QUANTITATIVE AND QUALITATIVE COMPOSITION

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Ingredient	CAS #	%	Function
Aloe Barbadensis Leaf Juice	94349-62-9	20 - 40	Skin Conditioning
Glycerin	56-81-5	20 - 40	Humectant
Sodium Palmate	61790-79-2	20 - 40	Emulsifying
Sucrose	57-50-1	10 - 20	Humectant
Sodium Cocoate	61789-81-9	5 - 10	Surfactant - Cleansing
Decyl Glucoside	54549-25-6	1 – 2.5	Surfactant - Cleansing
Aqua	7732-18-5	1 – 2.5	Solvent
Sodium Chloride	7647-14-5	1 – 2.5	Bulking /Viscosity Controlling
Citric Acid	77-91-9	0.1 – 0.5	Buffering
Citrus Aurantium Dulcis Oil	8028-48-6	0.70	Perfuming
Citrus Aurantium Flower Oil	8016-38-4	0.70	Perfuming
Tocopherol		0.20	Antioxidant
TOTAL		**100%**	

Note: The ingredient names and listing may not be assumed to be in INCI format nor in descending order suitable for product labelling.

Physico-chemical Properties

Physical: Solid.
Odour: Characteristic Citrus

Function: Bar Soap.

Statement on Approval of the Cosmetic Product Safety Assessment - Part B

This product is considered safe for human health when it is used under normal and reasonably foreseeable condition of use. The product is in accordance with the cosmetics Regulation (EC) No. 1223/2009 as amended and the United Kingdom (UK) Cosmetics Regulation, Schedule 34 of Product Safety and Metrology etc. (Amendment etc.) (EU Exit) Regulations 2019, and it is produced following Good Manufacturing Practice as stated in ISO 22716 as amended, this

product is expected to give the consumer the kind of safety likely from a product of this type. The product is also expected to take account, particular presentation including conformity with Directive 87/357/EEC as amended Dangerous Food Imitation), labelling, instructions of use and disposal, and other information relevant to this specific product (Regulation (EC) No. 1223/2009 as amended, Article 3).

ALLERGENS REQUIRED TO BE DECLARED ON THE PRODUCT LABEL
Limonene, Geraniol and Linalool.

STABILITY OF THE COSMETIC PRODUCT
Solid Soap bar considered to be stable.

MICROBIOLOGICAL TEST
Microbiological Test Report was not supplied. This can be justified on the grounds that this solid product is non-aqueous and unlikely to promote or sustain microbial growth.

PRESERVATIVE EFFICACY CHALLENGE TEST
Preservative Efficacy Challenge Test Report was not supplied. This can be on the justification that the solid product is non-aqueous and unlikely to promote or sustain microbial growth.

INFORMATION ABOUT THE PACKAGING MATERIAL
Inner packaging:

UNDESIRABLE EFFECT OR SERIOUS UNDESIRABLE EFFECT
New product none noted.

PRESENCE OF NANOMATERIAL IN THE PRODUCT
None present

NORMAL AND REASONABLY FORESEEABLE USE
This product, *Glycerine Soap Bar Sweet Orange & Neroli*, is a bar soap which is used to clean the body by washing of dirt and grease. The product comprises predominantly humectant, surfactants, bulking, chelating, viscosity controlling, emulsion stabilising, perfuming / perfuming agents. As supplied, it has the potential to cause skin and eye irritation. However, used diluted for bathing the skin, the diluted product will be only in brief contact with the skin and then rinsed off, thus would not be expected to pose a risk to health.
Used under normal and reasonably foreseeable condition of use, this product is not expected to pose a risk to health.

ASSESSMENT CONCLUSION

This product is considered safe for human health when it is used under normal and reasonably foreseeable condition of use. The product is in accordance with the cosmetics Regulation (EC) No. 1223/2009 as amended and the United Kingdom (UK) Cosmetics Regulation, Schedule 34 of Product Safety and Metrology etc. (Amendment etc.) (EU Exit) Regulations 2019, and it is

produced following Good Manufacturing Practice as stated in ISO 22716 as amended, this product is expected to give the consumer the kind of safety likely from a product of this type. The product is also expected to take account, particular presentation including conformity with Directive 87/357/EEC as amended Dangerous Food Imitation), labelling, instructions of use and disposal, and other information relevant to this specific product (Regulation (EC) No. 1223/2009 as amended, Article 3).

MARGIN OF SAFETY CONSIDERATION

Where a NOAEL was available for ingredient(s) in this product, the calculated Margin of Safety (MoS) was found to be several thousand-fold greater than the accepted 100 safe margin. This indicates the safe use of these ingredients in the product.

No Observed Adverse Effect Level (NOEAL) was available for some ingredients. The weight of evidence from other applications of the ingredients such as other cosmetic products, food or pharmaceutical fields was used to determine safe use of these ingredients in this product.

Toxicological Information - Summary

Skin: Irritating to skin.
Eyes: Irritating to eyes.

Exposure Information

Predominant: Skin.
Accidental: Eyes.
Unlikely route: Inhalation and ingestion.

Predominant Route of Exposure: Skin

Skin / Dermal:

Irritation - Exposure of the undiluted product to the skin is expected to cause skin irritation.
- Exposure of the diluted product to the skin is not expected to cause skin irritation

Sensitisation - Exposure of this product to the skin is not expected to induce nor elicit skin sensitisation.

Other Potential Routes of Exposure

Eyes: Accidental exposure of the undiluted and diluted product to eyes may cause eye irritation.

By Inhalation: Inhalation of the product is an unlikely route of exposure.

By Ingestion: If the undiluted (neat) product is accidentally ingested it may be expected to cause gastrointestinal discomfort or blockage if ingested in large amounts.

Information and Data on Exposure

Product category – Bar Soap (IFRA Class 9).
Product type – Rinse-off .
Target population – Adult.
Normal and reasonably foreseeable exposure routes – Skin.
Site of application – Whole body.
Frequency –Daily.

INCI	% Conc	SED	NOAEL	MOS
Aloe Barbadensis Leaf Juice	20 - 40	6.68	2000	299
Glycerin	20 - 40	6.68	2000	299
Sodium Palmate	20 - 40	6.68	1000	149
Sucrose	10 - 20	3.34	Not Available	Not Available
Sodium Cocoate	5 - 10	1.67	2070	1,239
Decyl Glucoside	1 – 2.5	0.4175	180	431
Aqua	1 – 2.5	N/A	-	N/A
Sodium Chloride	1 – 2.5	0.4175	Not Available	Not Available
Citric Acid	0.1 – 0.5	0.0835	1200	14,371
Citrus Aurantium Dulcis Oil	0.70	0.1169	Not Available	Not Available
Citrus Aurantium Flower Oil	0.70	0.1169	500	4,277
Tocopherol	0.20	0.0334	500	14,970

ASSESSMENT RATIONALE

A cosmetic product is considered an individual combination of cosmetic substances (SCCS Notes of Guidance, SCCS/1501/12).

This product, *Glycerine Soap Bar Sweet Orange & Neroli*, is a bar soap which is used to wash off dirt and grease from the body. The product comprises predominantly humectant, surfactants, bulking, chelating, viscosity controlling, emulsion stabilising, perfuming / perfuming agent. The active ingredients in the formulation are the surfactants which as supplied have the potential to cause skin and eye irritation. In this formulation, a range instead of exact concentrations are supplied for this safety assessment. Consequently, the highest concentrations are used for worse case scenario. If the overall actual concentration of the surfactants in this product results in its classification as a skin irritant, category 1, it is advisable that following in-use dilution, that the combined surfactants concentration is considerably less than 20% to avoid skin and less than 10% to avoid serious eye irritation. However, the characteristic of many surfactants is such that their irritancy potential in solution is reduced due to the formation of micellar structures. Furthermore, as a rinse-off product, the *Glycerine Soap Bar Sweet Orange & Neroli* will be used diluted (approximately by a dilution factor of three) and in brief contact with the skin (RIVM, 2006). Consequently, if used as

intended as a rinse-off and as advised, this product would not be expected to cause skin irritation. However, accidental exposure to eyes will result in eye irritation. The eyes should be rinsed with plenty of water; if irritation persists seek medical advice. Inhalation and ingestion are unlikely routes of normal exposure. Should the product be accidentally ingested in large quantities, seek medical assistance.

The majority of the ingredients used in the formulation are not controlled by the cosmetics Regulation (EC) No. 1223/2009 as amended, for use in this type of product. However, the predominant ingredients which are surfactants are required to be formulated such that they do not irritate the skin during normal use. Apart from the essential oils, generic detailed information and data were used in the safety assessment of this product.
It should be ensured that the specific available details for these ingredients are in accord with a compliant product as indicated in this report. The toxicological endpoints of the ingredients are detailed elsewhere in this report – see *Toxicological Profile Of Ingredients.*
In summary as supplied, the cosmetic substances in this formulation and at the concentrations advised, are not expected to pose a risk of adverse health effect if used as directed. For reasons of intra-species / genetic variations, a small number of individuals may adversely react to this product.

Warnings on Label –
Keep out of reach of children.
If product enters eyes, rinse with plenty of water.
For external use only.

The above list is not exhaustive.

INSTRUCTIONS OF USE

Use as directed by the manufacturer

TOXICOLOGICAL PROFILE OF INGREDIENTS

Ingredient – Aloe Barbadensis Leaf Juice

Aloe barbadensis Leaf Juice is the polysaccharide components of the aloe vera gel derived as a dried juice expressed from the leaves of aloe vera, (Aloe barbadensis Mill.). Not acutely toxic to mice and rats by the Oral route. However, Aloe barbadensis excessive ingestion may cause diarrhoea (https://echa.europa.eu/registration-dossier/-/registered-dossier/24771/9). Inhalation of Aloe vera dust can cause irritation of mucous membranes (ref. MSDS from The Chemistry Store, not dated). No acutely toxic by dermal contact. Not an immediate skin irritant but prolonged contact may cause mild transient irritation in some sensitive people can cause irritation on contact. There have been case reports which include acute eczema, contact urticaria, and dermatitis in individuals who applied Aloe-derived ingredients topically (CIR, 2007). Studies of mutagenicity / genotoxicity in bacterial and mammalian cell genotoxicity assays using Aloe barbadensis-derived material such as Aloe Fero-derived material, and various anthraquinones derived from Aloe resulted in negative and positive results. Aloin (an anthraquinone) did not produce tumours when included in the feed of mice for 20 weeks, nor did aloin increase the incidence of colorectal tumours induced with 1,2- dimethylhydrazine. Aloe-emodin (an anthraquinone) given to mice in which tumour cells had been injected inhibited growth of malignant tumors. Other animal data also suggest that components of Aloe inhibit tumor growth and improve survival. Various in vitro assays also demonstrated anticarcinogenic activity of aloe-emodin. In a 3-month reproduction toxicity study using mice, Aloe vera (extracted in ethanol) given orally in drinking water at 100 mg/kg produced reproductive toxicity, inflammation, and mortality above that

seen in control animals. Aloe vera extracted in methanol and given to mice at 100 mg/kg in drinking water for 3 months caused significant sperm damage compared to controls. Aloe barbadensis extracted with water and given to pregnant Charles Foster albino rats on gestational days (GDs) 0 through 9 was an abortifacient and produced skeletal abnormalities (CIR, 2007). Toxiciokinetics (ADME Studies) and Photo-induced toxicity – Data not available.

Ingredient – Glycerine

Glycerine is known also as 1,2,3 Propanetriol, Glycerol and Glycyl Alcohol (ref. MSDS for Glycerine from Lubrisolve Engineering Solutions Ltd., 12/05/18). Glycerine is exempt as a control chemical from the REACH registration under Annex V of Regulation 2006. This Glycerine has wide uses as follows: anti-freezing, chemical intermediate, chemical manufacturing, feed and food additive, and personal care. This Glycerine (99.9% pure) is a colourless viscous liquid with a barely perceptible odour, a boiling point of > 290 °C, a melting point of 18 °C and is also soluble in water. The Refined Glycerine 99.5% is manufactured to meet or exceed all requirements of the United States Pharmacopeia and the European Pharmacopeia (ref. Certificate of Analysis of Refined Glycerine 99.5% from Lubrisolve Engineering Solutions Ltd., 02 March 2020). Glycerin / Glycerol is an edible fat. Glycerin produces low order of acute oral and dermal toxicity; it causes irritation from inhalation (Ref. OECD SIDS Glycerol UNEP Publications, SIDS Initial Assessment Report For SIAM 14 2002). Skin and eye irritation studies, absence of case reports for sensitisation all indicate that Glycerin has low potential to irritate the skin and eyes nor cause sensitisation. Two generational oral repeated dose toxicity studies with in experimental models demonstrated a high no observable adverse effect level (NOAEL) of 2000 mg/kg bw. Glycerin was
not found to be mutagenic, not toxic to reproduction, but showed potential to be both tumorigenic (e.g. in pulmonary tumorigenesis in presence of a carcinogen) and anti-tumorigenic (protective against tobacco smoke induced cancer). Glycerin has a NOAEL of 2000 mg/kg bw/day based on oral gavage studies.

Ingredient – Sodium Palmate

Acute Toxicity of Sodium Palmate. Oral – LD50, rat, > 2000 mg/kg bw based on an OECD TG 401 (that is, acute oral toxicity) study, a group of five rats/sex was administered docosanoic acid (CAS No 112-85-6) at a dose of 2000 mg/kg bw. There were no clinical signs, deaths, or findings at necropsy CoCAM 6 September 30 – October 3, 2014. Italy/ICCA). Sodium and Sodium salts (supporting substances): In a study similar to OECD TG 401 study, a group of five rats/sex was administered Fatty acids, C16-18 and C18-unsaturated, sodium salts (CAS No 68424-26-0) (in carboxymethylcellulose) by gavage at a dose of 2000 mg/kg bw. There were no deaths or clinical signs. The LD50 was > 2000 mg/kg bw (CoCAM 6 September 30 – October 3, 2014. Italy/ICCA). Dermal and Inhalation – Data not available. Skin Irritation: According to read across information from a related compound, Tetradecanoic acid (CAS No. 544-63-8), Sodium Palmate is not expected to be irritating to the skin (CoCAM 6 September 30 – October 3, 2014. Italy/ICCA). In the study by the Federal Hazardous Substance Act (FHSA), groups of five male albino rats given Tetradecanoic acid at doses up to 10,000 mg/kg bw. No deaths; no clinical signs at 464, 1000, 2150 mg/kg bw. Transient slight diarrhoea and excessive salivation was observed at 4640 mg/kg bw. The majority of animals in the 10,000 mg/kg group showed slight depression, mucoid diarrhoea, unkempt fur stained with diarrhoea, and serum and blood discharge from the nose and eyes the first three days of dosing. There were no findings at gross necropsy (CoCAM 6 September 30 – October 3, 2014. Italy/ICCA). Eye Irritation – According to read across to a related compound, Tetradecanoic acid (CAS No. 544-63-8), Sodium Palmate was not expected to be irritating to eyes (CoCAM 6 September 30 – October 3, 2014. Italy/ICCA). Skin Sensitisation and Dermal / Percutaneous Absorption – Data not available. Repeated Dose Toxicity – In an OECD TG 422 study, groups of male and female rats (13/sex/group), were administered Docosanoic acid (CAS No 112-85-6) which is a single component in support of oral gavage at doses of 0, 100, 300, 1000 mg/kg/day. For males the exposure period was 42 days; for females the exposure period was from 14 days prior to mating to day 3 of lactation (minimum of 39 days of exposure). There were no deaths or changes in general condition, no changes in body weight gain or food consumption, and no adverse histopathological, haematological or biochemical effects. The NOAEL was 1000 mg/kg bw, the highest dose tested (cited in CoCAM 6 September 30 – October 3, 2014. Italy/ICCA). Mutagenicity / Genotoxicity – In an OECD TG 471 study with a single

component (supporting substances), Docosanoic acid (CAS No 112-85-6):, S. typhimurium TA 100, TA 1535, TA 98, TA 1537 and E. coli WP2 uvrA were exposed to Docosanoic acid (CAS No 112-85-6) at concentrations up to 5000 ug/plate in the presence and absence of metabolic activation (liver, induced with phenobarbital and 5,6-benzoflavone). Negative and solvent controls were included and valid; there was no data located regarding positive controls. The test substance was not mutagenic (cited in CoCAM 6 September 30 – October 3, 2014. Italy/ICCA). Weight of evidence based on in vivo chromosome aberration test with Dicarboxylic acid was negative for mutagenicity (cited in CoCAM 6 September 30 – October 3, 2014. Italy/ICCA). Carcinogenicity – Data not available. Reproduction Toxicity – Single component (Supporting substances): In an OECD TG 422 study, rats (13/sex/dose) were exposed to 0, 100, 300, or 1000 mg/kg bw/day of docosanoic acid, CAS No 112-85-6 via oral gavage. For males the exposure period was 42 days; for females the exposure period was from 14 days prior to mating to day 3 of lactation (minimum of 39 days of exposure). There were no effects on gonadal function, mating behaviour, conception, development of the conceptus or parturition. The NOAEL for reproductive toxicity is >= 1000 mg/kg bw/day, the highest dose tested (cited in CoCAM 6 September 30 – October 3, 2014. Italy/ICCA). Read across data from another reproduction toxicity study with 9,12-Octadecadienoic acid (CAS 60-33-3), derived a NOAEL = 467-

Ingredient - Sucrose

Sucrose is a white, odourless dissacharide (alpha(1 → 4) glucosyl-fructose) solid crystal soluble in water with a neutral pH (ref. MSDS of Sucrose from TS Corp, 6/2/2020; Intl J Toxicol. 2019. Vol. 38(Supplement 1) 5S-38S. Safety Assessment of Monosaccharides, Disaccharides, and Related Ingredients as Used in Cosmetics). When heated, Sucrose may have a characteristic caramel odour. Sucrose has a pKa of 12.62, a specific gravity (d254) of 1.587, it is stable in air and hydrolyses to glucose and fructose by diluted acids and by the enzyme, invertase. Sucrose is commonly obtained from sugar cane and sugar beet: sugar cane (Saccharum officinarum) contains 10% to 15% sucrose, sugar beet (Beta vulgaris) contains 10% to 17% sucrose. Sucrose is also obtained by crystallization from sugar cane or sugar beet juice that has been extracted by pressing or diffusion, then clarified and evaporated. Sucrose is the most abundant carbohydrate in the sap of land plants. In cosmetic products, Sucrose is generally used as a humectant, skin conditioning, soothing and as a flavouring agent. In the USA, Sucrose is generally recognized as safe (GRAS) food additive or approved direct food additive (ref. Intl J Toxicol. 2019. Vol. 38(Supplement 1) 5S-38S. Safety Assessment of Monosaccharides, Disaccharides, and Related Ingredients as Used in Cosmetics). The purity specification for Sucrose is as follows: For food use: Not more than (NMT) 1 mg/kg arsenic; NMT 0.1 mg/kg lead; NMT 0.1% invert sugars; NMT 0.15% residue on ignition (sulfated ash); NMT 0.1% loss on drying3 USP: NMT 5 ppm heavy metals; NMT 0.05% residue on ignition (Intl J Toxicol. 2019. Vol. 38(Supplement 1) 5S-38S).
Sucrose is a relatively efficient source of energy; rapidly metabolisable for utilization and storage. Sucrose hydrolyzes in the small intestine to yield dextrose and fructose, which are then absorbed. Also, there is evidence to suggest that sucrose can be absorbed unchanged to a small extent, particularly at a high dietary level; nearly all ingested sucrose is absorbed as glucose and fructose, its metabolism is essentially that of these 2 monosaccharides excreted unchanged in the urine when administered intravenously. In an HRIPT of a rinse-off hair product containing 29% sucrose (tested as a 50% dilution), an irritation was observed in 16% of the 102 participants during induction but no sensitization reactions were reported. Data on ocular irritation were not available but extrapolation from Lactose suggest that it is unlikely to be an eye irritant. Sucrose at 156-5000 mg/mL in Mouse Lymphoma Assay was negative for mutagenesis. General study of a number of the monosaccharides and disaccharides evaluated in in vitro and in vivo, overwhelmingly suggest that they are negative for genotoxicity. Based on occupational exposure, Sucrose is classified as category A4, that is, not classifiable as a human carcinogen.

Ingredient – Sodium Cocoate

Acute Toxicity of Sodium Cocoate. Oral: LD50: rat, > 2000 mg/kg bw. Data was obtained from a weight of evidence and using a read across from a related compound, CAS 68424-26-0 (Fatty acids, C16-18 and C18-unsaturated, sodium salts) (cited in CoCAM 6 September 30-October 3, 2014 Italy/ICCA). Another read

across data were from Octadecanoic acid (CAS No 57-11-4). A group of five rats/sex administered Octadecanoic acid as a 50% suspension in DMSO) at a dose of 5000 mg/kg bw using an OECD TG 401 study, resulted in one death. Animals exhibited transient piloerection, excessive salivation, and diminished activity. At necropsy, the male animal that died exhibited a stomach full of test substance; surviving animals showed remnants of test substance in the stomach with swelling of the mucous membrane (cited in CoCAM 6 September 30-October 3, 2014 Italy/ICCA). Dermal: Data not available. Inhalation: Data not available. Skin Irritation & Corrosivity – Suspected to be corrosive to skin based on read across date to CAS # 124-07-2 (Octanoic acid). Eye Irritation – Suspected to be irritating to eyes based on read across date to CAS # 124-07-2 (Octanoic acid) (CoCAM 6 September 30-October 3, 2014 Italy/ICCA). Skin Sensitisation – No data were available for sensitisation potential cited in CoCAM 6 September 30-October 3, 2014 Italy/ICCA). Dermal / Percutaneous Absorption – Data not available. Repeated Dose Toxicity – Read across oral data from a 42 day study using CAS 112-85-6 (Docosanoic acid) derived a NOAEL of 1000 mg/kg bw/day. Also, data were obtained from a group of twenty male rats administered with 9,12-Octadecadienoic acid (CAS No 60-33-3) in the diet at a dose of 1.5 % (ca. 467 - 1970 mg/kg bw/day) for 36 weeks. There were no adverse findings; the NOAEL was = 467 - 1970 mg/kg bw/day (CoCAM 6 September 30-October 3, 2014 Italy/ICCA). Mutagenicity / Genotoxicity – A negative genotoxicity was expected based on a weight of evidence from a single component (saturated fatty acid) in a Chromosome aberration in vitro study using Fatty acids, tall-oil (CAS 61790-12-3) read across cited in CoCAM 6 September 30-October 3, 2014 Italy/ICCA). In a Bacterial Reverse Mutation Assay (no guideline specified), S. typhimurium TA 98, TA 100, TA 1535, and TA 1537 were exposed to 9-Octadecenoic acid, (Z)- (CAS No 112-80-1) at concentrations up to 10,000 ug/plate in the presence and absence of metabolic activation (Aroclor 1254 induced rat or hamster liver S-9 mix). Positive, negative and solvent controls were included but results of the controls were not located. The test substance was not mutagenic (https://hpvchemicals.oecd.org/UI/handler.axd?id=5b206f57-624e- 413b-8fb2-e29bf53ecfb2). Carcinogenicity – No data were available. Reproduction Toxicity – Effects on fertility and/or reproductive organs were obtained from read across data from CAS 60-33-3 ((9Z,12Z)-Octadeca-9,12dienoic acid; 9,12Octadecadienoic acid) from which a NOAEL of 467-1970 mg/kg was derived for male; also from chemical components CAS # 112-85-6 (Docosanoic acid) and CAS # 693-23-2 (Dodecanedioic acid), a NOAEL of 1000 mg/kg was derived for both male and female cited in CoCAM 6 September 30-October 3, 2014 Italy/ICCA. Read across data suggest no effects on fertility or on reproductive organs (similar to OECD TG 408 or 422), or developmental effects (similar to OECD TG 422 or 416) were observed in studies on the sponsored or supporting aliphatic acids and the NOAELs correspond to the maximum dose tested. The weight of evidence supports the lack of reproductive and developmental toxicity potential of the aliphatic acids category. For example, in a 90 day study (no guideline specified), groups of ten rats/sex/group were administered 9-Octadecenoic acid, (Z)- (CAS No 112-80-1) in the diet at 0, 3300, 6100, 14,000 mg/kg bw/day. There were no effects on gonads weights, and no gross or histopathological findings for testes, seminal vesicle, ovary, uterus, or prostate. The NOAEL for reproductive effects was 14,000 mg/kg bw, the highest dose tested. In another study, a group of twenty male 344 rats were administered 9,12-octadecadienoic acid (CAS No 60-33-3) in the diet at a dose of ca. 467 - 1970 mg/kg bw/day for 36 weeks. There were no effects on testes weights, no findings at gross necropsy or histopathological findings in the testes; the NOAEL for male reproductive effects was = 467 - 1970 mg/kg bw/day, the highest dose tested (https://hpvchemicals.oecd.org/UI/handler.axd?id=5b206f57- 624e-413b-8fb2-e29bf53ecfb2). Developmental Toxicity – Read across data from oral study with Docosanoic acid (CAS 112-85-6), produced a NOAEL of 1000 mg/kg bw/day for both maternal and developmental groups. In a study following the Chernoff/Kavlock Developmental Toxicity Screen, groups of female mice (26-30/dose) were treated via oral gavage on gestation days 8-12 with 10,000 mg/kg bw/day of 9,12-octadecadienoic acid (CAS No 60-33-3). There were no effects on number of litters, number of resorptions, number of pups/litter, number of live and dead births, postnatal survival rates, pup weights at days 1 and 3 or external abnormalities among dead pups. The NOEL for developmental toxicity is >= 10,000 mg/kg bw/day for mice with exposure on gestation days 8-12 (https://hpvchemicals.oecd.org/UI/handler.axd?id=5b206f57-624e-413b-8fb2-e29bf53ecfb2). From another read across study with … (CAS # 112-85-6), a NOAEL of 1000 was derived for both maternal and developmental. Toxiciokinetics (ADME Studies) and Photo-induced toxicity – Data not found.

Ingredient – Decyl Glucoside

Decyl Glucoside belongs to a family of compounds known as Alkyl Glucosides (ref. Alfalah, M *et al*. 2017.

Alkyl Glucosides. Dermatitis, Jan/Feb 2017;28(1):3-4). Alkyl Glucosides are surfactants synthesized through the condensation of long-chain fatty alcohols and glucose, extracted from vegetal, renewable sources. Decyl Glucoside has been considered a mild surfactant and used in various leave-on and rinse-off cosmetic products as a result of its considered low irritancy and allergenicity. However, since the early 2000s, cases of allergic contact dermatitis to this family of molecules have been repeatedly reported. Decyl glucoside was found to be a "hidden" allergen in the sunscreen ingredient Tinosorb M and is likely responsible for most allergic contact dermatitis reported to this compound. As North American Contact Dermatitis Group observe steady increase in the rate of sensitization to Decyl glucoside, cross-reactions with other glucosides have also been noted although not found to be automatic. In a retrospective study with 897 patients suspected of having a cosmetic-related dermatitis and patch tested with both Decyl and Lauryl glucosides between 2009 and 2016, 48 patients (5%) had positive reactions to Decyl glucoside and/or Lauryl glucoside. Of the Alkyl glucoside-allergic patients, 65% had positive reactions to both Decyl and Lauryl glucosides. Patch testing multiple compounds was thus recommended.

Ingredient – Aqua

Aqua - Commonly known as water is not toxic. Excessive consumption could result in Hyponatremia (low serum sodium ion, electrolyte) (ref. HSDB). TDLo in Infant, oral - 333g/kg (333000mg/kg), TDLo in Man, oral - 42.86g/kg (42860mg/kg). Study of oral LD50 in rat, > 90mL/kg (90mL/kg). Aqua is not a skin or an irritant. It is not a skin sensitiser. Aqua is not toxic on repeated dosing. It is non- mutagenic nor genotoxic; non-carcinogenic. Whilst study of six new types of drinking water could impact on health, namely body weight of new born mice whose parents were fed with (1) magnetized mineral water, (2) activated water, (3) purified water, (4) mineral water, (5) alkaline ionized water and (6) natural water respectively for 3 months. No effects were observed on pregnancy rate, in gestation rate and birth liveability of mice. However, extensive water testing did not identify any known reproductive toxicant in tap water although differences in bacterial content and trace elements were noted. Toxiciokinetics (ADME Studies) – Readily absorbed throughout the body following ingestion. Aqua is not phototoxic.

Ingredient - Sodium Chloride

The safe and adequate intake for adults is reported as 1,875 to 5,625 mg. The National Academies recommends that Americans consume a minimum of 500 mg/day of sodium to maintain good health (Feldman SR et al; Sodium Chloride. Kirk-Othmer Encyclopedia of Chemical Technology. (1999-2013). New York, NY: John Wiley & Sons. Online Posting
Date: 14 Oct 2011 cited in https://toxnet.nlm.nih.gov/cgi- bin/sis/search2/f?./temp/~1UStY4:3).
In the USA, the Federal drinking water guidelines is as follows: EPA 250,000 ug/L /Chloride ion/(USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93) To Present cited in https://toxnet.nlm.nih.gov/cgi-bin/sis/search2/f?./temp/~1UStY4:3).); the State of California drinking water guidelines is as follows 250,000 ug/L (Recommended); 500,000 ug/L (Upper); Short-term 600000 ug/l /Chloride ion/ [USEPA/Office of Water; Federal-State Toxicology and Risk Analysis Committee (FSTRAC). Summary of State and Federal Drinking Water Standards and Guidelines (11/93) cited in https://toxnet.nlm.nih.gov/cgi-bin/sis/search2/f?./temp/~1UStY4:3).
Sodium is essential in diet to maintain chloride balance in body (Lewis, R.J. Sr.; Hawley's Condensed Chemical Dictionary 15th Edition. John Wiley & Sons, Inc. New York, NY 2007., p. 1140 cited in https://toxnet.nlm.nih.gov/cgi-bin/sis/search2/f?./temp/~1UStY4:3).
A review article on acute toxicity of Sodium Chloride in the general people and infant where NaCl was accidently used in place of sugar in preparing infant feeding formulas resulted in deaths (Sodium and potassium Melvin J.fregly. 1981. Ann.rev.Nutr. 1981.1:69-93 cited in https://echa.europa.eu/registration-dossier/-/registered-dossier/15467/7/11/2). Also, death occurred from the use of NaCl as an emetic where vomiting did not occur. The use of hypertonic saline injections to induce abortion has also resulted in the death of some women. In addition, an excessively high concentration of sodium ions resulting from Sodium bicarbonate therapy for Salicylate poisoning or for excessive diarrhoea and vomiting in infants has produced permanent brain damage and other pathologic effects. The major pathologic findings in deaths resulting from NaCl toxicity were subarachnoid haemorrhages and multiple small intracerebral haemorrhages, shrinkage of

the convoluted tubular cells from the basement membrane of the kidneys, and diffuse reddening of the mucosa of the stomach and small intestine.
The author stated that 3 g/kg is regarded as lethal and that smaller amounts have been known to kill. The probable lethal dose for adult humans ranges from 0.5 to 5.0 g/kg. The visible oedema occurs in the healthy adult man with 35-40 g of NaCl per day. It has also been described that an oral ingestion of larger quantities of Sodium chloride, eg 1000 g in 600 mL of water, is harmful and can induce irritation of the gastrointestinal tract, vomiting, hypernatremia, respiratory distress, convulsions, and death (Rowe, R.C., Sheskey, P.J., Quinn, M.E.; (Eds.), Handbook of Pharmaceutical Excipients 6th edition Pharmaceutical.

Ingredient – Citric Acid

Citric Acid has the chemical name, 2-Hydroxy-1,2,3-propanetricarboxylic Acid. Citric Acid is a white to almost white crystalline, odourless organic solid which has a melting point of 152–159 °C, a flash point of 345 °C, very soluble in water (576–771 g/l at 20 °C/room temp) and freely soluble in Ethanol (ref. CoA of Citric Acid Anhydrous from Weifang Ensign Industry Co. Ltd., 17 Nov. 2017). Citric Acid has the chemical name, 2-Hydroxy-1,2,3-propanetricarboxylic acid, monohydrate (MSDS of Citric Acid from Weifang Yingxuan Co.,Ltd., not dated). The potential health effects for Citric Acid include: causes irritation to the respiratory tract (MSDS of Citric Acid from Weifang Yingxuan Co.,Ltd., not dated). Symptoms may include coughing, shortness of breath. Ingestion: Causes irritation to the gastrointestinal tract. Symptoms may include nausea, vomiting and diarrhoea. Extremely large oral dosages may produce gastrointestinal disturbances. Calcium deficiency in blood may result in severe cases of ingestion. Causes irritation to skin. Symptoms include redness, itching, and pain. Highly irritating to eyes and may also be abrasive. Chronic or heavy acute ingestion may cause tooth enamel erosion. Citric Acid has a low acute oral toxicity (oral: LD50: rat, 3,000 - 12,000 mg/kg, details not supplied (OECD SIDS on Citric Acid, 2000); 11700 in rats (male only) (Yokotani et al. 1971); LD50: mouse, 5,400 mg/kg for males and females; 5 males, 5 females, based on gavage of 5 concentrations of Citric Acid in water, controls; LD50: mouse, 5790 mg/kg (male only) (Yokotani et al. 1971); lethal dose for rabbits = 7,000 mg/kg (probably lowest lethal dose). Single oral high doses of Citric Acid causes severe damage to the stomach lining and nervous system effects in rats, mice and rabbits (OECD SIDS on Citric Acid, 2000). When 14 guinea-pigs were exposed for 30 minutes to atmospheric Citric Acid concentrations of 31.1 or 81mg/m3 (obtained by aerosolizing 4 or 6% solutions respectively), only one cough was recorded at the lower concentration, but significant coughing occurred in the top group (OECD SIDS on Citric Acid, 2000). Coughing was produced in guinea-pigs exposed to 75 mg Citric Acid/ml as an aerosol for 3 minutes. Bronchoconstriction occurred after 3-4 minutes. Coughing occurred frequently when 1 ml of an aqueous 0.27 M (about 52 g/l; 5.2%) solution of Citric Acid was instilled into the lower trachea (windpipe) of lambs, an effect which was not apparently seen when the acid was instilled into the mid-trachea or laryngeal area. (OECD SIDS on Citric Acid, 2000). Citric Acid applied as 500 mg/24 h was found to be slightly irritating to skin, effects reported as “mild” – details not supplied. In a Draize test in which 0.5 ml of 30% aq. solution was applied to the skin for 4 h under occlusive patch produced no effect in intact skin, slight to well defined effect in abraded skin; primary irritation index = 0.84 (OECD SIDS on Citric Acid, 2000). A 0.5 and 2% solution of Citric acid was found irritating to the eye of rabbit when applied repetitively over 7 days as demonstrated by the presence of sporadic non-persisting areas of necrosis (Carpenter et al. 1946). No effects were available for skin sensitisation and dermal / percutaneous absorption. In a repeated dose toxicity, a 5-day NOAEL and LOAEL values were identified in male and female rats as 4000 and 8000 mg/kg bw/day, respectively (ECHA, 2016 - http://echa.europa.eu/registration-dossier/-/registered-dossier/15451/4/12). Citric acid is not mutagenic in in vitro assays with and without metabolic activation in 4 – 5 defined strains of Salmonella typhimurium, yeast gene mutation assay”; no clastogenic effects reported in CHO fibroblast culture cells at concentrations up to 1 mg Citric acid/ml (OECD SIDS on Citric Acid, 2000). In vivo genetic toxicity assays demonstrated in rats no mutagenic potential after doses of 3 g/kg (possibly per day) for 5 days; no chromosomal damage in bone marrow of rats fed up to 3 g/kg/d for 5 days (OECD SIDS on Citric Acid, 2000). In a limited study, no evidence of carcinogenicity was reported in 20 male rats receiving up to 5% Citric Acid in the diet (about 2000 mg/kg bw/day) for 2 years (OECD SIDS on Citric Acid, 2000). Citric Acid is a metabolic intermediate vital to the TCA respiration pathway found in all animal and plant cells. There is little evidence that Citric Acid and the citrate salts have deleterious effects, even in large doses in reproduction. Indeed there is some support for the fact that Citric Acid in the human diet is favourable by inhibiting the

formation of calcium oxalate kidney and bladder stones. This statement is applicable to the citrate salts since once absorbed citrate salts will dissociate into Citric Acid and their counter-ion. There were no indications of teratogenicity (malformations in the offspring) or other adverse effects when female rats received up to 295 mg Citric Acid/kg bw/day on days 6 to 15 of pregnancy (OECD SIDS on Citric Acid, 2000). Data were not available for toxiciokinetics (ADME Studies) and photo-induced toxicity.
In humans, Citric Acid was found to be irritant skin dermatitis in waiters and bakers. This was attributed to Citric acid in solution, the acid may produce pain if applied to abraded skin (OECD SIDS on Citric Acid, 2000). It was reported that a 0.3 N solution (~2%) can "sting" intact skin. A patch testing of 60 eczema patients with 2.5% Citric acid in petrolatum (probably 24-h covered contact) did not produce any irritant reactions (OECD SIDS on Citric Acid, 2000). Citric Acid (of unspecified concentration) induced bronchoconstriction) in human asthmatics (OECD SIDS on Citric Acid, 2000).

References

Regulation (EC) No1223/2009 as amended
SCCS Notes of Guidance
ECHA
CosIng
CoA
MSDS

Assessor's credentials: Ph.D, C.Biol., MRSB, EurProBiol.

Proof of qualification: Sent upon request.

Signature: M U Iwobi **Date of issue of report:** 30th May 2025