Oxford Biosciences Ltd.
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COSMETIC PRODUCT SAFETY REPORT

PRODUCT: SMILEREX Teeth Whitening Gel

DATE: 17 March 2021

Responsible Person: **Unikos Global Ltd**
128 City Road
London
EC1V 2NX

OXFORD BIOSCIENCES
Safety Assessment, Analysis, Research & Testing

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PART A – Cosmetic Product Safety Information

1. Quantitative and qualitative composition

	Ingredient INCI name	CAS	Function	Limits	Amount
1	Sorbitol	50-70-4	Humectant, plasticiser, skin		40.00
2	Aqua	7732-18-5	Solvent		20.10
3	Phthalimidoperoxycaproic acid	128275-31-0	Oxidising		12.00
4	Propylene glycol	57-55-6	Humectant, skin		10.00
5	Glycerin	56-81-5	Denaturant, hair		6.00
6	Potassium nitrate	7757-79-1	Oral care, soothing		5.00
7	PEG-8	5117-19-1 /	Humectant, solvent		3.00
8	Hydroxyapatite	1306-06-5	Abrasive, bulking, oral		1.00
9	Cellulose gum	9004-32-4	Binding, emulsion		1.00
10	Hydroxyethylcellulose	9004-62-0	Binding, emulsion		0.50
11	Xanthan gum	11138-66-2	Binding, emulsifying,		0.35
12	Sodium saccharin	128-44-9 / 6155	Flavouring, fragrance, oral		0.20
13	Menthol	1490-04-6 / 2216	Denaturant, fragrance,		0.20
14	Methylparaben	99-76-3	Preservative	V/12	0.15
15	Aloe barbadensis leaf juice	85507-69-3 /	Skin conditioning		0.10
16	Chamomilla recutita leaf extract	84082-60-0	Fragrance, skin		0.10
17	Punica granatum seed oil	84961-57-9	Emollient		0.10
18	Sodium bicarbonate	144-55-8	Abrasive, buffering,		0.10
19	Propylparaben	94-13-3	Perfuming, preservative	V/12	0.05
20	trans-Anethole	4180-23-8	Perfumiing		0.015
21	Eucalyptol	470-82-6	Denaturing, perfuming,		0.005
22	Isomenthone	491-07-6	Perfuming		0.005
23	Menthone	89-80-5	Perfuming		0.005
24	Carvone	6485-40-1 / 99	Flavouring, fragrance,		0.005
25	d-Limonene	5989-27-5	Fragrance, perfuming	III/88	0.005
26	alpha-Pinene	80-56-8	Fragrance		0.005
27	beta-Pinene	127-91-3	Perfuming	III/130	0.005

Allergens present in this product and estimated amounts*:
d-Limonene: 0.005%

* The presence of these allergens must be indicated in the list of ingredients when their concentration exceeds: 0.001% in leave-on products or 0.01% in rinse-off products

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2. Physical & chemical properties and stability

2.1.1 Physical/chemical properties of ingredients (substances or mixtures)

See section 1. Quantitative and qualitative composition – additional specification of ingredients.

Ref. 1. 1 **Sorbitol**

Sorbitol, also known as glucitol, is a sugar alcohol, which is a polyol organic compound. Its molecular formula is $C_6H_{14}O_6$. Sorbitol, a humectant, is also commonly used as a sugar substitute in the food industry and presents no safety concerns in its present use and concentration in this product.

Ref. 1. 2 **Aqua**

Aqua (water) is a liquid at standard temperature and pressure with the chemical formula H_2O: one molecule of water has two hydrogen atoms covalently bonded to a single oxygen atom.

Ref. 1. 3 **Phthalimidoperoxycaproic acid**

Phthalimidoperoxycaproic acid (PAP), is an organic peracid containing a high potential of oxidation. Oxidation is necessary for the bleaching procedure as it neutralizes organic double bonds that cause dental discolourations . PAP has a history of safe use in dental products and presents no safety issues when used in its present concentration as described in this safety assessment.

Ref. 1. 4 **Propylene glycol**

Propylene glycol, (1,2-propanediol or propane-1,2-diol) is an organic compound (a diol or double alcohol) with the formula $C_3H_8O_2$. It is a colourless, nearly odourless, clear, viscous liquid with a faintly sweet taste, hygroscopic and miscible in water and ethanol. In 1994 the Cosmetic Ingredient Review Expert Panel concluded that Propylene glycol is safe, when formulated to be non-irritating at concentrations up to 50%, in the present practices of use and concentration as described in this safety assessment. In 2012 the CIR Expert Panel reaffirmed its 1994 conclusion.

Ref. 1. 5 **Glycerin**

Glycerin, or glycerol, is a simple polyol compound, with three hydroxyl groups, which is a colourless, odourless, viscous liquid. Glycerin is naturally occurring in all animals and plant matter in combined form as glycerides in fats and oils, or, in intracellular spaces, as lipids. The glycerol backbone is central to all triglycerides, and its molecular formula is $C_3H_8O_3$. In December 2014 the Cosmetic Ingredient Review (CIR) Expert Panel also noted the high frequency of use that is reported for glycerin and the low instances of reports of toxicity, irritation, and sensitisation and that glycerin is GRAS for food packaging and as a multiple-purpose food substance. When considering the safety of glycerin, the Panel noted that it is naturally occurring in animal and human tissues, including the skin and blood. The data demonstrated low oral and dermal toxicity for multiple animal species and humans, in both acute and long-term studies. The CIR Expert Panel concluded that glycerin is safe in the present practices of use and concentration described in this safety assessment.

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2. Physical & chemical properties and stability

2.1.1 Physical/chemical properties of ingredients (substances or mixtures)

See section 1. Quantitative and qualitative composition – additional specification of ingredients.

Ref. 1. 6 **Potassium nitrate**

Potassium nitrate is an ionic salt of potassium ions K^+ and nitrate ions $NO3^-$. It occurs in nature as a mineral, niter. When used as a food additive in the European Union, Potassium nitrate is referred to as E252. Its molecualr formula is KNO_3.

Ref. 1. 7 **PEG-8**

PEG-8 is the a polymer of Ethylene glycol, Poly(oxy-1,2-ethanediyl), with a 8 mol EO average molar ratio.

The safety of PEG-8 has been assessed by the Cosmetic Ingredient Review (CIR) Expert Panel. The CIR Expert Panel evaluated the scientific data and concluded that PEG-8 was safe for use in cosmetics and personal care products.

Ref. 1. 8 **Hydroxyapatite**

Hydroxyapatite is the hydroxyl end member of the complex apatite group. Its molecular formula is $Ca_5(PO_4)_3(OH)$.

Ref. 1. 9 **Cellulose gum**

Cellulose gum is highly purified carboxymethyl cellulose manufactured from naturally occurring substances. Molecular formula: $C_8H_{16}NaO_8$

Ref. 1. 10 **Hydroxyethylcellulose**

Hydroxyethycellulose, a modified cellulose polymer, is used as a gelling and thickening agent. Hydroxyethycellulose is prepared by reacting alkali cellulose with ethylene oxide in the presence of alcohol or acetone. Being nonionic in character, Hydroxyethycellulose does not react with polyvalent cations, and in solution is generally unaffected by moderate shifts in pH. The US FDA has also approved the use of Hydroxyethylcellulose for use as ophthalmic demulcents in over-the-counter (OTC) drug products for the eyes. In 1986 the Cosmetic Ingredient Review (CIR) Expert Panel concluded that Hydroxyethylcellulose is safe for use as a cosmetic ingredient in the present practice of use and concentration detailed in this safety assessment. In March 2009 the CIR Expert Panel re-reviewed the data on Hydroxyethylcellulose and noted that Hydroxyethylcellulose passes essentially unchanged through the gastrointestinal tract following oral administration to rats, dogs, and humans. The Panel also noted acute, subchronic, chronic toxicity, reproductive and developmental toxicity, genotoxicity, and carcinogenicity studies of Hydroxyethylcellulose indicate that it is practically non-toxic when administered by oral, intraperitoneal, subcutaneous, or dermal routes. While no clinical inhalation studies have been conducted, long-term exposure to the dust of cellulose ethers in manufacturing operations has not led to any significant adverse effects. Ocular and dermal irritation studies indicate that the cellulose derivatives are, at most, minimally irritating and are not dermal sensitisers. Clinical studies confirm these findings. Therefore the CIR Expert Panel reconfirmed their 1986 conclusion.

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2. Physical & chemical properties and stability

2.1.1 Physical/chemical properties of ingredients (substances or mixtures)

See section 1. Quantitative and qualitative composition – additional specification of ingredients.

Ref. 1. 11 **Xanthan gum**

Xanthan gum is a high molecular weight heteropolysaccharide gum secreted by the bacterium Xanthomonas campestris, commonly used as a food additive, rheology modifier, and a stabiliser with the molecular formula $C_{35}H_{49}O_{29}$. It is composed of pentasaccharide repeat units, comprising glucose, 6-acetyl mannose, 4,6-pyruvylated mannose and glucuronic acid in the molar ratio 2.0:2.0:1.0. Xanthan gum is produced by a pure culture fermentation of a carbohydrate (glucose, sucrose, or lactose) with Xanthomonas campestris and is composed of glucose, glucuronic acid, 6-acetyl mannose and 4,6-pyruvylated mannose residues. After a fermentation period, the polysaccharide is precipitated from a growth medium with isopropyl alcohol, dried, and ground into a fine powder. Xanthan gum has a long history of safe use worldwide. It was approved for use in foods in 1968 and is accepted as a safe food additive in the USA, Canada, and European countries, with the E number E415. In 2016 the Cosmetic Ingredient Review (CIR) Expert Panel concluded that Xanthan gum is safe in the present practices of use and concentration, as described in this safety assessment.

Ref. 1. 12 **Sodium saccharin**

Sodium saccharin, also known as 1,2-Benzisothiazol-3(2H)-one 1,1-dioxide, sodium salt, is the sodium salt of the artificial sweetener saccharin. The U.S. Food and Drug Administration (FDA) permits Saccharin and its ammonium, calcium and sodium salts to be used in foods. The use of Saccharin and its salts in food has been reviewed and determined to be safe by the Joint Expert Committee on Food Additives (JECFA) of the World Health Organization (WHO).

Ref. 1. 13 **Menthol**

Menthol is an organic compound obtained from corn mint, peppermint or other mint oils. A waxy, crystalline substance, clear or white in color, it is solid at room temperature. The main form of menthol occurring in nature is (–)-menthol. Menthol has local anesthetic and counter-irritant qualities. Molecular formula: $C_{10}H_{20}O$

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2. Physical & chemical properties and stability

2.1.1 Physical/chemical properties of ingredients (substances or mixtures)

See section 1. Quantitative and qualitative composition – additional specification of ingredients.

Ref. 1. 14 **Methylparaben**

Methylparaben is a preservative with the chemical formula $CH_3(C_6H_4(OH)COO)$. It is the methyl ester of p-hydroxybenzoic acid. The paraben esters, as a generic class, are rare skin sensitizers when applied to the intact skin of man. Application to the damaged skin is a more common cause of sensitization. Methylparaben and a methyl:ethyl:propylparaben mixture have been shown on oral administration to exacerbate pre-existing skin complaints. A limited number of more severe reactions have been reported from ingestion or injection of methylparaben in preparations. The ester demonstrated a low acute oral toxicity in laboratory animals. Limited studies involving repeated oral administration indicated a low toxicity in dogs and rats. Repeated oral administration was without reproductive toxic potential in a range of species. Methylparaben was not mutagenic in the Ames bacterial test. It was able to induce chromosomal damage in mammalian cells in culture, but no similar activity was seen in rats or mice treated orally.

Ref. 1. 15 **Aloe barbadensis leaf juice**

Aloe barbadensis leaf juice is the juice obtained from leaves of the aloe vera plant, Aloe barbadensis, Xanthorrhoeaceae. In 2007, the Cosmetic Ingredient Review (CIR) Expert Panel concluded that anthraquinone levels in the several Aloe Barbadensis extracts are well understood and can conform to the industry-established level of 50 ppm. Although the phototoxicity anthraquinone components of Aloe plants have been demonstrated, several clinical studies of preparations derived from Aloe barbadensis plants demonstrated no phototoxicity, confirming that the concentrations of anthraquinones in such preparations are too low to induce phototoxicity and therefore Aloe barbadensis leaf juice is safe as a cosmetic ingredient in its current practice of use and concentration as described in this safety assessment.

Ref. 1. 16 **Chamomilla recutita leaf extract**

Chamomilla recutita leaf extract is an extract of the leaves of Chamomilla recutita (L.), Compositae.

Ref. 1. 17 **Punica granatum seed oil**

Punica granatum seed oil is the oil expressed from the seeds of the Pomegranate, Punica granatum L., Punicaceae.

Pomegranate seed oil contains punicic acid (65.3%), palmitic acid (4.8%), stearic acid (2.3%), oleic acid (6.3%) and linoleic acid (6.6%). Punicic acid, an Omega 5 conjugated fatty acid, is a rare plant based source of CLA.

Ref. 1. 18 **Sodium bicarbonate**

Sodium bicarbonate or sodium hydrogen carbonate is the chemical compound with the formula $NaHCO_3$. It is edible and commonly known as bicarbonate of soda or baking soda.

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2. Physical & chemical properties and stability

2.1.1 Physical/chemical properties of ingredients (substances or mixtures)

See section 1. Quantitative and qualitative composition – additional specification of ingredients.

Ref. 1. 19 **Propylparaben**

Propylparaben is a preservative with the chemical formula $C_{10}H_{12}O_3$. It is the n-propyl ester of p-hydroxybenzoic acid. Propylparaben is prepared by esterifying p-hydroxybenzoic acid with n-propyl (the three-carbon alkyl substituent with the chemical formula $–CH_2CH_2CH_3$ obtained by removing one hydrogen atom attached to the terminal carbon of propane) in the presence of an acid catalyst, such as sulfuric acid, and an excess of n-propyl. The acid is then neutralised with caustic soda, and the product is crystallised by cooling, centrifuged, washed, dried under vacuum, milled, and blended. The safety of Parabens has been assessed by the Cosmetic Ingredient Review (CIR) Expert Panel. The CIR Expert Panel evaluated scientific data and concluded that Methylparaben, Ethylparaben, Propylparaben, Isopropylparaben, Butylparaben and Isobutylparaben were safe as for use as ingredients in cosmetics and personal care products. In December 2011, the renamed Scientific Committee for Consumer Safety (SCCS formerly SCCP) released their draft final opinion on propylparaben and butylparaben. They concluded that these are considered safe for use in cosmetics to a maximum total concentration of 0.19% (of these two parabens) – this concentration is independent of the concentration of methylparaben and ethylparaben, but with a total maximum parabens concentration of 0.8%, as before.

Ref. 1. 20 **trans-Anethole**

trans-Anethole ((E)-anethol, 1-methoxy-4-[(E)-prop-1-enyl]benzene) C10 H12 O

IFRA Code of Practice Notification of the 49th Amendment to the IFRA Code of Practice
Recommendation for (E)-anethol usage levels up to:
10.0000 % in the fragrance concentrate.

Use levels for FEMA GRAS flavoring substances on which the FEMA Expert Panel based its judgments that the substances are generally recognized as safe (GRAS).

Ref. 1. 21 **Eucalyptol**

Eucalyptol (1,8-cineole)

IFRA Code of Practice Notification of the 49th Amendment to the IFRA Code of Practice
Recommendation for 1,8-cineole usage levels up to:
20.0000 % in the fragrance concentrate.

Maximised Survey-derived Daily Intakes (MSDI-EU): 1200.00 (µg/capita/day)
Maximised Survey-derived Daily Intakes (MSDI-USA): 1954.00 (µg/capita/day)
Structure Class: II
Use levels for FEMA GRAS flavoring substances on which the FEMA Expert Panel based its judgments that the substances are generally recognized as safe (GRAS).

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2. Physical & chemical properties and stability

2.1.1 Physical/chemical properties of ingredients (substances or mixtures)

See section 1. Quantitative and qualitative composition – additional specification of ingredients.

Ref. 1. 22 **Isomenthone**

Isomenthone, C_{10} $H_{18}O$, Mr 154.25, exists as two stereoisomers, trans-menthone [89-80-5] and cis-isomenthone [491-07-6], each of which occurs as a pair of enantiomers, due to the two asymmetric centers present in the molecule. Both stereoisomers occur in many essential oils, often as a single enantiomer species. A particularly high concentration (sometimes >50%) is found in oils from Mentha species. The menthones are colorless liquids that possess a typically minty odor; the odor of isomenthone is slightly musty. They have a strong tendency to interconvert and are, therefore, difficult to obtain in high purity. Industrial products are mixtures of varying composition. The menthones are converted into the corresponding menthols by means of hydrogenation; for example, (–)-menthone yields (+)-neomenthol and (–)-menthol. (–)-Menthone can be obtained by distillation of dementholized cornmint oil or by oxidation of (–)-menthol (e.g., with chromic acid). Dehydrogenation of (–) menthol (e.g., with copper chromite) yields a mixture of (–)-menthone and (+) isomenthone. rac-Menthone is prepared analogously to rac-menthol. However, it can also be synthesized by hydrogenation of thymol in the presence of palladium–carbon ca talysts [189]. Menthone and isomenthone are used for synthetic peppermint oils and bases.

In the notification of the 49th amendment to the IFRA code of practice, the recommendation for 491-07-6 usage levels in category 4: products related to fine fragrance is up to 8.00% in the fragrance concentrate.

Ref. 1. 23 **Menthone**

Menthone is a monoterpene that occurs naturally in a number of essential oils. l-Menthone (or (2S,5R)-trans-2-isopropyl-5-methylcyclohexanone) is the most abundant in nature of the four possible stereoisomers. It is structurally related to menthol, which has a secondary alcohol in place of the carbonyl. Menthone is used in flavoring, perfume and cosmetics for its characteristic aromatic and minty odor. Its molecular formula is $C_{10}H_{18}O$

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2. Physical & chemical properties and stability

2.1.1 Physical/chemical properties of ingredients (substances or mixtures)

See section 1. Quantitative and qualitative composition – additional specification of ingredients.

Ref. 1. 24 **Carvone**

Carvone ((5R)-2-methyl-5-prop-1-en-2-ylcyclohex-2-en-1-one, Mr 150.22, bp101.3kPa 230◦C, d204 0.960, n20D 1.499) is a cylclic terpene with the molecular formula $C_{10}H_{14}O$.

The optical isomers occur in high percentages in a number of essential oils. (+)-Carvone is the main component of caraway oil (about 60%) and dill oil; (–) Carvone occurs in spearmint oil at a concentration of 70–80%.

Carvone synthesis utilises the selective addition of nitrosyl chloride to the endocyclic double bond of limonene. If a lower aliphatic alcohol is used as solvent, limonene nitrosochloride is obtained in high yield. It is converted into Carvone oxime by elimination of hydrogen chloride in the presence of a weak base. Acid hydrolysis in the presence of a hydroxylamine acceptor, such as acetone, yields Carvone.

The Tier I toxicology data suggest that l-Carvone is acutely non toxic (Toxicology Category IV) and has very low acute dermal and inhalation concerns (Toxicology Category III). This compound is a mild-slight dermal sensitiser, and a negative mutagen. There is no evidence of inhalation toxicity (Toxicology Category IV) and primary eye irritation cleared in seven days (Toxicology Category III).

In the Notification of the 49th Amendment to the IFRA Code of Practice, the recommendation for Carvone usage levels in Category 4: Products related to fine fragrance is up to 0.59% in the fragrance concentrate due to dermal sensitisation and systemic toxicity.

Ref. 1. 25 **d-Limonene**

Limonene is a colourless liquid hydrocarbon classified as a cyclic terpene. The more common D-isomer has the aroma of oranges. Limonene is a chiral molecule, and biological sources produce one enantiomer: the principal industrial source, citrus fruit, contains D-limonene ((+)-limonene), which is the (R)-enantiomer. Racemic limonene is known as dipentene. Limonene is a relatively stable terpene and can be distilled without decomposition, although at elevated temperatures it cracks to form isoprene. It oxidises easily in moist air to produce carveol, carvone, and limonene oxide. With sulphur, it undergoes dehydrogenation to p-cymene.

In the notification of the 49th amendment to the IFRA code of practice, the recommendation for d-Limonene usage levels in category 4: products related to fine fragrance is up to 20.00% in the fragrance concentrate.

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2. Physical & chemical properties and stability

2.1.1 Physical/chemical properties of ingredients (substances or mixtures)

See section 1. Quantitative and qualitative composition – additional specification of ingredients.

Ref. 1. 26 **alpha-Pinene**

alpha-Pinene (DL-pin-2(3)-ene, 4,7,7-trimethylbicyclo[3.1.1]hept-3-ene, M_r 136.24, $bp_{101.3kPa}$ 156◦C, d204 0.8553, $n_{20}D$ 1.4662, $\alpha_{20}D$ + or –51.9◦) is the most widespread pinene isomer. (+)-α-Pinene, (1R,5R)-2,6,6-trimethyl bicyclo[3.3.1] hept-2-ene, [7785-70-8] occurs, for example, in oil from Pinus palustris Mill., at a concentration up to 65%; oil from Pinus pinaster Soland and American oil from Pinus caribaea contain 70% and 70–80%, respectively, of the laevorotatory isomer, (–)-α-Pinene, (1S,5S)-2,6,6-trimethylbicyclo[3.3.1]hept-2 ene. α-Pinene undergoes many reactions, of which the following are used in the fragrance industry: upon hydrogenation, α-pinene is converted to pinane, which has become an important starting material in the industrial processes used in the fragrance and flavour industry. α-Pinene can be isomerised to β-pinene with high selectivity for β-pinene formation. Hydration with simultaneous ring opening yields terpineol and cis-terpin hydrate. Pyrolysis of α-pinene yields a mixture of ocimene and alloocimene. Pure α-pinene is obtained by distillation of turpentine oils. As a fragrance substance, it is used to improve the odour of industrial products. However, it is far more important as a starting material in industrial syntheses, for example, terpineols, borneol, and camphor.

In the notification of the 49th amendment to the IFRA code of practice, the recommendation for alpha-Pinene usage levels in category 4: products related to fine fragrance is up to 10.00% in the fragrance concentrate.

Ref. 1. 27 **beta-Pinene**

beta-Pinene (β-Pinene, M_r 136.24, $_{bp101.3kPa}$ 164◦C, d204 0.8712, $n_{20}D$ 1.4763, $\alpha_{20}D$ + or −22.6◦) is a monoterpene alcohol, an isomer of pinene, with the molecular formula $C_{10}H_{16.}$ Optically active and racemic β-pinenes are present in turpentine oils, although in smaller quantities than α-pinene. (+)-β-Pinene, (1R,5R)-6,6-dimethyl-2-methylenebicycloheptane; (−)-β Pinene, (1S,5S)-6,6-dimethyl-2-methylenebicycloheptane. β-Pinene is similar to α-pinene in its reactions. Pyrolytic cleavage to myrcene, the starting material for acyclic terpenes, is used on an industrial scale. Addition of formaldehyde results in the formation of nopol; nopylacetate is used as a fragrance material. β-Pinene is produced in large quantities by distillation of turpentine oils. It is used as a fragrance material in household perfumery. However, most β-pinene is used in the production of myrcene.

In the Notification of the 49th Amendment to the IFRA Code of Practice, the recommendation for beta-Pinene usage levels in Category 4: Products related to fine fragrance is up to 12.00% in the fragrance concentrate.

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PART A – Cosmetic Product Safety Information *continued*

2. Physical & chemical properties and stability *continued*

2.1.2 Physical/chemical properties of the cosmetic product

Appearance	Cream/Paste/Gel
Colour	White
Aroma	Fresh
pH	7.55

*RP: Responsible Person: Unikos Global Ltd

2.2 Stability of the cosmetic product

The ingredients used in the production of the cosmetic product comply with the relevant legal regulations.

Both the product and constituent ingredients are stable under normal use and warehousing conditions during the entire time of the BBE period.

2.2.1 Unikos Global Ltd confirms that all product stability tests reflect the stability of the product which is to be placed on the market.

2.2.2 Unikos Global Ltd uses a BBE based on the results of Unikos Global Ltd 's stability testing, including shelf life stability testing.

2.2.3 This product was subjected to Preservative Efficacy Testing and proved that it did not support microbial growth. PET reference: OxBio PET 2561

3. Microbiological quality

3.1.1 Microbiological specification of ingredients (substances and mixtures).

Based on available information from the ingredient specification (see section 1. Quantitative and qualitative composition – specification of ingredients), the ingredients used can be assessed as microbiologically safe.

3.1.2 Microbiological specification of the finished product

The given cosmetic product can be regarded as microbiologically safe for consumers' health

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under the ISO 29621:2010 standard “Cosmetics -- Microbiology -- Guidelines for the risk assessment and identification of microbiologically low-risk products”.

The microbiological harmlessness of the ingredients and the cosmetic product is assessed according to COLIPA: Guideline for Microbiological Quality Management (MQM).

This product was subjected to Preservative Efficacy Testing and proved that it did not support microbial growth. PET reference: OxBio PET 2561

4. Impurities, trace amounts of forbidden substances, & information about packaging material

4.1 Impurities and trace amounts of forbidden substances

According to specifications (see section 2.1.1 Physical/chemical properties of ingredients (substances or mixtures) submitted by ingredient suppliers, the ingredients do not contain impurities or trace amounts of forbidden substances.

Any impurities or traces identified in any ingredient above standard tolerances are noted against each respective ingredient in section 2.1.1.

4.2 Information about packaging material

The packaging material applied is suitable for the given type of cosmetic product and meets the predictable use requirements.

Container	Syringe
Container Material	PP
Airless Container	No

Polypropylene is resilient and resistant to most solvents and represents a low hazard in terms of chemical leaching. Since polypropylene is liable to chain degradation from exposure to heat and sunlight (a source of UV radiation) unless antioxidants have been added to the polymer to prevent polymer degradation, normal label warnings to store the product in cool and dark conditions apply.

Unikos Global Ltd confirms that the results of reference sample monitoring show no reaction between the packaging material and the product during the product’s stated minimum useable life. During that life no changes to physical and chemical properties of the product were noticed that would affect its usability and safety.

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5. Normal and reasonably foreseeable use

The current label advice:

Placce a small drop of gel per tooth in the tray. The total amount should be about 0.4ml-0.5ml. Do not spread the gel around the tray. When you apply the gel, make sure not to fill the trays completely. Give priority of the treatment to your front teeth. Insert the trays into your mouth. If any gel comes into contact with your gums, wipe it off with your finger, or tissue, or it can cause a burning sensation.
Leave the trays in your mouth for 30 minutes. Use our kit for 30 minutes a day for no more than 5 consecutive days. Check your teeth against the teeth shade guide and if you want to improve your shade even more, repeat the 5 days process one more time following a 2 day break. Do not use more than 10ml of gel per course. You can repeat the course after 1-2 months. WARNING: Keep out of reach of children. Not to be used under 18 years old. Avoid contact with lips and gums for maximum effect and minimal irritation. Do not use while sleeping. Do not use if pregnant or lactating. Caps, crown or veneers will whiten minimally. Consult a doctor or dentist if in doubt. Temporary tooth sensitivity/irritation may occur. This will disappear: 1. Within a few hours after discontinuing use. 2. Decreasing the time you bleach your teeth. 3. Increasing the amount of time between bleaching sessions. For external use only. Store in a cool and dry place or keep refrigerated. Keep away from sunlight and excessive room temperature.

The label of this cosmetic product should include this special note regarding its use, in compliance with Article 19(1)(d) of *Cosmetic Regulation* (EC) No. 1223/2009:

For external use only. Keep out of reach of children.

6. Exposure to the cosmetic product

Area of application	Teeth
Product type: Leave-on or Rinse-off	Rinse Off
Duration and frequency	1/month
Possible additional routes of exposure	Mouth
Estimated skin surface area (cm^2)	0
Estimated amount of the product applied according to the SCCS (g/day)	.09 g
Estimated retention factor according to the SCCS	.05
Target group	Adult
Calculated relative daily exposure according to the SCCS (mg/kg bw/day)	.045

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7. Exposure to the ingredients

	Ingredient INCI name	Concentration	SED
1	Sorbitol	0.40000	0.00090
2	Aqua	0.20100	0.00045
3	Phthalimidoperoxycaproic acid	0.12000	0.00027
4	Propylene glycol	0.10000	0.00023
5	Glycerin	0.06000	0.00014
6	Potassium nitrate	0.05000	0.00011
7	PEG-8	0.03000	0.00007
8	Hydroxyapatite	0.01000	0.00002
9	Cellulose gum	0.01000	0.00002
10	Hydroxyethylcellulose	0.00500	0.00001
11	Xanthan gum	0.00350	0.00001
12	Sodium saccharin	0.00200	0.00000
13	Menthol	0.00200	0.00000
14	Methylparaben	0.00150	0.00000
15	Aloe barbadensis leaf juice	0.00100	0.00000
16	Chamomilla recutita leaf extract	0.00100	0.00000
17	Punica granatum seed oil	0.00100	0.00000
18	Sodium bicarbonate	0.00100	0.00000
19	Propylparaben	0.00050	0.00000
20	trans-Anethole	0.00015	0.00000
21	Eucalyptol	0.00005	0.00000
22	Isomenthone	0.00005	0.00000
23	Menthone	0.00005	0.00000
24	Carvone	0.00005	0.00000
25	d-Limonene	0.00005	0.00000
26	alpha-Pinene	0.00005	0.00000
27	beta-Pinene	0.00005	0.00000

***SED**: Systemic Exposure Dose*

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8. Toxicological profile of the ingredients in the formulation

	Ingredient INCI name	MOS
1	Sorbitol	17777777.77780
2	Aqua	221116639.02710
3	Phthalimidoperoxycaproic acid	9444444.44440
4	Propylene glycol	88888888.88890
5	Glycerin	93333333.33330
6	Potassium nitrate	33333333.33330
7	PEG-8	651851851.85190
8	Hydroxyapatite	88888888.88890
9	Cellulose gum	222222222.22220
10	Hydroxyethylcellulose	888888888.88890
11	Xanthan gum	5714285714.28570
12	Sodium saccharin	3777777777.77780
13	Menthol	706666666.66670
14	Methylparaben	888888888.88890
15	Aloe barbadensis leaf juice	7111111111.11110
16	Chamomilla recutita leaf extract	2222222222.22220
17	Punica granatum seed oil	888888888.88890
18	Sodium bicarbonate	1875555555.55560
19	Propylparaben	5628444444.44440
20	trans-Anethole	6192592592.59260
21	Eucalyptol	22044444444.44440
22	Isomenthone	11422222222.22220
23	Menthone	14222222222.22220
24	Carvone	14577777777.77780
25	d-Limonene	39111111111.11110
26	alpha-Pinene	32888888888.88890
27	beta-Pinene	32888888888.88890

***MOS**: Margin of Safety*

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8. Toxicological profile of the ingredients in the formulation - continued

Based on the calculation of MoS (Margin of Safety) for ingredients that can be classified as hazardous to human health, the product does not contain ingredients with toxicologically significant profiles in terms of consumer health.

An ingredient with an MoS above 1000 is considered safe. An ingredient with an MoS above 100 but lower than 1000 must be further considered by the assessor.

Since all of the ingredients have a margin of safety above 1,000 this product is considered safe for consumers to use.

9. Undesirable effects and serious undesirable effects

The cosmetic product with a similar composition has been supplied to the market in the long term and until nowadays, no undesired effects to human health have been noticed in relation to the use of this product. Therefore, no undesired effects are anticipated at the common and reasonably predictable application of the given cosmetic product.

After its launch, the cosmetic product will be further monitored by Unikos Global Ltd in accordance to procedures detailed in *Cosmetic Regulation* (EC) No 1223/2009. The safety of the product should be reviewed on a regular basis. To that end, undesirable and serious undesirable effects on human health during in market use of the product should be filed (complaints during normal and improper use, and the follow-up done) and details forwarded to the safety assessor.

The safety assessor will then update the Cosmetic Product Safety Report (CPSR) based on the new findings and the adopted corrective measures.

10. Additional information on the product

No additional information is available and no additional studies were carried out.

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11. References

- THE SCCS'S NOTES OF GUIDANCE FOR THE TESTING OF COSMETIC SUBSTANCES AND THEIR SAFETY EVALUATION 8TH REVISION
  http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2009:342:0059:0209:en:PDF
- MSDS of ingredients
- Commission Implementing Decision of 25th November 2013 Guidelines on Annex I to Regulation (EC) No 1223/2009 of the European Parliament and of the Council on cosmetic products
- SCCS - Opinions
  http://ec.europa.eu/health/scientific_committees/consumer_safety/opinions/index_en.htm
- CosIng: the European Commission database on cosmetic substances
  http://ec.europa.eu/consumers/cosmetics/cosing/index.cfm?fuseaction=search.simple
- REGULATION 1223/2009 ANNEXES
  http://ec.europa.eu/consumers/cosmetics/cosing/index.cfm?fuseaction=ref_data.annexes_v2

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PART B – Cosmetic Product Safety Assessment

1. Assessment conclusion

Based on the information supplied, the cosmetic product detailed in this report is safe for human health when used in common or reasonably predictable conditions in compliance with the instructions provided for the consumer.

This conclusion is only applicable to this cosmetic product with the composition, properties, purpose, and method of use of which are detailed in this documentation, and laboratory tests attached to this assessment, including the detailed production and labelling which has been assessed as meeting the requirements of *Cosmetic Regulation* (EC) No. 1223/2009 effective on the date this report was issued.

2. Labelled warnings and instructions of use

The label of this cosmetic product should include this special note regarding its use, in compliance with Article 19(1)(d) of *Cosmetic Regulation* (EC) No. 1223/2009:

For external use only. Keep out of reach of children.

Allergens present in this product and estimated amounts*:

d-Limonene: 0.005%

* The presence of these allergens must be indicated in the list of ingredients when their concentration exceeds: 0.001% in leave-on products or 0.01% in rinse-off products. Only the allergen, not the estimated amount, is required on the label.

3. Reasoning

Based on the formulation of this cosmetic product, its qualitative and quantitative composition according to its INCI ingredients, basic physical and chemical characteristics and microbiology, Preservation Challenge Test performed, classification of the cosmetic product type, including its purpose and method of application, and available toxicological information and safety sheets of the ingredients used, the cosmetic product safety has been assessed for the consumer by assessing the toxicological profile of all ingredients, their chemical structure, exposure level and Margin of Safety (MoS) depending on the purpose of use in this cosmetic product.

This cosmetic product contains only the allowed ingredients in allowed concentrations. For ingredients with safety limits as specified in Annexes to *Cosmetic Regulation* (EC) No. 1223/2009, no ingredient exceeds the allowable safety limit therefore is a safe concentration in this cosmetic product. The evaluation of the entire composition and applied ingredient concentrations indicate that as a whole the composition of this cosmetic product complies with the requirements of *Cosmetic Regulation* (EC) No. 1223/2009 of the European Parliament and of the Council.

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4. Assessor's credentials and approval of Part B

Safety Assessor: Allison Wild
Oxford Biosciences Ltd.
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Oxfordshire
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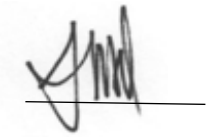
Experience and qualifications:

- MSc in Clinical Pharmacology, University of Oxford
- 15+ years experience formulating cosmetic products
- Full member of the Society of Cosmetic Scientists (SCS)
- Member of the British Pharmacological Society



Signature

17 March 2021

Date