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COSMETIC PRODUCT SAFETY REPORT

According to EC Regulation 1223/2009

GLUTANEX-GLOW

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SAFETY ASSESSOR

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PART A - COSMETIC PRODUCT SAFETY INFORMATION

Product name	GLUTANEX-GLOW
Shade names	/
Product type	Face care product
Formula number	/
Category of the product	Face care product
Physical form of the product	Liquid
Target population	Adults
Primary site of application	Face area
Packaging type and size	5ml glass vial with rubber cap
Manufacturer name and address	BIO-FD&C Co., Ltd., Korea
Producer name and address	BIO-FD&C Co., Ltd., Korea

1. QUANTITATIVE AND QUALITATIVE COMPOSITION OF THE COSMETIC PRODUCT

INCI name	CAS	EINECS/ELINCS	% active in the raw material	Concentration in the final product	Function
AQUA	7732-18-5	231-791-2	100	84,7304	Solvent
DEFINED CELL CULTURE MEDIA 7	Not available	Not available	100	10	SKIN CONDITIONING
HYDROLYZED COLLAGEN	92113-31-0 / 73049-73-7	295-635-5 / -	100	4	ANTISTATIC, EMOLLIENT, FILM FORMING, HAIR CONDITIONING, HUMECTANT, SKIN CONDITIONING
1,2-HEXANEDIOL	6920-22-5	230-029-6	100	1	SOLVENT
GLYCERIN	56-81-5	200-289-5	100	0,1	Denaturant, Hair Conditioning, Humectant, Masking, Oral Care, Perfuming, Skin Protecting, Viscosity Controlling
GLUCOSE	50-99-7	200-075-1	100	0,1	HUMECTANT
ADENOSINE	58-61-7	200-389-9	100	0,04	SKIN CONDITIONING
SODIUM CHLORIDE	7647-14-5	231-598-3	100	0,01	BULKING, MASKING, ORAL CARE, VISCOSITY CONTROLLING
SODIUM HYALURONATE	9067-32-7	Not available	100	0,01	HUMECTANT, SKIN CONDITIONING
SODIUM DNA	Not available	Not available	100	0,001	SKIN CONDITIONING
ACETYL HEXAPEPTIDE-8	616204-22-9	Not available	100	0,001	HUMECTANT, SKIN CONDITIONING
OCTAPEPTIDE-7	Not available	Not available	100	0,001	SKIN CONDITIONING
COPPER TRIPEPTIDE-1	Not available	Not available	100	0,001	SKIN CONDITIONING
SH-OLIGOPEPTIDE-9	Not available	Not available	100	0,001	HUMECTANT, HAIR CONDITIONING, SKIN CONDITIONING

SH-OCTAPEPTIDE-4	Not available	Not available	100	0,001	ANTIOXIDANT, BUFFERING, CHELATING, HAIR CONDITIONING, REDUCING, SKIN PROTECTING
SH-DECAPEPTIDE-7	Not available	Not available	100	0,001	ANTIOXIDANT, BUFFERING, CHELATING, HAIR CONDITIONING, REDUCING, SKIN PROTECTING
GLUTATHIONE	70-18-8	200-725-4	100	0,001	REDUCING
OLIGOPEPTIDE-1	Not available	Not available	100	0,001	SKIN CONDITIONING
SH-POLYPEPTIDE-1	Not available	Not available	100	0,0001	SKIN CONDITIONING
SH-POLYPEPTIDE-22	Not available	Not available	100	0,0001	SKIN CONDITIONING
SH-POLYPEPTIDE-9	Not available	Not available	100	0,0001	SKIN CONDITIONING
SH-POLYPEPTIDE-3	Not available	Not available	100	0,0001	SKIN CONDITIONING
SH-OLIGOPEPTIDE-1	Not available	Not available	100	0,0001	SKIN CONDITIONING
SH-OLIGOPEPTIDE-2	Not available	Not available	100	0,0001	SKIN CONDITIONING, SKIN PROTECTING

2. PHYSICAL/CHEMICAL CHARACTERISTICS AND STABILITY OF THE COSMETIC PRODUCT

a. PHYSICAL/CHEMICAL CHARACTERISTICS AND STABILITY OF SUBSTANCES OR MIXTURES

Substance (INCI) / Mixture	Chemical NAME	Physical form	Molecular weight (g/mol)	Water Solubility /Solubility	Partition coefficient	Absorption spectra (UV absorbers)
AQUA	Water	Liquid	18.02 g/mol	Soluble in alcohol	Not available	Not applicable
DEFINED CELL CULTURE MEDIA 7	Not available	Transparent solution	Not available	Soluble	Not available	Not available
HYDROLYZED COLLAGEN	Not available		1000 - 10000	Not available	Not available	Not applicable
1,2-HEXANEDIOL	(RS)-1,2-Dihydroxyhexane	Colorless liquid	118,17 g/mol	Miscible	log Pow= 0.58	
GLYCERIN	Glycerol	Liquid	92.09	Completely miscible with water at 25 °C. The compound is also completely miscible with methanol, ethanol, and the isomers of propanol, butanol, and pentanol.	log POW = -1.75 at 25 °C	Not applicable
GLUCOSE	Glucose	Crystalline, powder	180.16	alpha-form anhydrous: soluble in hot glacial acetic acid, pyridine, aniline; very sparingly soluble in absolute alcohol, ether, acetone	log POW = -3.24	Not applicable
ADENOSINE	6-Amino-9-beta-D-ribofuranosyl-9H-purine	White liquid	267.245 g/mol	Dispersible	Not available	Not available
SODIUM CHLORIDE	Sodium chloride	Solid (crystalline)	58.44	Very soluble in water	Not available	Not applicable
SODIUM HYALURONATE	Hyaluronic acid, sodium, salt	Powder	403.31 g/mol	Soluble	Not available	Not available
SODIUM DNA	Deoxyribonucleic acid, sodium salts	Ivory white powder	Not available	Soluble in water	Not available	Not available
ACETYL HEXAPEPTIDE-8	Not applicable		Not available	Not available	Not available	Not applicable
OCTAPEPTIDE-7	Not available	White-yellowish powder	Not available	Not soluble	Not available	Not available
COPPER TRIPEPTIDE-1	Not available	Blue powder	130.9 g/L in water	485.986 g/mol	Not available	Not available
SH-OLIGOPEPTIDE-9	Not available	Liquid	Not available	Soluble	Not available	Not available
SH-OCTAPEPTIDE-4	Not available	Liquid	Not available	Soluble	Not available	Not available
SH-DECAPEPTIDE-7	Not available	Liquid	Not available	Soluble	Not available	Not available
GLUTATHIONE	Glycine, N-(N-L-.gamma.-glutamyl-L-cysteinyl)-	Solid	307,3235 g/mol	20mg/ml at 25°C	Not available	Not available
OLIGOPEPTIDE-1	Glycine, oligomer with histidine and lysine	white lyophilized mass	Not available	Soluble	Not available	Not available
SH-POLYPEPTIDE-1	Not available	White Mily solution	17.2 kDa	Not soluble	Not available	Not available
SH-POLYPEPTIDE-22	Not available	White Mily solution	Not available	Not soluble	Not available	Not available
SH-POLYPEPTIDE-9	Not available	Liquid	Not available	Not soluble	Not available	Not available
SH-POLYPEPTIDE-3	Not available	White Mily solution	17.2 kDa	Not soluble	Not available	Not available
SH-OLIGOPEPTIDE-1	Not available	Colorless liquid	Not available	Soluble	Not available	Not available
SH-OLIGOPEPTIDE-2	Not available	Powder	Not available	Not soluble	Not available	Not available

b. PHYSICAL/CHEMICAL CHARACTERISTICS OF THE FINISHED COSMETIC PRODUCT

Analytical tests	Specifications	Results
Description	Transparent solution	comfirm
pH	5 ~ 9	comfirm
Odour	Typical	comfirm
Microbes	≤ 100 cfu/ml	0 cfu/ml
State of packing	Same as a standard	comfirm
Appearance	Same as a standard	comfirm
Viscosity	Same as a standard	comfirm
Weight	4ml ± 5%	comfirm
Note on storage	Keep in a cool place (4℃ ~ 25℃) away from direct sunlight.	Pass

c. STABILITY OF THE COSMETIC PRODUCT

The physical stability of the finished product is justified on the basis of the stability report document, which is ensuring that no changes in physical state of the finished product occur during transport, storage or handling of the product.

The stability testing was performed according to the accelerated method (12 weeks at 40 °C, room temperature and 5 °C), results below were obtained:

EVALUATION OF PHYSICHAL PROPERTIES OF THE PRODUCT IN GLASS CONTAINER (ORIGINAL PACKAGING)

PARAMETER	INITIAL	ACCELERATED STUDY 40°C				ACCELERATED STUDY 5°C			
		2 weeks	6 weeks	10 weeks	12 weeks	2 weeks	6 weeks	10 weeks	12 weeks
DATE	10.11.2020	24.11.2020	22.12.2020	19.1.2021	2.2.2021	24.11.2020	22.12.2020	19.1.2021	2.2.2021
APPEARANCE	Liquid	Liquid	Liquid	Liquid	Liquid	Liquid	Liquid	Liquid	Liquid
COLOUR	Colorless transparent	Colorless transparent	Colorless transparent	Colorless transparent	Colorless transparent	Colorless transparent	Colorless transparent	Colorless transparent	Colorless transparent
ODOUR	Characteristic	Characteristic	Characteristic	Characteristic	Characteristic	Characteristic	Characteristic	Characteristic	Characteristic
PH (at 22°C)	5,67	5,34	5,66	5,38	5,49	6,03	6,11	5,84	5,71
PHASE SEPARATION	None	None	None	None	None	None	None	None	None
DENSITY (at 22°C)	1,00	0,99	0,98	0,99	1,00	1,00	0,99	0,98	1,00

Based on the test results, the date of minimum durability is equal to 36 months.

3. MICROBIOLOGICAL QUALITY

a. MICROBIOLOGICAL QUALITY OF SUBSTANCES AND MIXTURES

Substances and mixtures susceptible to microbial growth (water based mixtures, protein - rich materials, plant or animal raw materials)	Present
Raw materials which do not support microbial growth (organic solvents)	Not present

b. MICROBIOLOGICAL QUALITY OF THE FINISHED COSMETIC PRODUCT

According to the 'Guidelines on Microbiological Quality of the finished product' (SCCS Notes of Guidance), the following limits apply:

Category 1: Products specifically intended for children under 3 years, eye area and mucous membranes.

Category 2: Other cosmetic products.

Types of microorganism	Products specifically intended for children under three years of age, the eye area or the mucous membranes	Other products
Total Aerobic Mesophilic Microorganisms (Bacteria plus yeast and mould)	**≤ 1 x 10^2 CFU per g or ml [a]**	**≤ 1 x 10^3 CFU per g or ml [b]**
Escherichia coli	Absence in 1 g or 1 ml	Absence in 1 g or 1 ml
Pseudomonas aeruginosa	Absence in 1 g or 1 ml	Absence in 1 g or 1 ml
Staphyloccocus aureus	Absence in 1 g or 1 ml	Absence in 1 g or 1 ml
Candida albicans	Absence in 1 g or 1 ml	Absence in 1 g or 1 ml
Due to inherent variability of the plate count method, according to USP Chapter 61 or EP Chapter 2.6.12, Interpretation of results, results considered out of limit if **a > 200 CFU/g or ml,** **b > 2 000 CFU/g or ml.** NOTE When colonies of bacteria are detected on Sabouraud Dextrose agar, Sabouraud Dextrose agar containing antibiotics may be used.		

(Source: The SCCS Notes of Guidance for testing of cosmetic ingredients and their safety evaluation, SCCS/1602/18, October 2018)

This product was evaluated according to the category 2, and the following results were obtained:

TEST	METHOD	RESULT
TOTAL AEROBIC MESOPHILIC BACTERIA	According to ISO 21149:2017	< 100 CFU/g
ENUMERATION OF YEAST AND MOULD	According to ISO 16212:2017	< 100 CFU/g
PRESENCE OF CANDIDA ALBICANS	According to ISO 18416:2015	Absent in 1g
PRESENCE OF PSEUDOMONAS AERUGINOSA	According to ISO 22717:2016	Absent in 1g
PRESENCE OF STAPHYLOCOCCUS AUREUS	According to ISO 22718:2016	Absent in 1g
PRESENCE OF ESCHERICCHIA COLI	According to ISO 21150:2015	Absent in 1g

The results show, that the microbiological purity of the product is acceptable and meets the criteria listed above.

The efficacy of the preservation of a finished cosmetic product was assessed experimentally in order to ensure microbial stability and preservation during storage and use. The challenge test was performed according to the ISO 11930 method and meets the industry requirements specified in the Notes of guidance for testing of cosmetic ingredients for their safety evaluation, 10th revision (SCCS/1602/18, October 2018)

4. IMPURITIES, TRACES, INFORMATION ABOUT THE PACKAGING MATERIAL

a. IMPURITIES AND TRACES

The test stability and compatibility test was performed according to the generally acceptable method.

This product is manufactured according to Good Manufacturing Practice (ISO 22716). Ingredients used throughout must be of a high quality and (where specified) they have to meet purity criteria listed in the Cosmetics legislation. Information provided on ingredient purity and representative certificates of analysis are held in the PIF and are acceptable.

b. THE RELEVANT CHARACTERISTICS OF PACKAGING MATERIAL

The product is packaged in a 5ml glass vial with rubber cap. These packaging components are widely used for consumer products. They are non-porous to inks and adhesives and are unlikely to react chemically with this product. They are considered to be safe since there is no evidence of a possible migration of packaging components into the product.

5. NORMAL AND RESONABLY FORSEEABLE USE

This product is a leave on face care product intended to be used by adults on daily basis.

Instructions for use written on the label	Facial serum
Precautions for use written on the label	/

A clear explanation of the normal intended use and the reasonably foreseeable use is provided on the product label and therefore a mistaken use (not a misuse) is not recognisable.

6. EXPOSURE TO THE COSMETIC PRODUCT

Product Type:	Face Cream
Targeted Population:	Adults
Estimated daily amount applied (g):	1,54*
Skin Surface Area of Application/cm^2:	565*
Calculated daily exposure (g/day)	1,54*
Calculated relative daily exposure (mg/kg bw/day):	24,14*
Amount Per Unit Area of Skin per day mg/cm^2/day:	2,73
Exposure time:	12h
Frequency of application:	2,14*
Part of the body exposed:	1/2 area head*

* SCCS, face cream

7. EXPOSURE TO THE SUBSTANCES

INCI	Retention factor	POD	SED	MoS
AQUA	1	Not available	21,74747	/
DEFINED CELL CULTURE MEDIA 7	1	Not available	2,56667	/
HYDROLYZED COLLAGEN	1	Not available	1,02667	/
1,2-HEXANEDIOL	1	500	0,25667	1948,051948
GLYCERIN	1	2000	0,02567	77922,07792
GLUCOSE	1	Not available	0,02567	/
ADENOSINE	1	Not available	0,01027	/
SODIUM CHLORIDE	1	1330	0,00257	518181,8182
SODIUM HYALURONATE	1	Not available	0,00257	/
SODIUM DNA	1	Not available	0,00026	/
ACETYL HEXAPEPTIDE-8	1	Not available	0,00026	/
OCTAPEPTIDE-7	1	Not available	0,00026	/
COPPER TRIPEPTIDE-1	1	Not available	0,00026	/
SH-OLIGOPEPTIDE-9	1	Not available	0,00026	/
SH-OCTAPEPTIDE-4	1	Not available	0,00026	/
SH-DECAPEPTIDE-7	1	Not available	0,00026	/
GLUTATHIONE	1	Not available	0,00026	/
OLIGOPEPTIDE-1	1	Not available	0,00026	/
SH-POLYPEPTIDE-1	1	Not available	0,00003	/
SH-POLYPEPTIDE-22	1	Not available	0,00003	/
SH-POLYPEPTIDE-9	1	Not available	0,00003	/
SH-POLYPEPTIDE-3	1	Not available	0,00003	/
SH-OLIGOPEPTIDE-1	1	Not available	0,00003	/
SH-OLIGOPEPTIDE-2	1	Not available	0,00003	/

Calculations of Margin of Safety (MoS) have been determined for all ingredients where this is possible from published toxicity information. The method used to do this is:

SED (whole product)*% ingredient = SED (ingredient)

MoS = POD (ingredient)/SED (ingredient).

In every case, the MoS is >100 which is considered to be acceptable. In addition, calculations are also presented to show by how much each ingredient is below the recommendations of industry (CTFA) and those required by European cosmetic legislation. All ingredients fall below any recommended maxima.

8. TOXICOLOGICAL PROFILE OF THE SUBSTANCES

INCI name	AQUA
Restriction	None
General description	Simply water unlikely to cause irritation, allergy or harm. Used in many cosmetic products as a solvent and necessary to sustain biological life. The source of water should be known, monitored to GMP and either a deionised or high purity grade free from toxins, pollutants and bacteriological contamination should be used in cosmetic products.
Acute toxicity via relevant routes of exposure	Not toxic. The actual or estimated LD50 value: 100000 mg/kg. Oral Rat LD50: >90 mL/kg.
Skin irritation and skin corrosivity	Not irritating
Mucous membrane irritation (eye irritation)	Not irritating
Skin Sensitization	Not sensitizing
Dermal/ percutaneous absorption	Non-permeator by skin
Repeated dose toxicity (normally 28- or 90-day studies)	Not available
Mutagenicity/ genotoxicity	Not available
Carcinogenicity	Not available
Reproduction toxicity	Not available
Toxicokinetics (ADME studies)	Not available
Phototoxicity / Photosensitization	Not available
Nanomaterials	Not applicable
Reference	(1) Dweck A. C. Handbook of Cosmetics Ingredients - their use, safety and toxicology. Third edition, 2012.

INCI name	DEFINED CELL CULTURE MEDIA 7
Restriction	None
General description	Defined Cell Culture Media 7 is a cell culture phase consisting of: Arginine HCl (q.v.), Calcium Chloride (q.v.), cystine HCl, Folic Acid (q.v.), Glucose (q.v.), Glycine (q.v.), Histidine HCl (q.v.), Inositol (q.v.), Isoleucine (q.v.), Leucine (q.v.), Lysine HCl (q.v.), Methionine (q.v.), Niacinamide (q.v.), Phenylalanine (q.v.), Potassium Chloride (q.v.), Pyridoxine HCl (q.v.), Riboflavin (q.v.), Serine (q.v.), Sodium Bicarbonate (q.v.), Sodium Chloride (q.v.), Sodium Phosphate (q.v.), Sodium Pyruvate (q.v.), Thiamine HCl (q.v.), Threonine (q.v.), Tryptophan (q.v.), tyrosine disodium salt dehydrate, and Valine (q.v.).

Acute toxicity via relevant routes of exposure	The actual or estimated LD50 value: 5000 mg/kg
Skin irritation and skin corrosivity	Healthy young women (n = 29) were allocated to a group (n = 14) receiving an amino-acid supplement (600 mg l-leucine, 250 mg l-arginine, and 300 mg l-glutamine) and a placebo group (n = 15) receiving a supplement not-containing the amino acids. The amino-acid supplement and placebo were given twice/day for 6 weeks. After a wash-out (2 months) from the 1st test, the amino-acid group received the placebo and the placebo group the amino-acid supplement. The body compositions/skin conditions were measured 4 times (day 1 and weeks 2, 4, and 6) in each test. Percentage-change of muscle mass in the amino-acid group increased up to 4 weeks (p = 0.05) and was higher than that in the placebo group (p = 0.09). Skin texture estimated by the image processing of neck skin replica tended to increase in the amino-acid group at 6 weeks compared with that at 0 week, though there was no significant intergroup difference. In conclusion, the young adult women having no fitness habit showed the significant increase of the muscle amount and improvement tendency of the skin texture by the continuous intake of the amino-acid supplement.
Mucous membrane irritation (eye irritation)	Not expected to cuase irritation
Skin Sensitization	Not expected to cause sensitization
Dermal/ percutaneous absorption	Not available
Repeated dose toxicity (normally 28- or 90-day studies)	Not available
Mutagenicity/ genotoxicity	Not available
Carcinogenicity	Not available
Reproduction toxicity	Not available
Toxicokinetics (ADME studies)	Not available
Phototoxicity / Photosensitization	Not available
Nanomaterials	Not available
Reference	(1) Defined Cell Culture Media 7 MSDS, BIO-FD&C Co., Ltd., version 1 (2) Takaoka M, Okumura S, Seki T, Ohtani M. Effect of amino-acid intake on physical conditions and skin state: a randomized, double-blind, placebo-controlled, crossover trial. J Clin Biochem Nutr. 2019;65(1):52-58. doi:10.3164/jcbn.18-108

INCI name	HYDROLYZED COLLAGEN

Restriction	None
General description	Substance obtained by acidic, alkaline, or enzymatic hydrolysis of hoofs and horns composed primarily of amino acids, peptides, and proteins. It may contain impurities consisting chiefly of carbohydrates and lipids along with smaller quantities of miscellaneous organic substances of biological origin. The safety of hydrolyzed collagen has been assessed by the CIR Expert Panel. The CIR Expert Panel evaluated the scientific data and concluded that this ingredient is safe as used in cosmetics at concentrations up to 6%.
Acute toxicity via relevant routes of exposure	Practically nontoxic when administered orally or dermally in acute animal toxicity studies. The actual or estimated LD50 value: 5000 mg/kg
Skin irritation and skin corrosivity	Non to minimally irritating (undiluted, rabbit). Not irritating in clinical studies.
Mucous membrane irritation (eye irritation)	Minimally irritating (undiluted, rabbit)
Skin Sensitization	Not sensitizing (guinea pig). Not sensitizing in clinical studies.
Dermal/ percutaneous absorption	Not available
Repeated dose toxicity (normally 28- or 90-day studies)	Subchronic dermal studies on 2 cosmetic formulations containing 2% hydrolyzed collagen were negative for systemic toxicity.
Mutagenicity/ genotoxicity	Not available
Carcinogenicity	Not available
Reproduction toxicity	Not available
Toxicokinetics (ADME studies)	Not available
Phototoxicity / Photosensitization	No indication of phototoxicity based on clinical studies.
Nanomaterials	Not applicable
Reference	(1) CIR Expert Panel. Final Report on the Safety Assessment of Hydrolyzed Collagen. JACT 4(5)199- 221, 1985 confirmed 06/04 IJT 25(S2), 2006. (2) Dweck A. C. Handbook of Cosmetics Ingredients - Their Use, Safety and Toxicology. Third edition, 2012.

INCI name	1,2-HEXANEDIOL
Restriction	None
General description	Solvents/diluents for flavour and/or fragrance agents. According to a patent filed by Proctor and Gamble, hexanediol or 1,2-hexanediol is a

	highly effective and mild coupling agent and humectant. It is especially useful when bonding silicone products and can be used at lower concentrations than many other coupling agents, therefore reducing its irritation likeliness. There are no safety warnings for Hexanediol, 1,2-hexanediol (OSHA). However, it has been known to be an irritant in some cases, especially to the eyes at 100%. It can also cause dermatitis, although the Cosmetics Working Group offers no warnings for its use. At the levels used in cosmetic products it reperesent no concerns and no adverse reactions are expected from its topical use.
Acute toxicity via relevant routes of exposure	Oral LD50 (mouse): 3,097mg/kg.
Skin irritation and skin corrosivity	The substance 1,2-hexanediol is not irritating to rabbit skin
Mucous membrane irritation (eye irritation)	The substance 1,2-hexanediol was shown to be irritant to rabbit eyes
Skin Sensitization	Not sensitizing
Dermal/ percutaneous absorption	Not available
Repeated dose toxicity (normally 28- or 90-day studies)	the systemic no-observable-adervse-effect-level(NOAEL) is 500 mg/kg/day followin OECD guideline and GLP regulations
Mutagenicity/ genotoxicity	The results of the Salmonella/Mammalian Microsome (Ames test) and Escherichia coli WP2 mutagenesis assay indicate that test article did not cause a positive respone with any of the tester strains with and without metabolic activation.
Carcinogenicity	Not available
Reproduction toxicity	no effects on estrous cycle of female and sperm obility and sperm count of males has been observed up to the highest tested dose of 1000 mg/kg bw/day and thus the substance is considered not to effect fertility
Toxicokinetics (ADME studies)	Not available
Phototoxicity / Photosensitization	Not available
Nanomaterials	
Reference	(1) Dweck A. C. Handbook of Cosmetics Ingredients - Their Use, Safety and Toxicology. Third edition, 2012. (2) ECHA Information on Chemicals. REACH Registered Substance CAS 6920-22-5. Joint Submission. First published 30 Julij 2013, Last modified 29 Jul 2013

INCI name	GLYCERIN

Restriction	None
General description	Glycerol is widely distributed in food as a natural constituent, and it has undergone review and approval for use as both a direct and indirect food additive and is GRAS by US FDA. Animal studies involving single or repeated exposure by various routes indicated a low order of toxicity, the possible target sites (particularly following repeated oral administration) being the kidney and gastrointestinal tract. Glycerol appears to be of generally low oral toxicity in humans.
Acute toxicity via relevant routes of exposure	The reported oral LD50 of glycerin ranged from 2530-58400 mg/kg in rats, 4090-38000 mg/kg in mice, 27000 mg/kg in rabbits, and 77500 mg/kg in guinea pigs. The dermal LD50 of glycerin in rats was reported to be > 21900 mg/kg and >18700 mg/kg in rabbits. The approximate Lt50 for rats was determined to be 423 min for exposure to glycerin vapors at 11.0 mg/L. The intraperitoneal LD50 of glycerin in rats ranged from 4420-10100 mg/kg and 8600-9500 mg/kg in mice. The subcutaneous LD50 of glycerin was 100 mg/kg in rats and ranged from 91-10000 mg/kg in mice. The intravenous LD50 of glycerin ranged from 5200-6600 mg/kg in rats, 4250-6700 mg/kg in mice, and 53000 mg/kg in rabbits.
Skin irritation and skin corrosivity	Not dermally irritating to rabbits when applied at concentrations up to 100% to up to 30% of the body surface. Mild dermal irritant at 100% in guinea pigs.
Mucous membrane irritation (eye irritation)	Undiluted glycerin was not irritating when administered to the eyes of human subjects. There was a strong burning and stinging sensation, with tear production but no injury was observed.
Skin Sensitization	A moisturizer containing 65.9% glycerin was not sensitizing to human subjects. Natural and synthetic glycerin were not sensitising to white male guinea pigs at 0.1%.
Dermal/ percutaneous absorption	No data
Repeated dose toxicity (normally 28- or 90-day studies)	There were no signs of toxicity or effects on blood or on urine production when human subjects were orally administered approximately 1300-2200 g/kg/d glycerin for 50 days. The NOAEL was ≥2200 mg/kg/d. There were no treatment effects when 100% glycerin was topically applied daily to 30% of the body surfaces of rabbits for 45 weeks. The inhalation

	LOAEL was 1000 mg/m3 for glycerin administered 6 h/d, 5 d/week for 2 weeks in rats. The inhalation NOAEL was 0.167 mg/L for glycerin administered for 5 h/d, 5 d/week for 13 weeks in rats.
Mutagenicity/ genotoxicity	Glycerin was not genotoxic in multiple Ames tests using multiple strains of S. typhimurium at concentrations up to 50 mg/plate. It was not genotoxic in a cytogenetic assay, X-linked HGPRT, sister chromatid exchange assay, unscheduled DNA synthesis assay, and chromosome aberration test at concentrations up to 1.0 mg/mL.
Carcinogenicity	Glycerin administered in the feed of rats at doses up to 20% in feed for 1 year or up to 10 g/kg for 2 years did not increase the incidence of tumors. Orally administered glycerin, in concentrations up to 5%, had a potentiating effect on the carcinogenicity of 4NQO in mice.
Reproduction toxicity	No convincing evidence of reproductive effects have been seen in rats treated orally or dermally, or in mice fed glycerol during pregnancy. Glycerin is transferred across the plancenta in small amounts. May cause some adverse reproductive effects based on animal data, but there was no evidence of teratogenicity. No effects on fertility and reproductive performance were observed in a two generation study with glycerol administered by gavage (NOAEL 2000 mg/kg bw/day).
Toxicokinetics (ADME studies)	Glycerin is rapidly absorbed in the intestine and the stomach, distributed throughout the extracellular fluids through much of the body. It is mostly metabolized by the liver and kidneys with the remainder excreted in urine. Free glycerin is naturally present in humans, primarily in plasma.
Phototoxicity / Photosensitization	No data
Nanomaterials	Not applicable
Reference	(1) CIR Expert Panel. Safety assessment of glycerin as used in cosmetics - final report (January 14,2015). (2) ECHA. Retrieved from http://echa.europa.eu/information-on-chemicals/registered-substances

INCI name	GLUCOSE

Restriction	None
General description	Approved by US FDA as a GRAS direct food additive. Listed in the Annex IV of the Regulation (EC) No 1907/2006 (REACH) which sets out substances that are exempted from the registration as sufficient information is known about these substances that they are considered to cause minimum risk because of their intrinsic properties. The CIR Expert Panel evaluated the scientific data and concluded that this ingredient is safe as used in cosmetics and personal care products.
Acute toxicity via relevant routes of exposure	Oral LD50 (rat): 25800 mg/kg; Oral LD50 (dog): 10000 mg/kg
Skin irritation and skin corrosivity	Not irritating (HRIPT)
Mucous membrane irritation (eye irritation)	Not irritating
Skin Sensitization	Not sensitizing (HRIPT)
Dermal/ percutaneous absorption	Not available
Repeated dose toxicity (normally 28- or 90-day studies)	Not available
Mutagenicity/ genotoxicity	Not available
Carcinogenicity	Not available
Reproduction toxicity	Not available
Toxicokinetics (ADME studies)	Rapidly absorbed from the small intestine, principally by an active mechanism.
Phototoxicity / Photosensitization	Not available
Nanomaterials	Not applicable
Reference	(1) CIR Expert Panel. Safety Assessment of Monosaccharides, Disaccharides, and Related Ingredients as Used in Cosmetics. April 4, 2014. (2) EC. Appendix 2, Review of Annex IV of the Regulation No. 1907/2006 (REACH), Evaluation of existing entries. 2009. Retrieved from http://ec.europa.eu/environment/chemicals/reach/pdf/6b_appendix_2.pdf

INCI name	ADENOSINE
Restriction	None
General description	Adenosine is a purine nucleoside comprising a molecule of adenine attached to a ribose sugar molecule (ribofuranose) moiety via a β-N9-glycosidic bond. Adenosine plays an important

	role in biochemical processes, such as energy transfer —as adenosine triphosphate (ATP) and adenosine diphosphate (ADP)—as well as in signal transduction as cyclic adenosine monophosphate, cAMP. It is also an inhibitory neurotransmitter, believed to play a role in promoting sleep and suppressing arousal, with levels increasing with each hour an organism is awake. Extracellular adenosine concentrations from normal cells are approximately 300 nM; however, in response to cellular damage (e.g. in inflammatory or ischemic tissue), these concentrations are quickly elevated (600–1,200 nM). Thus, in regard to stress or injury, the function of adenosine is primarily that of cytoprotection preventing tissue damage during instances of hypoxia, ischemia, and seizure activity. Activation of A2A receptors produces a constellation of responses that in general can be classified as anti-inflammatory.
Acute toxicity via relevant routes of exposure	Oral LD50 (rat): 2,000 mg/kg; Oral LD50 (mouse): 2,000 mg/kg.
Skin irritation and skin corrosivity	Rabbit: mild irritation
Mucous membrane irritation (eye irritation)	Rabbit: mild irritation
Skin Sensitization	Not available
Dermal/ percutaneous absorption	Not available
Repeated dose toxicity (normally 28- or 90-day studies)	Not available
Mutagenicity/ genotoxicity	Not available
Carcinogenicity	Not available
Reproduction toxicity	Not available
Toxicokinetics (ADME studies)	Not available
Phototoxicity / Photosensitization	Not available
Nanomaterials	
Reference	(1) Dweck A. C. Handbook of Cosmetics Ingredients - their use, safety and toxicology. Third edition, 2012. (2) NLT AdenoSphere 2.0 MSDS, BioSpectrum, Inc.

INCI name	SODIUM CHLORIDE
Restriction	None
General description	The US FDA reviewed the safety of Sodium Chloride and approved its use as an active ingredient in OTC drug products for eyes at concentrations of 2 to 5%. US FDA includes

	Sodium Chloride on its list of substances considered GRAS as a substance migrating to food from packaging.
Acute toxicity via relevant routes of exposure	Oral LD50 (rat): 3000 mg/kg; Dermal LD50 (rabbit) > 10000 mg/kg
Skin irritation and skin corrosivity	May cause skin irritation.
Mucous membrane irritation (eye irritation)	In contact with eyes can cause irritation or redness due to abrasion.
Skin Sensitization	Not available
Dermal/ percutaneous absorption	Not available
Repeated dose toxicity (normally 28- or 90-day studies)	NOEL value of 1330 mg/kg/day was determined in a study in which non-iodized sodium chloride was fed to rats in their diets for periods of 90 days (study report).
Mutagenicity/ genotoxicity	Not available
Carcinogenicity	Not available
Reproduction toxicity	
Toxicokinetics (ADME studies)	Not available
Phototoxicity / Photosensitization	Not available
Nanomaterials	Not applicable
Reference	(1) ECHA. REACH, Registration Dossier, CAS 7647-14-5. Joint Submission (Akzo, Archroma...) First published 17 Mar 2011, Last modified 13 Apr 2015. (2) Dweck A. C. Handbook of Cosmetics Ingredients - Their Use, Safety and Toxicology. Third edition, 2012.

INCI name	SODIUM HYALURONATE
Restriction	None
General description	The safety of Hyaluronic Acid, Sodium Hyaluronate and Potassium Hyaluronate has been assessed by the Cosmetic Ingredient Review (CIR) Expert Panel. The CIR Expert Panel evaluated the scientific data and concluded that Hyaluronic Acid, Sodium Hyaluronate and Potassium Hyaluronate were safe as cosmetic ingredients.
Acute toxicity via relevant routes of exposure	The actual or estimated LD50 value: 800 mg/kg body weight.
Skin irritation and skin corrosivity	Not irritating
Mucous membrane irritation (eye irritation)	Not available
Skin Sensitization	Not sensitizing (rabbits)
Dermal/ percutaneous absorption	Not available
Repeated dose toxicity (normally 28- or 90-day studies)	Not available
Mutagenicity/ genotoxicity	Not genotoxic

Carcinogenicity	No evidence of cytotoxicity form sodium hyaluronate to mouse bone marrow cells
Reproduction toxicity	Not toxic for the reproduction
Toxicokinetics (ADME studies)	Not available
Phototoxicity / Photosensitization	Not available
Nanomaterials	
Reference	(1) CIR Expert Panel. Final Report of the Safety Assessment of Hyaluronic Acid, Potassium Hyaluronate, and Sodium Hyaluronate. IJT 28(Suppl. 1):5-67, 2009. (2) Dweck A. C. Handbook of Cosmetics Ingredients - Their Use, Safety and Toxicology. Third edition, 2012.

INCI name	SODIUM DNA
Restriction	None
General description	Deoxyribonucleic acid, sodium salts
Acute toxicity via relevant routes of exposure	Male rats Wistar 520 mg/kg(Russian study)
Skin irritation and skin corrosivity	non irritant (Patch Test method, February 2007, DNA gel 2,5%)
Mucous membrane irritation (eye irritation)	non irritant (Het Cam method, January 2007, Sodium DNA gel 2,5%)
Skin Sensitization	Allergic reactions can occur in sensitive people. Conditions that can be aggravated from exposure to the substance: asthmatics or those predisposed to allergies should be careful of material of a biological origin.
Dermal/ percutaneous absorption	Not available
Repeated dose toxicity (normally 28- or 90-day studies)	Not available
Mutagenicity/ genotoxicity	Not carcinogenic
Carcinogenicity	Not available
Reproduction toxicity	Not available
Toxicokinetics (ADME studies)	Not available
Phototoxicity / Photosensitization	Not available
Nanomaterials	Not available
Reference	(1) KALINAT AW POWDER MSDS; KALICHEM srl - Via Alessandrini 8, 25086 Rezzato (BS), July 2018

INCI name	ACETYL HEXAPEPTIDE-8
Restriction	None
General description	Acetyl hexapeptide-8 is the synthetic peptide consisting of arginine, methionine, and

	acetylated glutamic acid residues. Except for acute toxicity estimate, no known or reported toxicological information available for this ingredient.
Acute toxicity via relevant routes of exposure	The actual or estimated LD50 value: 2000 mg/kg
Skin irritation and skin corrosivity	Not available
Mucous membrane irritation (eye irritation)	Not available
Skin Sensitization	Not available
Dermal/ percutaneous absorption	Not available
Repeated dose toxicity (normally 28- or 90-day studies)	Not available
Mutagenicity/ genotoxicity	Not available
Carcinogenicity	Not available
Reproduction toxicity	Not available
Toxicokinetics (ADME studies)	Not available
Phototoxicity / Photosensitization	Not available
Nanomaterials	Not applicable
Reference	(1) Dweck A. C. Handbook of Cosmetics Ingredients - Their Use, Safety and Toxicology. Third edition, 2012.

INCI name	OCTAPEPTIDE-7
Restriction	None
General description	Octapeptide-7 is the synthetic peptide consisting of glycine, hydroxyproline, lysine, proline, serine and threonine
Acute toxicity via relevant routes of exposure	The actual or estimated LD50 value: 2,000 mg/kg body weight.
Skin irritation and skin corrosivity	Not considered irritant
Mucous membrane irritation (eye irritation)	Not considered irritant
Skin Sensitization	Not considered sensitizing
Dermal/ percutaneous absorption	Not available
Repeated dose toxicity (normally 28- or 90-day studies)	Not available
Mutagenicity/ genotoxicity	Not available
Carcinogenicity	Not available
Reproduction toxicity	Not available
Toxicokinetics (ADME studies)	Not available
Phototoxicity / Photosensitization	Not available
Nanomaterials	Not available
Reference	(1) Octapeptide-7, powder MSDS, BIO-FD&C Co., Ltd., version 1

INCI name	COPPER TRIPEPTIDE-1

Restriction	None
General description	Copper Peptide is a naturally occurring human tripeptide. In plasma, the level of Copper peptide is about 200 ng/ml at age 20. By the age of 60, the level drops to 80 ng/ml. Scientific studies conducted have established that human tripeptide. Copper peptide possesses a plethora of biological actions such as activation of wound healing, attraction of immune cells, antioxidant and anti-inflammatory effects, stimulation of collagen etc. Is widely used in cosmetics as a reparative and anti-aging ingredient.
Acute toxicity via relevant routes of exposure	Acute toxicity: LD50 mouse (I.P.): =160mg/kg
Skin irritation and skin corrosivity	May cause irritation. To the best of our knowledge the chemical, physical, and toxicological properties have not been completely investigated.
Mucous membrane irritation (eye irritation)	Not available
Skin Sensitization	Moderate irritant to skin on direct contact.
Dermal/ percutaneous absorption	Not available
Repeated dose toxicity (normally 28- or 90-day studies)	Not available
Mutagenicity/ genotoxicity	Not available
Carcinogenicity	Not available
Reproduction toxicity	Not available
Toxicokinetics (ADME studies)	Not available
Phototoxicity / Photosensitization	Not available
Nanomaterials	Not availabe
Reference	(1) Copper Peptide MSDS, Jiangsu Highhope International Group Sunshine Chemical Corporation

INCI name	SH-OLIGOPEPTIDE-9
Restriction	None
General description	sh-Oligopeptide-9 is a single chain recombinant human peptide, produced by fermentation in E. coli. The starting gene is synthesized to be identical to the human gene which codes for Enkephalin which contains a maximum of 267 amino acids. This protein contains 11 amino acids consisting of arginine, glutamic acid, glutamine, glycine, leucine, methionine, phenylalanine, and tyrosine and may contain disulfide bonds and/or sugar. The protein consists of the proper sequence of the 20

	standard amino acids. Adverese effects are not expected after topical application.
Acute toxicity via relevant routes of exposure	Not available
Skin irritation and skin corrosivity	Not expected to cause skin irritation (0,5% dilution in water)
Mucous membrane irritation (eye irritation)	Not expected to cause eye irritation (0,5% dilution in water)
Skin Sensitization	Not available
Dermal/ percutaneous absorption	Not available
Repeated dose toxicity (normally 28- or 90-day studies)	Not available
Mutagenicity/ genotoxicity	Not available
Carcinogenicity	Not available
Reproduction toxicity	Not available
Toxicokinetics (ADME studies)	Not available
Phototoxicity / Photosensitization	Not available
Nanomaterials	
Reference	(1) Neuropeptide Complex H MSDS, BIO-FD&C Co.,Ltd., October 2018

INCI name	SH-OCTAPEPTIDE-4
Restriction	None
General description	SH-Octapeptide-4 is a recombinant human peptide produced synthetically to be identical to the protein, Enkephalin. It contains 8 amino acids consisting of glycine, histidine, leucine, lysine, phenylalanine, and tyrosine Adverese effects are not expected after topical application.
Acute toxicity via relevant routes of exposure	Not available
Skin irritation and skin corrosivity	Not expected to cause skin irritation (0,5% dilution in water)
Mucous membrane irritation (eye irritation)	Not expected to cause eye irritation (0,5% dilution in water)
Skin Sensitization	Not available
Dermal/ percutaneous absorption	Not available
Repeated dose toxicity (normally 28- or 90-day studies)	Not available
Mutagenicity/ genotoxicity	Not available
Carcinogenicity	Not available
Reproduction toxicity	Not available
Toxicokinetics (ADME studies)	Not available
Phototoxicity / Photosensitization	Not available
Nanomaterials	

Reference	(1) Neuropeptide Complex H MSDS, BIO-FD&C Co.,Ltd., October 2018

INCI name	SH-DECAPEPTIDE-7
Restriction	None
General description	sh-Decapeptide-7 is a single chain recombinant human peptide, produced synthetically to be identical to the protein, Enkephalin. It contains 10 amino acids consisting of glycine, leucine, lysine, phenylalanine, serine, threonine and tyrosine. Adverese effects are not expected after topical application.
Acute toxicity via relevant routes of exposure	Not available
Skin irritation and skin corrosivity	Not expected to cause skin irritation (0,5% dilution in water)
Mucous membrane irritation (eye irritation)	Not expected to cause eye irritation (0,5% dilution in water)
Skin Sensitization	Not available
Dermal/ percutaneous absorption	Not available
Repeated dose toxicity (normally 28- or 90-day studies)	Not available
Mutagenicity/ genotoxicity	Not available
Carcinogenicity	Not available
Reproduction toxicity	Not available
Toxicokinetics (ADME studies)	Not available
Phototoxicity / Photosensitization	Not available
Nanomaterials	
Reference	(1) Neuropeptide Complex H MSDS, BIO-FD&C Co.,Ltd., October 2018

INCI name	GLUTATHIONE
Restriction	None
General description	Glutathione is a tripeptide that contains an unusual peptide linkage between the amine group of cysteine (which is attached by normal peptide linkage to a glycine) and the carboxyl group of the glutamate side-chain. It is an antioxidant, preventing damage to important cellular components caused by reactive oxygen species such as free radicals and peroxides
Acute toxicity via relevant routes of exposure	Oral LD50 (mouse):5000 mg/kg
Skin irritation and skin corrosivity	Not expected to cause irritation
Mucous membrane irritation (eye irritation)	Not expected to cause irritation
Skin Sensitization	Not available

Dermal/ percutaneous absorption	Not available
Repeated dose toxicity (normally 28- or 90-day studies)	Not available
Mutagenicity/ genotoxicity	Not available
Carcinogenicity	Not available
Reproduction toxicity	Not available
Toxicokinetics (ADME studies)	Not available
Phototoxicity / Photosensitization	Not available
Nanomaterials	
Reference	(1) Glutathione MSDS, ScienceLab

INCI name	OLIGOPEPTIDE-1
Restriction	None
General description	Glycine, oligomer with histidine and lysine. OLI-1602 rh-EGF is the human Epidermal Growth Factor expressed on methyl yeast system produced by bio engineering technology. It can accelerate the growth for the cells of ectoderm and blood capillary, promote the growth of epidermis, and heals the wounded cuticle as well. OLI-1602 rh-EGF is an important ingredient of cosmetics for anti-wrinkle and anti-aging purposes.
Acute toxicity via relevant routes of exposure	LD50: >15g/kg, oral, rat
Skin irritation and skin corrosivity	Not available
Mucous membrane irritation (eye irritation)	Not available
Skin Sensitization	Not available
Dermal/ percutaneous absorption	Not available
Repeated dose toxicity (normally 28- or 90-day studies)	Not available
Mutagenicity/ genotoxicity	Not available
Carcinogenicity	Not available
Reproduction toxicity	Not available
Toxicokinetics (ADME studies)	Not available
Phototoxicity / Photosensitization	Not available
Nanomaterials	
Reference	(1) OLI-1602 RECOMBINED HUMAN EPIDERMAL GROWTH FACTOR (rh-EGF) MSDS, Shanghai OLI Enterprises Co., Ltd, September 2009

INCI name	SH-POLYPEPTIDE-1
Restriction	None

General description	sh-Polypeptide-1 is a single chain synthetic human peptide, produced by fermentation in E. coli. The starting gene is a synthesized copy of the human gene which codes for Basic Fibroblast Growth Factor used as such or adapted to the production host. It contains a maximum of 288 amino acids which may contain disulfide bonds and/or glycosylation. The protein consists of the proper sequence of the 20 standard amino acids. Placebo-controlled clinical tests with some sh-Polypeptide-containing formulations clearly revealed statistically significant differences in their cosmeceutical efficacies
Acute toxicity via relevant routes of exposure	Polypeptides are present in or are parts of human tissues, and thus intrinsically compatible and biodegradable, therefore this class of ingredients should be the most natural as well as safest to human skin
Skin irritation and skin corrosivity	Cultured cells were treated with serial dilution of the active ingredient (2mg/ml down to 0,03 mg/ml) for 24h + 4h. Treated cell viability was calculated and compared to untreated cells (positive control); Experimental results: No toxic effect, No irritating potential
Mucous membrane irritation (eye irritation)	Not expected to cause irritation
Skin Sensitization	Not available
Dermal/ percutaneous absorption	Sh-Polypeptides can not and in fact does not penetrate the epidermal barrier of intact human skin under normal conditions, therefore their topical application should be all the safer as these ingredients affect only the limited skin area in their direct contacts
Repeated dose toxicity (normally 28- or 90-day studies)	Not available
Mutagenicity/ genotoxicity	Not available
Carcinogenicity	Not available
Reproduction toxicity	Not available
Toxicokinetics (ADME studies)	Not available
Phototoxicity / Photosensitization	Not available
Nanomaterials	Not available
Reference	(1) Bio Placenta MSDS, LABIO. Co., Ltd. (2) Truly Natural and Safe Ingredients to Human Skin from Regeron, Regeron October 2013

INCI name	SH-POLYPEPTIDE-22
Restriction	None

General description	sh-Polypeptide-22 is a single chain recombinant human peptide, produced by fermentation in E. coli. The starting gene is synthesized to be identical to the human gene which codes for Transforming Growth Factor Beta 1. It contains a maximum of 390 amino acids which may contain disulfide bonds and/or glycosylation. The protein consists of the proper sequence of the 20 standard amino acids.
Acute toxicity via relevant routes of exposure	Polypeptides are present in or are parts of human tissues, and thus intrinsically compatible and biodegradable, therefore this class of ingredients should be the most natural as well as safest to human skin
Skin irritation and skin corrosivity	Cultured cells were treated with serial dilution of the active ingredient (2mg/ml down to 0,03 mg/ml) for 24h + 4h. Treated cell viability was calculated and compared to untreated cells (positive control); Experimental results: No toxic effect, No irritating potential
Mucous membrane irritation (eye irritation)	Not expected to cause irritation
Skin Sensitization	Not available
Dermal/ percutaneous absorption	Sh-Polypeptides can not and in fact does not penetrate the epidermal barrier of intact human skin under normal conditions, therefore their topical application should be all the safer as these ingredients affect only the limited skin area in their direct contacts
Repeated dose toxicity (normally 28- or 90-day studies)	Not available
Mutagenicity/ genotoxicity	Not available
Carcinogenicity	Not available
Reproduction toxicity	Not available
Toxicokinetics (ADME studies)	Not available
Phototoxicity / Photosensitization	Not available
Nanomaterials	Not available
Reference	(1) Bio Placenta MSDS, LABIO. Co., Ltd. (2) Truly Natural and Safe Ingredients to Human Skin from Regeron, Regeron October 2013

INCI name	SH-POLYPEPTIDE-9
Restriction	None
General description	

	It is a single chain recombinant human peptide, produced by fermentation in E. Coli. The starting gene is a synthesized copy of the human gene which codes for Vascular Endothelial Growth Factor A used as such or adapted to the production host.
Acute toxicity via relevant routes of exposure	Polypeptides are present in or are parts of human tissues, and thus intrinsically compatible and biodegradable, therefore this class of ingredients should be the most natural as well as safest to human skin
Skin irritation and skin corrosivity	Cultured cells were treated with serial dilution of the active ingredient (2mg/ml down to 0,03 mg/ml) for 24h + 4h. Treated cell viability was calculated and compared to untreated cells (positive control); Experimental results: No toxic effect, No irritating potential
Mucous membrane irritation (eye irritation)	Not expected to cause irritation
Skin Sensitization	Not available
Dermal/ percutaneous absorption	Sh-Polypeptides can not and in fact does not penetrate the epidermal barrier of intact human skin under normal conditions, therefore their topical application should be all the safer as these ingredients affect only the limited skin area in their direct contacts
Repeated dose toxicity (normally 28- or 90-day studies)	Not available
Mutagenicity/ genotoxicity	Not available
Carcinogenicity	Not available
Reproduction toxicity	Not available
Toxicokinetics (ADME studies)	Not available
Phototoxicity / Photosensitization	Not available
Nanomaterials	Not available
Reference	(1) Bio Placenta MSDS, LABIO. Co., Ltd. (2) Truly Natural and Safe Ingredients to Human Skin from Regeron, Regeron October 2015

INCI name	SH-POLYPEPTIDE-3
Restriction	None
General description	It is a single chain recombinant human peptide, produced by fermentation in E. Coli. The starting gene is a synthesized copy of the human gene which codes for Keratinocyte Growth Factor used as such or adapted to the production host
Acute toxicity via relevant routes of exposure	Polypeptides are present in or are parts of human tissues, and thus intrinsically

	compatible and biodegradable, therefore this class of ingredients should be the most natural as well as safest to human skin
Skin irritation and skin corrosivity	Cultured cells were treated with serial dilution of the active ingredient (2mg/ml down to 0,03 mg/ml) for 24h + 4h. Treated cell viability was calculated and compared to untreated cells (positive control); Experimental results: No toxic effect, No irritating potential
Mucous membrane irritation (eye irritation)	Not expected to cause irritation
Skin Sensitization	Not available
Dermal/ percutaneous absorption	Sh-Polypeptides can not and in fact does not penetrate the epidermal barrier of intact human skin under normal conditions, therefore their topical application should be all the safer as these ingredients affect only the limited skin area in their direct contacts
Repeated dose toxicity (normally 28- or 90-day studies)	Not available
Mutagenicity/ genotoxicity	Not available
Carcinogenicity	Not available
Reproduction toxicity	Not available
Toxicokinetics (ADME studies)	Not available
Phototoxicity / Photosensitization	Not available
Nanomaterials	Not available
Reference	(1) Bio Placenta MSDS, LABIO. Co., Ltd. (2) Truly Natural and Safe Ingredients to Human Skin from Regeron, Regeron October 2013

INCI name	SH-OLIGOPEPTIDE-1
Restriction	None
General description	sh-Oligopeptide-1 is a single chain recombinant human peptide, produced by fermentation in E. coli. The starting gene is synthesized to be identical to the human gene which codes for Epidermal Growth Factor. It contains a maximum of 53 amino acids which may contain disulfide bonds and/or sugar. The protein consists of the proper sequence of the standard amino acids
Acute toxicity via relevant routes of exposure	Not available
Skin irritation and skin corrosivity	Not irritating for the skin (OECD 439)
Mucous membrane irritation (eye irritation)	Not irritating for the eyes (NRU - Neutral Red Uptake test)
Skin Sensitization	Potentially not sensitizing for the skin. (Monocytes cell line THP-1)
Dermal/ percutaneous absorption	Not available

Repeated dose toxicity (normally 28- or 90-day studies)	Not available
Mutagenicity/ genotoxicity	No genotoxic. Ames test (OECD 471)
Carcinogenicity	Not available
Reproduction toxicity	Not available
Toxicokinetics (ADME studies)	Not available
Phototoxicity / Photosensitization	Not available
Nanomaterials	Not available
Reference	(1) plant-EGF MSDS, Plantaderma

INCI name	SH-OLIGOPEPTIDE-2
Restriction	None
General description	It is a single chain recombinant human peptide,produced by fermentation in E. coli. The starting gene is a synthesized copy of the human gene which codes for Insulin-Like Growth Factor used as such or adapted to the production host.
Acute toxicity via relevant routes of exposure	Not available
Skin irritation and skin corrosivity	Not irritating for the skin (OECD 439).
Mucous membrane irritation (eye irritation)	Not irritating for the eyes (NRU - Neutral Red Uptake test).
Skin Sensitization	Potentially not sensitizing for the skin. (Monocytes cell line THP-1).
Dermal/ percutaneous absorption	Not available
Repeated dose toxicity (normally 28- or 90-day studies)	Not available
Mutagenicity/ genotoxicity	No genotoxic. Ames test (OECD 471).
Carcinogenicity	Not available
Reproduction toxicity	Not available
Toxicokinetics (ADME studies)	Not available
Phototoxicity / Photosensitization	Not available
Nanomaterials	Not available
Reference	(1) Bio Placenta MSDS, LABIO. Co., Ltd. (2) Plantderma study on plant -EGF (in vitro efficacy test)

Perfume compliance to IFRA regulations:

This product is fragrance free.

9. UNDESIRABLE EFFECTS AND SERIOUS UNDESIRABLE EFFECTS

The product is available on the market, no undesirable effects have been reported till now. Rarely, reports of skin and eye irritation may be received on this type of product.

10. INFORMATION ON THE COSMETIC PRODUCT

- The product has not been tested on animals
- The products does (not) contain CMR, nanoparticles…
- Additional testing: /

PART B - COSMETIC PRODUCT SAFETY ASSESSMENT

1. ASSESSMENT CONCLUSION

The cosmetic product GLUTANEX-GLOW can be assessed as **SAFE** for normal and reasonably foreseeable use in accordance with the European Cosmetics Regulation (EC) No 1223/2009 (as amended) respectively.

2. LABELLED WARNINGS AND INSTRUCTIONS FOR USE

The following instructions for use and warnings are written on both, primary and secondary packaging:

Instructions for use written on the label	Facial serum
Precautions for use written on the label	Test 2

The labelled instructions for use and the general description of the product indicate the explicit use of the finished product as a leave on face care product intended for daily use. A reasonably foreseeable mistaken use additional to this use (not a misuse) is not recognisable

3. REASONING

a. SAFETY EVALUATION OF SUBSTANCES AND/OR MIXTURES

The margin of safety, which takes into account all systemic toxicity endpoints, has been calculated for each of the ingredient used in this cosmetic product. All ingredients (where the NOAEL value was available) have a sufficiently large MoS (>100), which is supporting the safety of the finished product. Specific exposure consideration for the targeted consumer group (adults) has been taken into account as documented in the exposure and MoS calculation.

b. SAFETY EVALUATION OF COSMETIC PRODUCT

Stability data

The stability data (microbiological and physical-chemical stability) of the formula after storage meet the previously specified characteristics. They confirm a sufficient stability of the formula. The shelf life for the final product is 36 months. Based on the above mentioned the product is rated as safe.

Packaging

The package consists of a 5ml glass vial with rubber cap. The packaging of the product is made to protect the product during shelf life and use and to enable the safe use of the product. No interaction with packaging material is expected as the packaging compatibility with the formulation was confirmed during its stability test. Based on that the packaging is rated to be suitable and safe for this specific product type. This package does not contain hazardous materials that require special markings or labelling on the shippers.

Normal and reasonably foreseeable use

A reasonably foreseeable mistaken use (not a misuse), is not recognizable.

Undesirable effects and serious undesirable effects

From the market launch until today the complaint statistics as documented in the Consumer Response System (CRS) of the manufacturer of this product show no remarkable consumer complaints regarding undesirable effects or serious undesirable effects in general.

Information on the cosmetic product

The product is a leave on face care product intended to be sued by adults on daily basis.

The packaging of cosmetic product should include the following information in indelible, easily legible and visible lettering:

- Brand name
- Name of the product
- Function of the cosmetic product (unless it is clear from its presentation)
- Ingredients list (ingredients present **in more than 1%** in the end product should follow in the same order as here): **AQUA, DEFINED CELL CULTURE MEDIA 7, HYDROLYZED COLLAGEN, 1,2-HEXANEDIOL,** GLYCERIN, GLUCOSE, ADENOSINE, SODIUM CHLORIDE, SODIUM HYALURONATE, SODIUM DNA, ACETYL HEXAPEPTIDE-8, OCTAPEPTIDE-7, COPPER TRIPEPTIDE-1, SH-OLIGOPEPTIDE-9, SH-OCTAPEPTIDE-4, SH-DECAPEPTIDE-7, GLUTATHIONE, OLIGOPEPTIDE-1, SH-POLYPEPTIDE-1, SH-POLYPEPTIDE-22, SH-POLYPEPTIDE-9, SH-POLYPEPTIDE-3, SH-OLIGOPEPTIDE-1, SH-OLIGOPEPTIDE-2
- Particular precautions for use: /
- Instructions for use: Facial serum.
- Date of minimum durability (for products with a minimum durability ≤ 30 months) or PAO (for products with a minimum durability > 30 months)
- Nominal quantity (except for packaging containing less than 5 grams or 5 millilitres, free samples and single-application packs)

- Batch number or the reference for identifying the cosmetic product
- Responsible person name and address
- Manufacturer name and address
- Products' country of origin

SUMMARY

The safety assessment is based on the chemical specification and toxicological profile of the ingredients as supplied at the time of assessment and an assessment of the final cosmetic product.

All statements in this safety assessment were elaborated on the recent level of knowledge. Every change in the formulation or changes and/or additional information of relevant data respectively will require an immediate re-evaluation of this safety assessment.

Concerning the skin tolerance, the final product is expected to be well tolerated and to have a good cosmetic acceptability.

Safety assessor: Tanja Židan, MPharm

Signature:

We confirm that the product is safe in the stated application when used under normal and reasonably foreseeable use. Its composition complies with EC Regulation 1223/2009 and all its annexes.