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MATRIXYL® synthe'6



English

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Product Information File

MATRIXYL® synthe'6

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RECOMMENDATIONS:

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1. PRODUCT INFORMATION

Description

MATRIXYL® synthe'6 evens out skin relief and smoothes wrinkles from the inside by rebuilding the skin where it is needed, particularly on the forehead and crow's feet.



Palmitoyl-Lysyl-Dioxymethionyl-Lysine, a matrikine-mimetic peptide, which stimulates the synthesis of matrix molecules and helps fill wrinkles.

INCI Name

Glycerin (and) Water (Aqua) (and) Hydroxypropyl Cyclodextrin (and) Palmitoyl Tripeptide-38

Proven cosmetic activity

In vitro

Study on the synthesis of matrix molecules

Study on boosting the effect of luminotherapy on UV-aged skins

Study on the synthesis of molecules at the dermal-epidermal junction

In vivo

Anti-wrinkle effect on the forehead determined by fringe projection (FOITS)

Anti-wrinkle effect on crow's feet determined by fringe projection or imprinting

Formulation guidelines

Appearance: colourless to pale yellow clear to slightly opalescent liquid

Solubility: water soluble

Recommended use level: 2%

Storage

Conditions: 15-25°C.

Re-evaluation date: 24 months from the date of manufacturing, if the storage conditions are respected.

Specifications

See selling specifications or contact your local sales representative.

Patents and publications

WO 2005/048968; WO 2012/164488; FR 2 975 904; EP 1 686 957; EP 2 714 001; US 6,974,799; JP 4256389; CN 1893911; KR 101045658.

For further information, please contact your local sales representative or refer to our technical dossier available upon request.

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2. MANUFACTURER / SUPPLIER INFORMATION

Supplier and/or Manufacturer

SEDERMA SAS
29 rue du Chemin Vert
78612 Le Perray en Yvelines cedex
France

Certifications

Environmental management systems	ISO 14001:2015
Quality management systems	ISO 9001:2015
Occupational health and safety management systems	OHSAS 18001:2007
Good Manufacturing Practices	EFfCI
Authorised Economic Operator (AEO)	Yes

Good Manufacturing Practices

SEDERMA realises their activities according to Good Manufacturing Practices for Cosmetic Ingredients and makes sure they are correctly implemented thanks to external audits.

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3. CORPORATE SOCIAL RESPONSIBILITY AND SUSTAINABILITY

Code of conduct for responsible relationships and purchasing

Within the framework of its Corporate Social Responsibility (CSR), the CRODA Group implements corporate governance that applies to its organisation and to its purchasing and supply chains (CRODA CSR report and code of Ethics).

As an affiliate of the CRODA Group, Sederma is naturally engaged in the implementation of such principles that reflect the corporate culture and values.

Our "Code of conduct for responsible relationships and purchasing" is available upon request.

Sustainability

According to its policy, SEDERMA is in favor of sustainable development based on the following objectives:

- decrease of energy and water consumption,
- respect of protected species (according to Washington's convention),
- respect of Convention on Biological Diversity and Nagoya Protocol,
- promotion of recycling of waste,
- use of cell plant culture to minimize the impact on the environment,
- use of renewable and sustainable raw materials whenever possible.

SEDERMA's ambition is to raise awareness about social and environmental responsibility of every actor along the value chain and to favor shared commitments to progress. In particular:

- to pursue traceability of raw materials, their processing, and of all those involved in these domains,
- to encourage sustainable partnerships between all those involved in the supply chain.

SEDERMA also signed the "Cosmetic Valley Charter for Sustainability" (please visit our website **www.sederma.fr**).

SEDERMA, as part of CRODA International Plc, is a member of the RSPO: Roundtable on Sustainable Palm Oil (**www.rspo.org/en/member/82/croda-international-plc**) and is certified according to the RSPO Supply Chain Certification Standard (Certificate available on request).

SEDERMA fully supports the objectives of the Convention on Biological Diversity and of the Nagoya Protocol, the international instrument adopted on 29 October 2010 by the Parties to the Convention.

In the European Union, compliance measures for users of genetic resources are laid down in the EU CM-ABS Regulation. Individual Member States may introduce legal or regulatory requirements governing the access to genetic resources and associated traditional knowledge on their territories, as well as the sharing of benefits arising from their utilisation in accordance to the Nagoya Protocol.

SEDERMA has naturally followed the elaboration of the different texts at European level and got involved in the discussions through its active participation in professional syndicate ASPA-INGRECOS as well as in several working groups at the EFfCI.

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SEDERMA has mapped and evaluated its active ingredients and is able to demonstrate their compliance with the Nagoya Protocol. In addition, the "Nagoya requirements" have been fully integrated in our R&D strategy and are already deployed for our future developments.

4. COMPOSITION AND MANUFACTURING PROCESS

Composition

INCI Name (PcPc)	CAS Nr	%	Origin*	Function
Glycerin	56-81-5	qsp 100	V	Solvent
Water	7732-18-5	≈ 25		Solvent
Hydroxypropyl Cyclodextrin	128446-35-5	≈1	S,V	Viscosity agent
Palmitoyl Tripeptide-38	1101175-36-3	≈ 0.025	S,V	Skin conditioning agent
Manufacturing additive: /				
Preservative: /				

* V: vegetable, S: synthetic, B: biotechnology, Mi: mineral

Country of origin

France

Simplified manufacturing process

MATRIXYL® synthe'6 is a mixture of Glycerin, Water, Hydroxypropyl Cyclodextrin and Palmitoyl Tripeptide-38.

Palmitoyl Tripeptide-38 (Pal-KMO2K-OH, 2HCl) is obtained by chemical synthesis: coupling of amino acids followed by a last coupling with palmitic acid. The last step is the substitution of acid function of lysine by Hydrochloride. This peptide is solubilised in a mixture of Glycerin, Water and Hydroxypropyl Cyclodextrin.

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5. REGULATORY INFORMATION

Note: This information is based on the knowledge of our raw materials and of the manufacturing process of the product. It is not part of the product's specifications and thus is likely to change.

Biodiversity

CITES:

MATRIXYL® synthe'6 does not contain ingredient obtained from endangered species listed on Annexes I, II and III of the Convention on International Trade in Endangered Species of wild fauna and flora (CITES).

IUCN:

The plant raw materials used are not derived from threatened species according to the International Union or Conservation of Nature (IUCN) red list.

Nagoya protocol:

MATRIXYL® synthe'6 is out of the scope of the Nagoya Protocol. The product was developed without utilisation of genetic resource, at the meaning of the Article 2 of the Nagoya Protocol.

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Chemical Inventory Status / REACH

		Chemical Inventory							REACH		
INCI Name (PcPc)	**CAS Nr**	**Europe** EINECS Nr	**US** TSCA	**Canada** DSL/NDSL /ICL	**China** IECSC	**Korea** KECI/K-REACH	**Japan** ENCS /ISHL	**Australia** AICS	**Exemption if any**	**Pre-registered**	**Registered**
Glycerin	56-81-5	200-289-5	X	DSL	X	X	X	X	Annex V.9		
Water	7732-18-5	231-791-2	X	DSL	X	X	X	X	Annex IV		
Hydroxypropyl Cyclodextrin	128446-35-5	ELINCS Nr: 420-920-1	X	DSL	X	X	-	X		Yes	01-0000016748-58
Palmitoyl Tripeptide-38	1101175-36-3	n/a	X	-	*	X	-	-	< 1t/year		

*X: listed or exempt -: unknown *: please contact your local sales representative*

Canada:

- Non listed DSL substances can be imported in quantities not exceeding 100kg/year/importer,
- NDSL substances can be imported in quantities not exceeding 1000kg/year/import,
- In-commerce list (ICL) substances can be used in cosmetics as regulated by the F&D Act,
- "Naturally occurring" substances according to the Health Canada definition are exempt of New Substances Regulation.

Australia:

- Non-hazardous substances introduced at 1% or less in cosmetic are exempt from AICS listing (annual report to NICNAS before or on 28 September each year),
- No unreasonable risk substances imported at not more than 10kg in a 12-month period are exempt from AICS listing (annual report to NICNAS before or on 28 September each year),
- No unreasonable risk substances imported at not more than 100kg in a 12-month period are exempt from AICS listing with notification (annual report to NICNAS before or on 28 September each year),
- "Naturally occurring" according to the NICNAS definition are exempt of AICS listing.

Cosmetic use covered according to the Cosmetics Europe (formerly COLIPA) use mapping.

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Cosmetic Status

Note: Users are responsible for determining the suitability of this product for their own particular purpose and claims.

Countries (Non-exhaustive list)	Cosmetic Regulatory Compliance
European Union Regulation (EC) No1223/2009 and its amendments	Yes
United States of America FD&C Act - 21 CFR 700 to 740	Yes
Canada F&D Act - Cosmetic Regulations c. 869 and Cosmetic Ingredient Hotlist	Yes (See chemical status above)
Australia Cosmetics Standard 2007	Yes (See chemical status above)
Japan Japanese Standards for Cosmetics	Yes
South Korea Cosmetics Act and Safety Standards for Cosmetics	Yes
MERCOSUR GMC Resolutions for personal hygiene products, cosmetics & perfumes	Yes
ASEAN ASEAN Cosmetics Directive	Yes
Taiwan Statute for Control of Cosmetic Hygiene	Yes
China (PRC) Safety and Technical Standards for cosmetics 2015 and IECIC 2015	No (Palmitoyl Tripeptide-38 not listed IECIC 2015)

ASEAN: Indonesia, Malaysia, the Philippines, Singapore, Thailand, Brunei, Burma (Myanmar), Cambodia, Laos and Vietnam

MERCOSUR: Argentina, Brazil, Paraguay, Uruguay and Venezuela

Nanomaterial

MATRIXYL® synthe'6 is not a nanomaterial and does not contain nanomaterial, according to the Cosmetic Regulation (EC) No 1223/2009 definition of a nanomaterial:

'Nanomaterial' means an insoluble or biopersistent and intentionally manufactured material with one or more external dimensions, or an internal structure, on the scale from 1 to 100 nm.

GMO

MATRIXYL® synthe'6 does not contain and is not produced from genetically modified organisms (GMO).

BSE / TSE

None of the ingredients used for the production of MATRIXYL® synthe'6 are of bovine, ovine, or caprine origin. Therefore, Bovine Spongiform Encephalopathy (BSE) / Transmitting Spongiform Encephalopathy (TSE) risk, as defined in the European Commission Decision 97/534/EC and EMEA/410/10, does not concern this product.

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6. IMPURITIES AND OTHER RESIDUES

Note: This information is based on the knowledge of our raw materials and of the manufacturing process of the product. Analyses are not part of the product's specifications and are thus not performed in routine.

Fragrance allergens according to the Annexes II and III of the Regulation (EC) No 1223/2009 and its amendments

Raw vegetables, raw vegetable derivatives and end products used as raw material in the manufacture of SEDERMA's products are monitored for the presence of fragrance allergens according to a risk assessment approach based on materials, processes, analytical availabilities and relevance.

MATRIXYL® synthe'6 contains ingredients obtained from vegetable derivatives but, according to our knowledge of our raw materials and of manufacturing process of the product, the presence of fragrance allergens residues is not expected. The product itself does not require a fragrance allergens residues monitoring.

Pesticides

Raw vegetables, raw vegetable derivatives and end products used as raw material in the manufacture of SEDERMA's products are monitored for the presence of pesticides according to a risk assessment approach based on materials, processes, analytical availabilities and relevance.

MATRIXYL® synthe'6 contains ingredients obtained from vegetable derivatives but, according to our knowledge of our raw materials and of manufacturing process of the product, the presence of pesticides residues is not expected. The product itself does not require a pesticides residues monitoring.

Heavy metals

Elements		Results (mg/kg) ICP-MS
Arsenic	(As)	<1.5 (1)
Cadmium	(Cd)	<0.5 (1)
Lead	(Pb)	<1.0 (1)
Mercury	(Hg)	<1.5 (1)
Chromium	(Cr)	<2.5 (1)
Antimony	(Sb)	<2.5 (1)
Molybdenum	(Mo)	<2.5 (1)
Tin	(Sn)	<2.5 (1)
Nickel	(Ni)	<2.5 (1)
Cobalt	(Co)	<2.5 (1)
Barium	(Ba)	<2.5 (1)

(1) *Internal limits of quantification*

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CMR

MATRIXYL® synthe'6 does not contain any ingredients classified CMR category 1A, 1B or 2 (Carcinogen, Mutagen, toxic for the Reproduction) according to the Regulation (EC) No 1272/2008 and adaptations. Nevertheless, potential traces of these substances are technically unavoidable due to the presence of Polysorbate 20.

MATRIXYL® synthe'6 fulfils the requirements of the article 15 of the Cosmetics Regulation (EC) No 1223/2009 and its amendments.

Residual Solvents

MATRIXYL® synthe'6 complies with ICH guideline for residual solvents CPMP/ICH/283/95 and Chapter <467> of USP/NF: Residual Solvents Limits.

VOC

MATRIXYL® synthe'6 does not contain one or more intentionally added Volatile Organic Compounds (VOC) in compliance with the Swiss ordinance and the definition of California. Nevertheless, potential traces of Ethyl Acetate and Cyclohexane are technically unavoidable due to the presence of Carbomer.

SVHC

No Substances of Very High Concern (SVHC) listed in annex 14 of the Regulation (EC) 1907/2006, or listed in candidate list published by ECHA of which we regularly follow the updates, are intentionally added in the manufacturing process of MATRIXYL® synthe'6. Therefore, MATRIXYL® synthe'6 would not be expected to contain these substances.

Proposition 65

The ingredients constituting MATRIXYL® synthe'6 are not known to the State of California to cause cancer or reproductive toxicity as listed under Proposition 65 State Drinking Water and Toxic Enforcement Act of which we regularly follow the updates.

Glycerin

Glycerin used for the production of MATRIXYL® synthe'6 meets specifications of accepted pharmacopoeias with respect to Diethylene Glycol impurity (DEG content NMT 0.1%).

Gluten

MATRIXYL® synthe'6 does contain raw materials derived from wheat, barley and/or rye.

Formaldehyde

Formaldehyde and Formaldehyde releasers (as described by the SCCNFP opinions 586/02 and 587/02) are not intentionally added in the manufacturing process, and so are not expected in MATRIXYL® synthe'6.

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Phthalates

The following Phthalates are not intentionally added in the manufacturing process of MATRIXYL® synthe'6. Therefore, MATRIXYL® synthe'6 would not be expected to contain these substances:

Substances		CAS Nr
Dibutyl Phthalate	(DBP)	84-74-2
Diethylhexyl Phthalate	(DEHP)	117-81-7
Benzyl Butyl Phthalate	(BBP)	85-68-7
Di-n-pentyl Phthalate	(DnPP)	131-18-0
Dimethylglycol Phthalate	(DMEP)	117-82-8
Diisopentyl Phthalate	(DIPP)	605-50-5
Diisobutyl Phthalate	(DIBP)	84-69-5
n-Pentyl-isopentyl Phthalate	(PIPP)	776297-69-9
Dihexyl Phthalate	(DHP)	84-75-3

Glycol Ethers

The following Glycol Ethers are not intentionally added in the manufacturing process of MATRIXYL® synthe'6. Therefore, MATRIXYL® synthe'6 would not be expected to contain these substances:

Substances		CAS Nr
2-Methoxyethanol / Ethylene Glycol Monomethyl Ether	(EGME)	109-86-4
2-Methoxyethyl Acetate / Methylglycol Acetate	(EGMEA)	110-49-6
2-Ethoxyethanol	(EGEE)	110-80-5
2-Ethoxyethyl Acetate	(EGEEA)	111-15-9
1,2-Dimethoxyethane / Ethylene Glycol Dimethyl Ether	(EGDME)	110-71-4
Oxybis(2-Methoxyethyl) / Dimethoxydiglycol	(DEGDME)	111-96-6
1,2-bis(2-Methoxyethoxy)ethane / Triethylene Glycol Dimethyl Ether	(TEGDME)	112-49-2
2-Butoxyethanol	(EGBE)	111-76-2
2-(2-Butoxyethoxy)ethanol	(DEGBE)	112-34-5
2-(2-Ethoxyethoxy)ethanol	(DEGEE)	111-90-0

Packaging

The packaging of MATRIXYL® synthe'6 is in compliance with Regulation (EC) No 1935/2004 of the European parliament and of the Council of October 27th, 2004 on materials and articles intended to come into contact with food.

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7. MICROBIOLOGICAL INFORMATION

Specifications

Total aerobic microbial count <100 cfu/g
Total combined yeasts / moulds count <10 cfu/g

Challenge Test

Strains	D7 (cfu/g)	D14 (cfu/g)	D28 (cfu/g)
Bacteria	<10	<10	<10
Yeast/mould	<10	<10	<10
Aspergillus niger	7000	1500	<10

Internal test method

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8. TOXICOLOGICAL INFORMATION

Animal testing

MATRIXYL® synthe'6 has not been tested on animals to fulfil the requirements of the European Cosmetics Regulation (EC) No 1223/2009 and its amendments, by or on behalf of SEDERMA.

Since 1998 and according to CRODA's policy, SEDERMA has decided not to perform any animal testing on its products (except for other specific regulatory purposes).

Toxicological tests results

Local toxicity	
Cutaneous primary tolerance (Patch-test) October 12th, 2010 Dilution to 40%	Very good skin compatibility
Ocular irritation (HETCAM) November 4th, 2010 Dilution to 10%	Practically non irritant
Ocular irritation (Neutral Red Release Method) October 18th, 2010	negligible cytotoxicity
Allergenicity	
Sensitization (HRIPT) (On formula containing the same concentration in Palmitoyl Tripeptide-38 / noHydroxypropyl Cyclodextrin) November 26th, 2008 Dilution to 40%	No allergic reaction
Systemic toxicity	
Mutagenicity (Ames test) (on solution of 500ppm of Palmitoyl Tripeptide-38 in ethanol) November 3rd, 2008	Non mutagenic
Phototoxicity	
According to OECD guideline 432: "it has been suggested that if the molar extinction/absorption coefficient is less than 10 litre/mol/cm the chemical is unlikely to be photoreactive. Such chemical may not need to be tested in the 3T3 NRU phototoxicity test or any other biological test for adverse photochemical effects." As the X Extract does not absorb in UV wavelength (between 290 and 400 nm), we did not carry out any phototoxicity test.	

Complete reports and Expert's certificates are available upon request.

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NOAEL

INCI Name (PcPc)	Dermal Absorption (%)	NOAEL[(a)] / NOEL[(b)] (mg/kg b.w./day)	Read across	Expert panel conclusion
Glycerin	50 [1]	8000 (b) [2]	No	Safe for use [3]
Water	n/a	n/a	No	-
Hydroxypropyl Cyclodextrin	50 [1]	500 (b) [4]	No	Safe for use [5]
Palmitoyl Tripeptide-38	50 [1]	[6]	No	-

[1] SCCS, 2015. SCCS notes of guidance for the testing of cosmetic ingredients and their safety evaluation, 9th revision, 29 September 2015, SCCS/1564/15, revision of 25 April 2016.

[2] EFSA, 2010. Panel on Contaminants in the Food Chain (CONTAM): Scientific Opinion on the abiotic risks for public and animal health of glycerin as co-product from the biodiesel production from Category 1 animal by-products (ABP) and vegetable oils. *EFSA Journal,* 8(12): 1934.

[3] CIR, 2014 Safety Assessment of Glycerin as Used in Cosmetics.

[4] Gould S., Scott R. C., (2005). "2-Hydroxypropyl-b-cyclodextrin (HP-b-CD): A toxicology review". Food Chem Toxicol., 43(10): pp. 1451-1459.

[5] CIR, 2015 Safety Assessment of Polysaccharide Gums as Used in Cosmetics.

[6] To the best of our current knowledge, NOAEL data can only be determined with animal experimentations. Since 1998 and according to CRODA's policy, SEDERMA has decided not to perform any animal testing on its products (except for other specific regulatory purposes).
Furthermore, Palmitoyl Tripeptide-38 has been worldwide used in SEDERMA product up to 0.05% since 2009 without any complaint concerning its innocuousness.

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9. VOLUNTARY COMMITMENT

Ecocert/Cosmos

Not applicable

Palm/palm oil derivatives

MATRIXYL® synthe'6 contains ingredient which is obtained from palm.

We confirm that the palm derivative used to produce the ingredient Palmitoyl Tripeptide-38 is certified CSPO Mass Balance.

Halal

MATRIXYL® synthe'6 is halal certified (Certificate available on request).

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Date	Rev #	Description
16 October 2018	0	Creation

Signed by:
Brice LECLERC
Regulatory Affairs Manager



For further information, don't hesitate to contact your local sales representative or to visit our website: **www.sederma.fr**

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Cosmetic
ACTIVE INGREDIENTS

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