Status: Not controlled
Canadian Cosmetics Status: Approved preservative (phenoxyethanol)

Regulatory Summary:

EU Classification: R41-52/53, R22-36
GHS Classification: Not Controlled
REACh SVHC Candidate List: Not Controlled

Systemic Exposure Dosage / Margin of Safety:

SED Adult mg/kg bw/day: 0.056 MoS - Adult 60kg: 1428.5 NO(A)EL mg/kg bw day: 80
SED Child mg/kg bw/day: 0.201 MoS - Child 16.7kg: 397.6
SED Baby mg/kg bw/day: 0.569 MoS - Baby 5.9kg: 140.4

Toxicological Summary:

A mixture of phenoxyethanol permitted under EU regulations together with a humectant. The active ingredient is permitted at 1%. Ethylhexylglycerin as supplied classified as severely irritating to eyes but a 5% solution in water is said to be non irritating to eyes . Not a skin sensitiser . Unlikely to cause irritancy or allergy when used at up to 5% in a cosmetic product. Phenoxyethanol a widely used preservative. Works well in combination with other preservatives. Max permitted concentration 1%. The manufacturer recommend the use of this preservative system within the range 0.5-1.0% for leave on products.

Profile of phenoxyethanol: Preservative / Fragrance Ingredient. A widely used and well accepted preservative. Described as a rare sensitiser with 2 reported cases in 1984 and 1998. Also report of Contact urticaria from the use of cosmetic products containing phenoxyethanol (Herna´ndez, B, Ortiz-Frutos, F J, Garcı´a, M, Palencia, S, Garcı´a, M C and Iglesias, L. 2002. Contact urticaria from 2-phenoxyethanol. CONTACT DERMATITIS, 47: 54). . Unlikely to cause irritancy or allergy at typical levels of use. Information from CIR review states phenoxyethanol is not a sensitizer, is a strong eye irritant when undiluted but non irritating at 2.2%. Maximum permitted concentration in EU is 1%. Toxicological data: Acute oral toxicity : LD50 rat 1250 mg/kg; Acute dermal toxicity : LD50: > 2000 mg/kg; Skin irritation : rabbit, Not considered as being a skin irritant. (OECD Test Guideline, 404); Eye irritation : rabbit, Irritating to eyes.(OECD Test Guideline, 405); Non mutagenic in the Ames test. Other gene mutation tests were also negative (IUCLID, 2000d; OECD SIDS, 2004). Sensitisation : Maximisation Test (GPMT) guinea pig, Did not cause sensitization on laboratory animals (Method: OECD Test Guideline, 406. A survey with patch tests showed only one positive response to phenoxyethanol (5% in petrolatum) corresponding to 0.2% out of the 501 patients (IUCLID, 2000d; De Groot et al, 1986).Human skin absorption of phenoxyethanol is tested in vitro and shows that about 60% of the substances is absorbed after 6 hours (Roper et al, 1997). After either oral or dermal exposure can be found unchanged in the urine together with small quantities of two substances to which the phenoxyethanol has metabolized. The oral (gavage), repeated-dose 90 day NOAEL in rats is 80 mg/kg bw/day. For this 90% solution the NOAEL can be adjusted to 89mg/kg/day.

Reference: A survey and health assessment of cosmetic products for children; Pia Brunn Poulsen & Anders Schmidt FORCE Technology Survey of Chemical Substances in Consumer Products, No. 88 2007

OECD SIDS ETHYLENE GLYCOL PHENYL ETHER; SIDS Initial Assessment Report For SIAM 18 Paris, France, 20-23 April 2004

Chemical Substance: DISODIUM EDTA

EU INCI NAME: Disodium EDTA

CAS: 139-33-3 / 6381-92-6 Function: Additive

EINECS 205-358-3

Appearance: White crystals Melting Point: 240

Water Solubility: Soluble in water. 100g/L at 20oC Boiling Point: >100

Cosmetic Regulatory Summary:

Saudi Cosmetics Status: Not controlled by Saudi legislation

US Cosmetics Status: <1% (CIR, 2009).

Regulatory Summary:

EU Classification: Xi R36-52/53

REACh Annex XVII controlled: Not Controlled

REACh SVHC Candidate List: Not Controlled

Systemic Exposure Dosage / Margin of Safety:

SED Adult mg/kg bw/day: 0.046 MoS - Adult 60kg: 10714.2 NO(A)EL mg/kg bw day: 500

SED Child mg/kg bw/day: 0.167 MoS - Child 16.7kg: 2982.1 NOAEL test method: Based on Trisodium EDTA in a two year dietary study (CSTEE, 2003).

SED Baby mg/kg bw/day: 0.474 MoS - Baby 5.9kg: 1053.5

Toxicological Summary:

Functions : Chelating / Viscosity Controlling. EDTA is used as a chelating agent in cosmetic formulations. The ability of these complexes to aid penetration of certain compounds, particularly calcium based compounds, must also be taken into account when used with other chemicals that are considered safe because they are not significantly absorbed. Unlikely to add to the toxicity of rinse off products. Comprehensive evaluations of disodium EDTA have been conducted by the FDA and approved for direct addition in specified foods under prescribed levels under 21 CFR 172.135. CIR, has also evaluated the safety of disodium EDTA. Acute Toxicity: Disodium EDTA is slightly toxic to rat through oral route and the oral LD50 studies in rats was determined to be >2000 mg/kg bw. Clinical signs of toxicity included convulsions, diarrhea, ataxia, intestinal hemorrhage were exhibited. The oral, intraperitoneal and intravenous LD50 in mouse is 400, 260 and 56 mg/kg bw respectively (CIR, 2002, RTECS AH4375000). Irritation and Corrosivity:Skin : Results of in vivo studies in rabbits applied with disodium EDTA showed no irritating effects and classified as a non irritant (CIR, 2002). Eye Irritation : Result of in vivo studies in rabbits applied into the conjunctival sac with disodium EDTA showed no irritation to the eyes and classified as non irritant (CIR, 2002). Skin Sensitisation: Results of both in vivo skin sensitization test with disodium EDTA showed no evidence of sensitization potential in guinea pigs (CIR, 2002). Dermal/Percutaneous Absorption: No data available. Repeated Dose Toxicity: Results of sub chronic and chronic animal studies indicate that disodium EDTA is practically non-toxic (CIR 2002). Mutagenicity/Genotoxicity: Disodium EDTA was non genotoxic in ames assay with all the strains of Salmonella typhimurium in the presence and absence of metabolic activation system. Similarly, no chromosomal aberrations were observed in Gesonula punctifrons germinal cells. In contrast to the above results, weak increase of aberrations was seen in germinal cells of male grasshopper. Increased micronuclei were observed in in vivo bone marrow micronucleus assay in mice. However, no incidence of mutations was observed in dominant lethal assay. It is predicted that EDTA and its salts are non mutagenic nor genotoxic provided that it does not deplete the trace elements essential for the enzymes involved in DNA synthesis and normal cell function (CIR, 2002). Carcinogenicity: Carcinogenicity study was conducted in both rats and mice fed with trisodiumEDTA trihydrate. The concentration of trisodium EDTA administered was approximately 535 and 1070 mg/kg/day in mice and 375 and 750 mg/kg/day for a period of 103 weeks. Neither compound related clinical signs of toxicity nor incidence of tumors were observed in both rats and mice indicating no carcinogenic potential (NCI, 1977) . Reproductive and Developmental Toxicity: Several reproductive and developmental toxicity studies were conducted with disodium EDTA where the final conclusion is the toxicity caused by disodium EDTA may be attributed to the zinc deficiency induced by disodium EDTA rather the toxicity of the substance itself. Impaired reproduction and increased incidence of malformations indicative of both reproductive and developmental toxicities were observed in animals administered with disodium EDTA (CIR, 2002). Toxicokinetics: Disodium EDTA administered to rats through diet at a dose levels of 0.5, 1.0 and 5.0% showed 99.4, 98.2 and 97.5% in the faeces suggesting that EDTA is poorly absorbed. In another study 93% of the administered dose (95 mg) was recovered from the colon. (WHO/FAO, 1967). Photo-Induced Toxicity:No data reported. Human Data:Clinical studies with 26 human volunteers applied with 0.2g of disodium EDTA in a 4-hour patch test did not showed any irritation potential in any of the subjects (CIR, 2002). No-Observed-Adverse Effect Level (NOAEL) and Rationale: Although sub-chronic oral studies were conducted with disodium EDTA, No-Observed Adverse Effect Levels were not calculated. The NOAEL of trisodium EDTA in a two year dietary study was derived to be 500 mg/kg/day (CSTEE, 2003). One study in mice fed with trisodium EDTA exhibited decrease in body weight gain in males. And the lowest-effect level (LEL) was determined to be 1125 mg/kg/day and the no observed effect level (NOEL) was 563 mg/kg/day (CIR, 2002). Evidence for reproductive toxicity has been shown in animal studies with EDTA salts (NOAEL: 750 mg/kg bw/d); clinical studies indicate that EDTA and its salt are not absorbed into the body from dermal or oral ingestion and thus not bioavailable to exert toxicity effects. Acting as chelator, disodium EDTA is expected to be consumed in reaction during the production with minimal free form in the finished product.

Chemical Substance: SODIUM BENZOATE

EU INCI NAME: SODIUM BENZOATE

CAS: 532-32-1
EINECS 208-534-8
Appearance: Crystalline powder
Log Kow: -2.27
Water Solubility: Soluble (550–630 g/l at 20 °C)

Function: preservatives

Melting Point: 330.6 °C
Boiling Point: 465°C
Vapour Pressure: N/A

Cosmetic Regulatory Summary:

EU Cosmetics Status:	Approved preservative
Saudi Cosmetics Status:	Permitted preservative - all products. Max conc 0.5%.
US Cosmetics Status:	Safe for use in all cosmetic formulations up to 5%; insufficient data to support safety in
Canadian Cosmetics Status:	Approved preservative

Regulatory Summary:

EU Classification:	Unclassified
GHS Classification:	Unclassified
REACh Annex XVII controlled:	Not Controlled
REACh SVHC Candidate List:	Not Controlled

Systemic Exposure Dosage / Margin of Safety:

SED Adult mg/kg bw/day: 0.041
SED Child mg/kg bw/day: 0.149
SED Baby mg/kg bw/day: 0.422

MoS - Adult 60kg: 19261.6
MoS - Child 16.7kg: 5361.1
MoS - Baby 5.9kg: 1894.0

NO(A)EL mg/kg bw day: 800
NOAEL test method: 90-day oral dose study - benzoic acid; rat

Toxicological Summary:

Cosmetic Functions : Anticorrosive / Masking / Preservative. Sodium benzoate is a hygroscopic salt produced by the neutralization of benzoic acid with sodium hydroxide. Benzoic acid and sodium benzoate are commonly used as preservatives in beverages, food products and condiments. Benzoic acid occurs naturally in many plants and in animals. It is therefore a natural constituent of many foods, including milk products. The WHO established an ADI of 5 mg/kg for Sodium Benzoate and benzoic acid. Given GRAS status in the US for food use. EU: SCCP/0891/05 opinion concludes that benzoic acid and sodium benzoate are safe to use in oral care products up to a maximum concentration of 1.7% and cosmetic rinse off products up to 2.5%. The maximum legal limits below apply for preservation purposes only. Rinse-off products, except oral care products: 2.5 % (acid); Oral care products: 1.7 %(acid); Leave-on products: 0.5 % (acid). Benzoic acid and the salts follow a common metabolic pathway and benzyl alcohol is metabolised to benzoic acid, thus the available data for the other compounds have been considered in establishing the toxicity profile of sodium benzoate. After oral uptake, benzoic acid and sodium benzoate are rapidly absorbed from the gastrointestinal tract and metabolized in the liver by conjugation with glycine, resulting in the formation of hippuric acid, which is rapidly excreted via the urine. To a lesser extent, benzoates applied dermally can penetrate through the skin. Owing to rapid metabolism and excretion, an accumulation of the benzoates or their metabolites is not to be expected (CICAD, 2000).

Acute toxicity: Not acutely toxic or harmful by oral, dermal or inhalative route. Sodium benzoate and benzoic acid were practically non-toxic in acute oral and dermal studies. The LD50 values were > 2000 mg/kg bw. 4 h of inhalation exposure to benzyl alcohol or benzoic acid at 4 and 12 mg/L aerosol/dust, respectively, did not cause death in rats (OECD, 2001). Thus, low acute toxicity was associated with the acid and its salts.

Irritation: Sodium benzoate is non-irritating to the skin but it is a slight eye irritant (CICAD, 2000; OECD, 2001).

Sensitisation: Non-sensitising in guinea pig maximization test (OECD, 2001). However, a low incidence of positive reactions was observed in dermatologic patients patch tested and, it has been suggested that the positive reactions observed were actually non-immunologic contact urticaria.

Mutagenicity/Genotoxicity: Sodium benzoate and benzoic acid were found negative in bacterial mutation assays (Ames test). Various results (negative and positive [chromosomal/chromatid responses]) for sodium benzoate, potassium benzoate, and benzyl alcohol were obtained in other in vitro genotoxicity assays. Sodium benzoate and potassium benzoate were positive in the spore rec-assay to assess DNA damaging activity. Also, sodium benzoate caused a significant increase in sister chromatid exchanges when compared to control cultures (OECD, 2001). However, while some mixed and/or equivocal in vitro chromosomal/chromatid responses have been observed, sodium benzoate was not genotoxic in the in vivo cytogenetic assay, the micronucleus test, or in other in vivo assays. The weight of evidence of the in vitro and in vivo genotoxicity data indicates that sodium benzoate is not mutagenic or clastogenic (OECD, 2001).

Repeat dose toxicity: Benzoic acid and its salts exhibited low repeated dose toxicity. According to the OECD SIDS initial assessment report on Benzoates (2001), repeated dose oral toxicity studies yielded a NOAEL of 800 mg/kg bw/day for benzoic acid and > 1000 mg/kg bw/day for the salts. At greater doses, increased mortality, reduced weight gain, and liver and kidney effects were observed. Systemic toxic effects of a similar nature (e.g. liver, kidney) were observed after dosing with benzyl alcohol, benzoic acid, sodium benzoate, and potassium benzoate. However, these effects were observed at higher doses of benzoic acid and its salts when compared to dosing with benzyl alcohol. Long-term studies on benzyl alcohol yielded a NOAEL of > 400 mg/kg bw/d for rats and > 200 mg/kg bw/d for mice. Systemic/dermal effects induced by benzyl benzoate were observed in rats receiving repeated dermal doses up to 2.0 g/kg and in rabbits receiving 2.2 g/kg doses. The following effects were observed in rats following dermal application of 0.188, 0.488, 0.781, 1.25, or 2.0 g/kg for 30 days: hyperplasia of squamous epithelium, degeneration of hair follicles and sebaceous glands, subcutaneous fibrosis, and hyperplasia of the thyroid gland. The NOEL was 0.781g/kg/d (CIR, 2011). A 4-week inhalation study on aerosolized benzoic acid was performed in rats exposed nose-only 5 days/week, 6h/day to concentrations of 2.5 or 12.5 mg/m3. No adverse toxicity or treatment-related effects were noted (references as cited in CIR, 2011). Several reproductive and developmental toxicity studies on different species have been conducted with sodium benzoate. Embryotoxic and fetotoxic effects as well as malformations were seen only at doses that induced severe maternal toxicity. In a dietary study in rats, a NO(A)EL of about 1310 mg/kg bw/d was established (CICAD, 2000). No evidence of carcinogenicity was seen in long-term dietary study in rats fed 1% or 2% sodium benzoate for 18 to 24 months (CIR, 2011). The NOAEL of 800 mg/kg bw/d determined in the oral study with benzoic acid is considered the most adequate in estimating the safety margin.

Phototoxicity: The photogenotoxicity of benzoic acid (0.5%) and sodium benzoate (0.5%) and other food additives was evaluated using Escherichia coli cell suspensions (CIR, 2011). Neither benzoic acid nor sodium benzoate affected cell viability (i.e. not cytotoxic) or the number of spontaneous mutations in the absence of sunlight. Exposure to sunlight resulted in cell death in the presence or absence of benzoic acid or sodium benzoate. The induced mutation in cells exposed to sunlight was increased in the presence of benzoic acid and sodium benzoate which suggests that these compounds may have photo-induced toxicity potential. The photohaemolytic activity of benzyl alcohol and sodium benzoate in vitro was evaluated in a test involving human erythrocyte suspensions, incubated with either chemical (10-3 mol/l) for 1 h and exposed to UVA or UVB radiation. Neither compound induced significant haemolysis (CIR, 2011).

Human data: In humans, the acute toxicity of benzoic acid and sodium benzoate is low. However, both substances are known to cause non-immunological contact reactions (pseudoallergy). This effect is scarce in healthy subjects; in patients with frequent urticaria or asthma, symptoms or exacerbation of symptoms was observed. A provisional tolerable intake of 5 mg/kg bw/day was derived by the WHO Panel (CICAD, 2000), although benzoates at lower doses can cause non-immunological contact reactions (pseudoallergy) in sensitive persons.

Dermal / percutaneous absorption: No data with sodium benzoate is available. Benzoic acid is not completely absorbed by the dermal route. In a study with six human subjects, an uptake of 36% of the applied dose (14C-labelled benzoic acid dissolved in acetone was reported within 12h. The total uptake within 5 days was 43%. This observation was confirmed in animal studies in vivo. The dermal absorption ranged from 25% in pig to 89% in rhesus monkey

Chemical Substance: ACACIA SENEGAL GUM

EU INCI NAME: ACACIA SENEGAL

CAS: 9000-01-5
EINECS 232-519-5
Appearance: A pale white to orange-brown solid
Log Kow: Not available
Water Solubility: Soluble (1 g in 2 ml of water, JECFA, 2006)

Function: viscosity controlling agents

Melting Point: Not available
Boiling Point: N/A
Vapour Pressure: N/A

Cosmetic Regulatory Summary:

EU Cosmetics Status: Not controlled
Saudi Cosmetics Status: Not controlled
US Cosmetics Status: Not controlled
Canadian Cosmetics Status: Not controlled

Regulatory Summary:

EU Classification: R36
GHS Classification: Unclassfied
REACh Annex XVII controlled: Not Controlled

Systemic Exposure Dosage / Margin of Safety:

SED Adult mg/kg bw/day: 0.018
SED Child mg/kg bw/day: 0.067
SED Baby mg/kg bw/day: 0.189

MoS - Adult 60kg: 36589.2
MoS - Child 16.7kg: 10184.0
MoS - Baby 5.9kg: 3597.9

NO(A)EL mg/kg bw day: 683
NOAEL test method: Base on the developmental study in rats(JECFA, 2006)

Toxicological Summary:

Widely used as a stabiliser/thickener in food. Reports of allergy usually caused by preservatives added to the material. When the resin is used at up to 1% as a thickener, unlikely to cause irritancy or allergy. As supplied, in powder form, this is severely irritating to the eyes and has been reported to be a respiratory allergen in printing workers. Ingested orally, acacia is non-toxic. It may also give rise to skin sensitisation in sensitive individuals. When used at a low concentration in a cosmetic product it is unlikely to produce skin irritation or allergy. However due to its potential as a respiratory allergen it should not be used in aerosols or spray preparations. Some institutions have classified this as R42, R36. Gum arabic is has been given GRAS status by the FDA and considered as suitable as a direct food additive. The CIR panel (2006) concluded that the toxicity data indicates little or no acute, short-term or sub-chronic toxicity. Tests have indicated that it has a very low acute oral toxicity (LD50: hamster, >18000 mg/kg/d, strain, sex and number were not specified) and >16000 mg/kg /d in mice, strain, sex and number were not specified (ChemIDplus 2012). No relevant information was available following the literature searching on its dermal and inhalation toxicity nor on its skin and eye irritation. It has a slow rate of dermal absorption of gum arabic due to its large molecular size and water solubility (CIR Compendium 2012). However there is some evidence of sensitisation in sensitive individuals. Some people are allergic to its dust and develop skin lesions and severe asthmatic attacks when in contact with it (HSDB, 2002). However, considering the extensive safety testing of this gum, the CIR concluded gum arabic was safe for use in cosmetic products. A negative result was given for all 25 subjects in a human maximisation study from a mascara contain 8% acacia gum and it was concluded that through normal use in a cosmetic product sensitisation is unlikely. It was not found to be mutagenic; a carcinogenesis bioassay of gum arabic using a 81 -86% purity was conducted by feeding diets containing 25,000 or 50,000 ppm of the test substance rats and mice of each sex for 103 weeks was negative for carcinogenicity (HSDB, 2002). It was not toxic to reproduction or development (CIR Compendium 2012; JECFA, 2006; JECFA, 1982a). In cosmetic products, it is considered as safe at up to 9% for the gum and 0.001% for the extract (CIR Compendium 2012).

Chemical Substance: DEXTRIN

EU INCI NAME: DEXTRIN

CAS: 9004-53-9
EINECS 232-675-4

Function: absorbents / binders / viscosity controlling agents

Cosmetic Regulatory Summary:

Saudi Cosmetics Status: Not controlled by Saudi legislation

Regulatory Summary:

EU Classification: Unclassified

Systemic Exposure Dosage / Margin of Safety:

SED Adult mg/kg bw/day: 3.313
SED Child mg/kg bw/day: 11.904
SED Baby mg/kg bw/day: 33.694

No NOAEL Available
No NOAEL Available
No NOAEL Available

NO(A)EL mg/kg bw day: -

Toxicological Summary:

Cosmetic Functions : Absorbent / Binding / Bulking / Viscosity Controlling / Viscosity Increasing Agent-Aqueous. A high molecular weight glucose polymer. Low potential to cause irritancy or allergy.

Chemical Substance: AQUA

Systemic Exposure Dosage / Margin of Safety:

SED Adult mg/kg bw/day: 0.233
SED Child mg/kg bw/day: 0.838
SED Baby mg/kg bw/day: 2.372

No NOAEL Available
No NOAEL Available
No NOAEL Available

NO(A)EL mg/kg bw day: -

Toxicological Summary:

Chemical Substance: MICA (CI 77019)

EU INCI NAME: MICA

CAS: 12001-26-2
EINECS 310-127-6
Appearance: Crystalline solid
Log Kow: N/A
Water Solubility: Insoluble

Function: Opacifying

Melting Point: Not available.
Boiling Point: N/A
Vapour Pressure: N/A

Cosmetic Regulatory Summary:

EU Cosmetics Status: Not controlled
ASEAN Cosmetics Status: Not controlled
Saudi Cosmetics Status: Not controlled
US Cosmetics Status: Mica No restrictions 73.2496.
Canadian Cosmetics Status: Not controlled

Regulatory Summary:

EU Classification: unclassified
GHS Classification: unclassified
REACh Annex XVII controlled: Not Controlled
REACh SVHC Candidate List: Not Controlled

Systemic Exposure Dosage / Margin of Safety:

SED Adult mg/kg bw/day: 1.633 No NOAEL Available
SED Child mg/kg bw/day: 5.868 No NOAEL Available
SED Baby mg/kg bw/day: 16.610 No NOAEL Available

NO(A)EL mg/kg bw day: -
NOAEL test method: -

Toxicological Summary:

Mica is silicate mineral with diverse chemical composition. Used in the production of pearlescent pigments and as a bulking agent in cosmetic products. The material is considered to be “chemically inert” and of a size unlikely to be inhaled (i.e. > 100 µm). There is low concern for systemic toxicity with non-respirable mica. It is not considered to be irritating to the skin or eyes and not known to cause skin sensitisation or elicitation of allergic reaction. Inhalation of mica dust over a period of years may cause fibrogenic response resulting in scarring of the lungs. Permitted for use in US, Canada and Saudi regulatory regimes.
High LD50 and not of toxicological concern (except for Mica that may contain crystalline quartz, which is known to be carcinogenic to humans [WHO, 2012; HSDB, 2012]. Margin of Safety (MoS): Inadequate data available to identify a NOAEL; therefore MoS cannot be calculated.

Chemical Substance: MAY CONTAIN (+/-)

EU INCI NAME: -

CAS: ----------
EINECS ----------
Appearance: -
Log Kow: -
Water Solubility: -

Function: ----------

Melting Point: -
Boiling Point: -
Vapour Pressure: -

Cosmetic Regulatory Summary:

EU Cosmetics Status: ----------
ASEAN Cosmetics Status: ----------
Saudi Cosmetics Status: ----------
US Cosmetics Status: ----------
Canadian Cosmetics Status: ----------

Regulatory Summary:

EU Classification: ----------
GHS Classification: ----------
REACh Annex XVII controlled: ----------
REACh SVHC Candidate List: ----------

Systemic Exposure Dosage / Margin of Safety:

SED Adult mg/kg bw/day: .000 No NOAEL Available
SED Child mg/kg bw/day: .000 No NOAEL Available
SED Baby mg/kg bw/day: .000 No NOAEL Available

NOAEL test method: -

Toxicological Summary:

Chemical Substance: CI 15850:1 (D&C RED NO.7 CALCIUM LAKE)

EU INCI NAME: CI 15850

CAS: 5858-81-1/ 5281-04-9
EINECS 226-109-5
Appearance: Red powder
Log Kow: 3.587 ± 0.796 (calculated) (SCCNFP, 2004)
Water Solubility: 1% soluble in water) (SCCNFP, 2004)

Function: Colour

Melting Point: Not available.
Boiling Point: N/A
Vapour Pressure: Not available.

Cosmetic Regulatory Summary:

EU Cosmetics Status: Approved colour all products
Saudi Cosmetics Status: Permitted colour field 1 All products
US Cosmetics Status: Cosmetics generally 74.2307 except eye area (CI 15850:1)
Canadian Cosmetics Status: Not controlled

Regulatory Summary:

EU Classification: R20/22
GHS Classification: Unclassified
REACh Annex XVII controlled: Not Controlled

Systemic Exposure Dosage / Margin of Safety:

SED Adult mg/kg bw/day: 0.096
SED Child mg/kg bw/day: 0.346
SED Baby mg/kg bw/day: 0.980

MoS - Adult 60kg: 1556.5
MoS - Child 16.7kg: 433.2
MoS - Baby 5.9kg: 153.0

NO(A)EL mg/kg bw day: 150
NOAEL test method: Based on a 2-year repeat dose study in rats demonstrating exacerbated spontaneous kidney disease at 1000 mg/kg bw/day (SCCNFP, 2004).

Toxicological Summary:

Cosmetic Function: Cosmetic Colorant. A monoazo pigment well tested in experimental studies and with a long history of safe use in cosmetics. It is insoluble in water and unlikely to cause adverse effects at the typical concentrations used in cosmetics. CI 15850:1 known also as D&C Red No. 7 Calcium Lake is not acutely toxic, a skin irritant, an eye irritant, a skin sensitizer, mutagenic nor a reproductive toxicant. It has a very low acute oral toxicity (LD50: rat, > 10,800 mg/kg bw for the Sodium salt and >5,000 - 9,800 mg/kg bw for the Calcium salt) (SCCNFP, 2004). It was not found to be acutely toxic by the dermal route (LD50: rat, > 2,500 mg/kg bw) (ECHA 2012a, December 20). It has a very low acute inhalation toxicity (LC50: rats, >1518 ± 176 mg/m^3). A 10% solution was not irritating to rabbit skin and a 1% solution in a HET-CAM study was not irritating to rabbit eyes; a 4% solution was not found to be a skin sensitiser in mice (SCCNFP, 2004). Carcinogenicity data was inconclusive (SCCNFP, 2004). No data was readily available on its bioaccumulation potential or phototoxicity. Based on this information and other scientific literature on this ingredient, safety concerns are not expected with this ingredient for use in cosmetics. It is unlikely to cause adverse effects at the typical concentrations used in cosmetics. Permitted for use in all cosmetic types under the EU Cosmetics Regulation 1223/2009, Annex IV). Unlikely to cause adverse effects at the typical concentrations used in cosmetic products.

For US only: Not approved for use in cosmetic products intended to come into contact with the eye area.

Chemical Substance: CI 77891 (TITANIUM DIOXIDE)

EU INCI NAME: CI 77891

CAS: 13463-67-7/1317-70-0/1317-80-2
EINECS 236-675-5/205-280-1/215-282-2
Appearance: Solid
Log Kow: N/A
Water Solubility: Insoluble (<0.1mg/L)

Function: Colour

Melting Point: 1843
Boiling Point: 2500 - 3000 °C (Calculated value).
Vapour Pressure: N/A

Cosmetic Regulatory Summary:

EU Cosmetics Status: Approved colour all products
ASEAN Cosmetics Status: Approved colour all products
Saudi Cosmetics Status: Permitted colour field 1 All products
US Cosmetics Status: CI 77891 No restrictions 73.2575
Canadian Cosmetics Status: Not controlled

Regulatory Summary:

EU Classification: unclassified
GHS Classification: Unclassified
REACh Annex XVII controlled: Not Controlled
REACh SVHC Candidate List: Not Controlled

Systemic Exposure Dosage / Margin of Safety:

SED Adult mg/kg bw/day: 0.002
SED Child mg/kg bw/day: 0.007
SED Baby mg/kg bw/day: 0.021

MoS - Adult 60kg: 1177394.0
MoS - Child 16.7kg: 327708.0
MoS - Baby 5.9kg: 115777.0

NO(A)EL mg/kg bw day: 2500
NOAEL test method: NOEL in 2-year gavage study in rat

Toxicological Summary:

Titanium dioxide may be in the anatase or rutile form. It is an approved food color (E171) with an unspecified acceptable daily intake. Bioaccessibility data on titanium released from titanium dioxide were determined when exposed to synthetic biological media of varying pH and composition. Only a small fraction of titanium was released / dissolved from the titanium dioxide powder during exposure to any of the media matrices of varying acidity and composition. A trend with somewhat higher release rates with increasing acidity and exposure period was evident. Not classified in the EU. Titanium dioxide (dust) is classified by IARC as Category 2B, "Possibly carcinogen to humans" (IARC, 2010). Food and Drug Administration (FDA) has authorized the use of titanium dioxide in food, in general, at a limit not to exceed 1% by weight of the food. It has approved the use of titanium dioxide for use in OTC sunscreen drug products at concentrations up to 25%.
Acute toxicity: Not acutely toxic or harmful by the oral, inhalation or dermal route. Acute oral toxicity studies in animals (rats or mice) with micro/non micro crystalline/coated/uncoated forms of titanium dioxide were conducted, in general, the LD50 >5000 mg/kg bw. The dermal LD50 for rats is determined to be >2000 mg/kg bw (SCCNFP, 2000). The inhalation LC50 in rats was > 2 mg/L (4 hour exposure).
Irritation: Non-irritating. Results of different skin irritation studies with various types of titanium dioxide showed varying degree of erythema and completely recovered at 72 hours after application. Results of animal studies demonstrated that coated and uncoated titanium dioxide is non-irritating to the eye (SCCNFP, 2000).
Sensitisation: No sensitisation was observed with both coated and uncoated titanium dioxide in both animal and human studies.
Mutagenicity/Genotoxicity: In vitro and in vivo studies indicate that titanium dioxide is non mutagenic or genotoxic. It was negative in a battery of standard assays.
Repeat dose toxicity: Results of subchronic feeding study in mice with anatase titanium dioxide demonstrates that it has no specific systemic effects. Titanium dioxide administered by oral gavage at a dose level of 24 g/kg bw/d to rats for 28 days showed no adverse effects (REACH Dossier). Benign tumours (bronchioloalveolar adenomas and cystic keratinising squamous cell carcinoma) were reported in a 2-year inhalation study in rats at 250 mg/m3. The NOEC (No observed effect concentration) for non-neoplastic changes was reported as 10 mg/m3. Titanium dioxide administered in the diet at doses of 25000 (~1250 mg/kg bw/d) or 50000 ppm (2500 mg/kg bw/d) to rats for 2 years showed no treatment-related increased in tumour incidence or any systemic toxicity effects. NOEL was > 2500 mg/kg bw/d.
Photo-induced toxicity: Titanium dioxide is neither photo-irritant nor photo-allergenic to rabbits and guinea pigs respectively. It showed no evidence of sensitization in human volunteers. Photo genotoxicity assays have been conducted with the results showing that titanium dioxide is not photogenotoxic (SCCNFP, 2000).
Human data: The working group of the International Agency for Research on Cancer (IARC) concluded that the epidemiological studies on titanium dioxide provide inadequate evidence of carcinogenicity (IARC Monograph, Volume 93).
Others: Derived No Effect Level (DNEL) of 700 mg/kg bw/d for long term systemic exposure to titanium dioxide is given in the REACH Dossier.
Dermal / percutaneous absorption: In vitro percutaneous absorption studies with coated or uncoated titanium dioxide indicate no dermal absorption. The in vitro absorption of microfine zinc oxide and titanium dioxide through porcine skin was reported in the REACH dossier (accessed on 05/03/2013 at http: //echa.europa.eu). Titanium dioxide was not recovered in the receptor fluid; the potentially absorbable dose (total in the skin, stratum corneum and epidermis) was 0.1- 0.5%. Titanium dioxide applied in an oil/water emulsion base to the external surface of the arms showed deposition of the substance in the upper layer of the stratum corneum without any evidence of absorption reported. “Worst case” dermal absorption value of 0.5% is assumed.
Margin of Safety (MoS): NOEL: 2500 mg/kg bw/d; Dermal absorption (Dap): 0.5%

Chemical Substance: CI 19140 (FD&C YELLOW 5)

Systemic Exposure Dosage / Margin of Safety:

SED Adult mg/kg bw/day: 0.196
SED Child mg/kg bw/day: 0.704
SED Baby mg/kg bw/day: 1.993

No NOAEL Available
No NOAEL Available
No NOAEL Available

NO(A)EL mg/kg bw day: -

Toxicological Summary:

Chemical Substance: CI 77510 (FERRIC FERROCYANIDE)

EU INCI NAME: CI 77510
CAS: 14038-43-8
EINECS 237-875-5
Appearance: Powder
Log Kow: N/A
Water Solubility: 6 mg/mL at 25ºC

Function: Colour

Melting Point: Not available
Boiling Point: N/A
Vapour Pressure: N/A

Cosmetic Regulatory Summary:

EU Cosmetics Status: Approved colour all products
Saudi Cosmetics Status: Permitted colour field 1 All products
US Cosmetics Status: Externally including eye area 73.2299
Canadian Cosmetics Status: Not controlled

Regulatory Summary:

EU Classification: R32
GHS Classification: Unclassified
REACh Annex XVII controlled: Not Controlled
REACh SVHC Candidate List: Not Controlled

Systemic Exposure Dosage / Margin of Safety:

SED Adult mg/kg bw/day: 0.003
SED Child mg/kg bw/day: 0.014
SED Baby mg/kg bw/day: 0.040

MoS - Adult 60kg: 629881.5
MoS - Child 16.7kg: 175317.0
MoS - Baby 5.9kg: 61938.3

NO(A)EL mg/kg bw day: 2500
NOAEL test method: 12 week repeated dose study in rats exposed orally via drinking water (ECHA, 2013)

Toxicological Summary:

An essentially inert iron pigment which is essentially insoluble in water and alcohol. Being inert and insoluble it has minimal toxic properties. Its use in powder form should have minimal amounts available for inhalation. Various GLP-compliant study following OECD 405 guideline using 0.1 g of a mixture containing 35% Fe3+, 3% NH4+ and ~1% Na+ , and non-guideline non-GLP study using 50 mg of Iron Blue and 50 mg of sodium ferrocyanide instilled into the eyes did not demonstrate eye irritation effect (ECHA 6 Nov. 2012). Skin irritation (using GLP-compliant study following OECD 404 guidelines and non-compliant methods) and sensitisation (GLP-compliant study following OECD 406 guidelines) studies also found the pigment to be non-irritating and non-sensitising to skin (ECHA 6 Nov. 2012). Various *in vitro* bacterial assay and *in vitro* mammalian chromosome aberration test did not find this pigment to be mutagenic. A NOAEL of 2500 mg/kg bw/day is assigned based on a 12 week repeated dose study in rats when exposed orally via drinking water where no adverse effects were observed at the highest dose of Prussian Blue tested (ECHA, 2013). No data was available regarding its carcinogenicity but it is not on the list of *Chemicals Known To The State* (of California*) To Cause Cancer Or Reproductive Toxicity, May 20, 2011.* The colour pigment is approved for use in the EU for all products and in the US for externally applied cosmetics including eye area.

Chemical Substance: CI 77499 (BLACK IRON OXIDE)

EU INCI NAME: CI 77499
CAS: 12227-89-3
EINECS 235-442-9
Appearance: Powder
Water Solubility: Insoluble

Function: Colour

Melting Point: >1000

Cosmetic Regulatory Summary:

EU Cosmetics Status: Approved colour all products
Saudi Cosmetics Status: Permitted colour field 1 All products
US Cosmetics Status: Iron Oxides No restrictions 73.2250

Regulatory Summary:

EU Classification: Unclassified

Systemic Exposure Dosage / Margin of Safety:

SED Adult mg/kg bw/day: 0.571
SED Child mg/kg bw/day: 2.053
SED Baby mg/kg bw/day: 5.813

No NOAEL Available
No NOAEL Available
No NOAEL Available

NO(A)EL mg/kg bw day: -

Toxicological Summary:

This inert iron oxide has minimal skin irritancy properties. It may cause mechanical eye irritation and is a nuisance dust. Its level of use and its inert nature makes it unlikely for this substance to provoke an adverse effect.

Chemical Substance: CI 77163 (BISMUTH OXYCHLORIDE)

EU INCI NAME: CI 77163
CAS: 7787-59-9
EINECS 232-122-7
Appearance: White solid powder
Log Kow: Not available.
Water Solubility: 500°C (932°F)

Function: cosmetic colorants

Melting Point: 500°C (932°F)
Boiling Point: Not available.
Vapour Pressure: Not available.

Cosmetic Regulatory Summary:

EU Cosmetics Status: Approved colour all products
Saudi Cosmetics Status: Permitted colour field 1 All products
US Cosmetics Status: No restrictions 73.2162-Cosmetics generally including eye area use.
Canadian Cosmetics Status: Not controlled

Regulatory Summary:

EU Classification: Unclassified
GHS Classification: Unclassified
REACh Annex XVII controlled: Not Controlled

Systemic Exposure Dosage / Margin of Safety:

SED Adult mg/kg bw/day: 0.081
SED Child mg/kg bw/day: 0.293
SED Baby mg/kg bw/day: 0.830

No NOAEL Available
No NOAEL Available
No NOAEL Available

NO(A)EL mg/kg bw day: -
NOAEL test method: -

Toxicological Summary:

Cosmetic Function : Colorant. An essentially inert white substance. Being inert it is unlikely to cause any adverse effects when used in cosmetics. Approved for use in the EU for all products and in the US for cosmetics including eye area use.

Chemical Substance: ZINC OXIDE (CI 77947)

EU INCI NAME: CI 77947

CAS: 1314-13-2 Function: cosmetic colorants

EINECS 215-222-5

Appearance: Odourless, non-flammable, white or faintly yellowish, amorphous powder Melting Point: 1975 °C

Log Kow: Data not available. Boiling Point: N/A

Water Solubility: Practically insoluble in water (0.00016 g/100 ml Vapour Pressure: Data not available.

Cosmetic Regulatory Summary:

EU Cosmetics Status: Approved colour all products
Saudi Cosmetics Status: Permitted colour field 1 All products
US Cosmetics Status: CI 77947 No restrictions 73.2991
Canadian Cosmetics Status: Not controlled

Regulatory Summary:

EU Classification: N R50/53
GHS Classification: Aquatic Acute 1 (H400), Aquatic Chronic 1 (H410).
REACh Annex XVII controlled: Not Controlled

Systemic Exposure Dosage / Margin of Safety:

SED Adult mg/kg bw/day: 0.001
SED Child mg/kg bw/day: 0.005
SED Baby mg/kg bw/day: 0.014

MoS - Adult 60kg: 40816.3
MoS - Child 16.7kg: 11360.5
MoS - Baby 5.9kg: 4013.6

NO(A)EL mg/kg bw day: 60
NOAEL test method: Zinc Sulfate - maternal and developmental toxicity

Toxicological Summary:

Cosmetic Functions: Colourant / Bulking / Skin Protecting / UV Absorber. In OTC drug products, it is used as a skin protectant and a sunscreen agent. Practically insoluble in water (0.00016 g/100 ml water), soluble in diluted mineral acids. Zinc Oxide works as a sunscreen agent by reflecting and scattering UV radiation. As supplied neat, some potential to irritate the skin and eyes. Normally used at levels less than 4% in a cosmetic but can be used at higher levels in skin creams and be unlikely to cause irritation. The SCCP considers that on basis of the dossier reviewed in 2003 the use of ZnO in its non-nano form (pigment grade, with particle sizes above 100 nm) is considered safe as a UV-filter up to 25%. The concern expressed in the SCCNFP opinion 0693/03 with regard to phototoxicity is not relevant for this form of ZnO due to the absence of dermal penetration (SCCP/1215/09).
In its most recent opinion the SCCS (SCCS/1489/12) further confirmed the following:
- On the basis of available evidence that the use of ZnO nanoparticles with the characteristics specified in the opinion publication, at a concentration up to 25% as a UV-filter in sunscreens, can be considered not to pose a risk of adverse effects in humans after dermal application. This does not apply to other applications that might lead to inhalation exposure to ZnO nanoparticles (such as sprayable products). Also, this assessment only applies to ZnO nanoparticles that are included in this dossier, or are similar materials that have the characteristics indicated in the published opinion.
-The use of larger (non-nano) forms of ZnO as a UV-filter with a concentration up to 25%, as stated in the SCCP clarification (SCCP/1215/09), is safe and is not of any additional safety concern compared to the nano-forms assessed in this Opinion.

However, the SCCS (SCCS/1489/12) further notes that in view of the lung inflammation induced by ZnO particles after inhalation exposure, the use of ZnO in cosmetic products which may result in inhalation is of concern. In addition the SCCS (SCCS/1489/12) points out that any cosmetic products containing ZnO particles (nano or non-nano) with coatings that can promote dermal penetration will also be of concern.

Acute Oral Toxicity: LD50 > 5000 mg/kg
Acute Dermal Toxicity:LD50 > 2000 mg/kg.
Conclusion: ZnO is non-toxic after a single oral ingestion and non toxic after a single dermal application.
Non skin irritating after repeated application in different animal species. Non skin sensitizing.
Inhalation: Occupational exposure standards of ZnO fume are 5 mg/m³ (long term) and 10 mg/m³ (short term).
According to EU criteria, ZnO is considered non irritating to the eyes.
No Observed Effect Level (NOEL) with regard to maternal and developmental toxicity of Zinc Sulfate was at least 60.0 mg/kg (corresponding to about 24 mg/kg if expressed as zinc.
The systemically available amount of zinc can be considered to be < 1 % of the applied dose.
ZnO is virtually non photo reactive and no photo toxicity observed in tests. Non-photosensitising.
No toxicity at 40 mg/kg bw/d for a period of 120 days in the diet. The FDA has also approved the use of Zinc Oxide for use in OTC skin protectants and ano-rectal skin protectant drug products at concentrations up to 25%, and in sunscreen drug products at concentrations up to 25%. It is a colorant in cosmetics that is exempt from certification for the US.

Note: In the absence of NO(A)EL data, the Margin of Safety (MoS) has not been calculated.
Unless otherwise determined and in the absence of literature or other experimental data, a Dermal Absorption (DAp) of 100% is taken as the worst case scenario.
NO(A)EL: No Observed Adverse Effect Level; MoS: Margin of Safety; SED Systemic Exposure Dosage
Calculation of Margin of Safety: MoS = NO(A)EL / SED

Reference for skin surface area, exposures and application quantities are derived from:

1. RIVM Report 320104001/2006
2. References sited in Dermal Sensitization Quantitative Risk Assessment (QRA) For Fragrance Ingredients, 2006 revision
3. Exposure factors handbook 2009 Update
4. SCCP Notes of Guidance For testing of Cosmetic Ingredients and their Safety Evaluation 6th Revision
5. Colipa Data SCCNFP/0321/02
6. McNamara et al, Food Chem. Tox; 2007, 45, 2086
7. Loretz et al, Food Chem. Tox; 2008, 46, 1516
N.B. Exposure times have been taken from RIVM Report 320104001/2006
8. Body weights taken from Exposure factors handbook 2009 Update and mean values have been used unless specified otherwise
9. ConsExpo database
10. New default values for the spray model, RIVM, March 2010
11. SCCP Notes of Guidance For testing of Cosmetic Ingredients and their Safety Evaluation 8th Revision, 2012

For European Legislation only: This formulation will be assessed by Intertek in accordance with PART B , Annex I to Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 Novembe 2009 on cosmetic products (Official Journal L 342, 22 December 2009, pp. 59–209). The safety assessment is based upon the chemical specification and toxicological profile of the ingredients as supplied at the time of assessment and an assessment of the final cosmetic product. The supplier to this safety assessment is advised to ask for a new safety evaluation if any change in formulation occurs, change in raw materials used, abnormally high number of adverse events are recorded, changes in recommended uses or other circumstances that may affect the safety of this product.