化粧品產品資訊檔案(範例)
<嫩膚沐浴乳>

＜PIF **無特定之格式**，本範例**僅提供參考用**＞

中華民國 112 年 10 月

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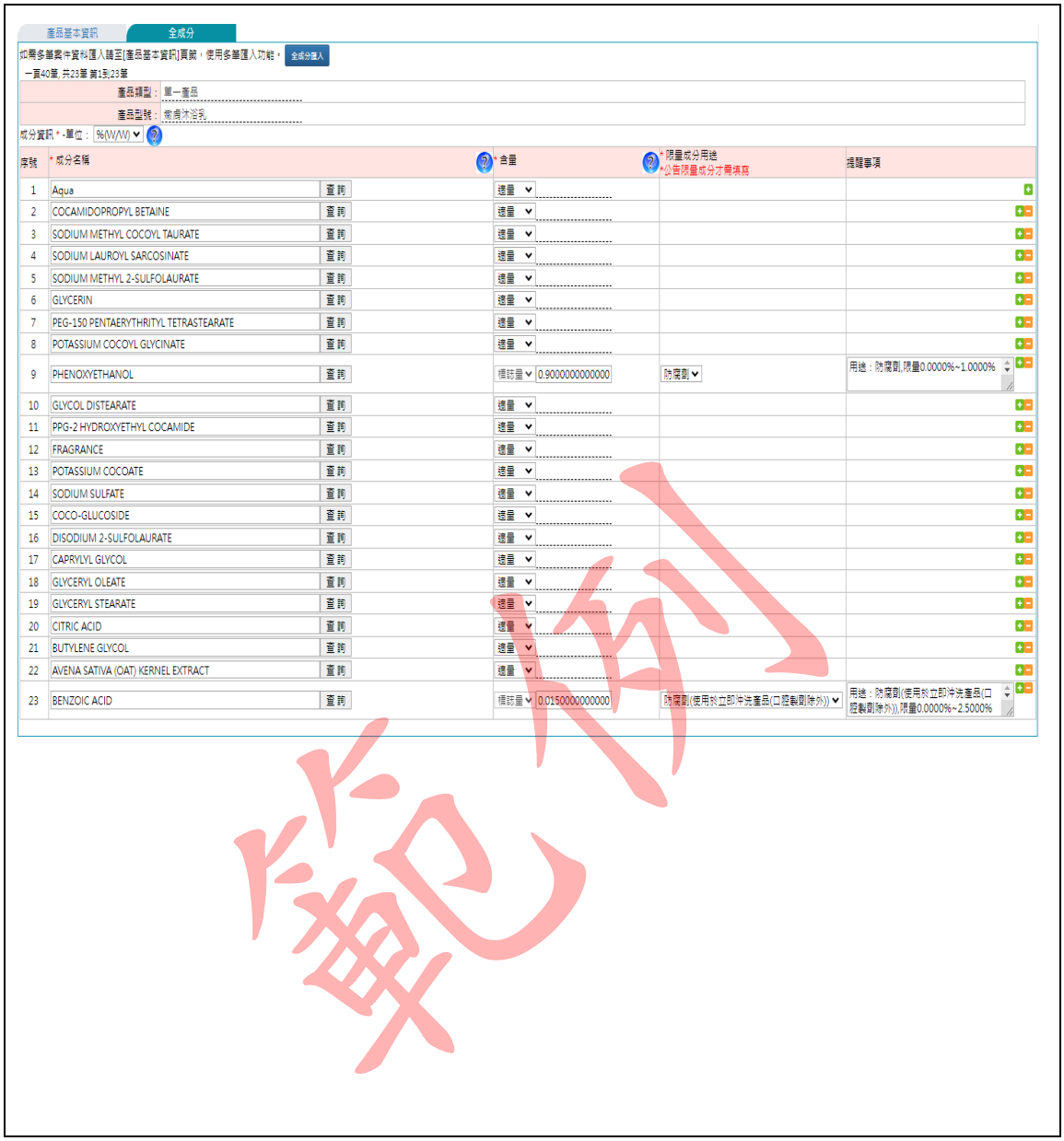
I. 產品敘述

(1) 產品基本資料

項目	內容描述
產品名稱	嫩膚沐浴乳
產品類別	沐浴油、沐浴乳、沐浴凝膠、沐浴泡沫、沐浴粉
產品劑型	乳劑
用途	清潔身體
製造作業場所資訊	製造廠名稱：XX 化粧品股份有限公司 廠址：〇〇市〇〇區〇〇路〇〇號 國別：台灣
包裝作業場所資訊	包裝廠名稱：YY 股份有限公司 廠址：〇〇市〇〇區〇〇路〇〇號 國別：台灣
產品製造業者資訊	製造業者：AJP 化粧品股份有限公司 地址：〇〇市〇〇路〇〇段 XX 號 公司負責人：李〇基 聯絡電話：02-2xxx-xxxx 統一編號：0123XXXX

(2) 完成產品登錄之證明文件

登錄號碼：0123XXXX TEST 1000000010



產品基本資訊 | 全成分

如需多筆資料匯入請至[產品基本資訊]頁籤，使用多筆匯入功能， 全成分匯入

一頁40筆, 共23筆 第1到23筆

產品類型： 單一產品

產品型號： 療癒沐浴乳

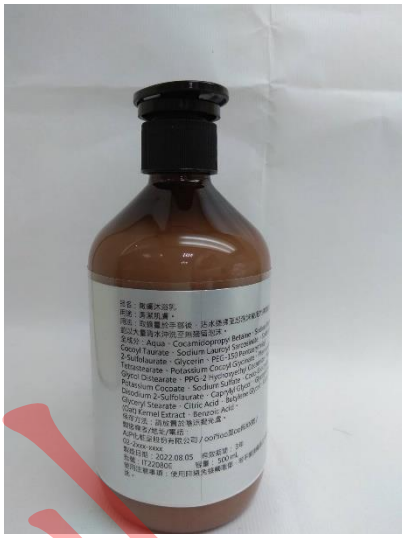
成分資訊 * -單位： %(W/W)

序號	* 成分名稱	* 含量	* 限量成分用途 *公告限量成分才需填寫	補充事項
1	Aqua 查詢	適量		
2	COCAMIDOPROPYL BETAINE 查詢	適量		
3	SODIUM METHYL COCOYL TAURATE 查詢	適量		
4	SODIUM LAUROYL SARCOSINATE 查詢	適量		
5	SODIUM METHYL 2-SULFOLAURATE 查詢	適量		
6	GLYCERIN 查詢	適量		
7	PEG-150 PENTAERYTHRITYL TETRASTEARATE 查詢	適量		
8	POTASSIUM COCOYL GLYCINATE 查詢	適量		
9	PHENOXYETHANOL 查詢	標註量 0.9000000000000	防腐劑	用途：防腐劑,限量0.0000%~1.0000%
10	GLYCOL DISTEARATE 查詢	適量		
11	PPG-2 HYDROXYETHYL COCAMIDE 查詢	適量		
12	FRAGRANCE 查詢	適量		
13	POTASSIUM COCOATE 查詢	適量		
14	SODIUM SULFATE 查詢	適量		
15	COCO-GLUCOSIDE 查詢	適量		
16	DISODIUM 2-SULFOLAURATE 查詢	適量		
17	CAPRYLYL GLYCOL 查詢	適量		
18	GLYCERYL OLEATE 查詢	適量		
19	GLYCERYL STEARATE 查詢	適量		
20	CITRIC ACID 查詢	適量		
21	BUTYLENE GLYCOL 查詢	適量		
22	AVENA SATIVA (OAT) KERNEL EXTRACT 查詢	適量		
23	BENZOIC ACID 查詢	標註量 0.0150000000000	防腐劑(使用於立即沖洗產品(口腔製劑除外))	用途：防腐劑(使用於立即沖洗產品(口腔製劑除外)),限量0.0000%~2.5000%

(3) 全成分名稱及其各別含量

INCI Name	Cas No.	w/w%	功能
Aqua	7732-18-5	73.255	溶劑
Cocamidopropyl Betaine	61789-40-0	5.55	界面活性劑
Sodium Methyl Cocoyl Taurate	12765-39-8	5.00	界面活性劑
Sodium Lauroyl Sarcosinate	137-16-6	4.50	界面活性劑
Sodium Methyl 2-Sulfolaurate	4016-21-1	3.04	起泡劑
Glycerin	56-81-5	2.12	保濕劑
PEG-150 Pentaerythrityl Tetrastearate	130249-48-8	1.30	界面活性劑
Potassium Cocoyl Glycinate	301341-58-2	1.05	界面活性劑
Phenoxyethanol	122-99-6	0.90	防腐劑
Glycol Distearate	627-83-8	0.66	肌膚調理劑
PPG-2 Hydroxyethyl Cocamide	201363-52-2	0.52	界面活性劑
Fragrance	-	0.50	香精
Potassium Cocoate	61789-30-8	0.45	界面活性劑
Sodium Sulfate	7757-82-6	0.32	黏度調節劑
Coco-Glucoside	110615-47-9	0.30	起泡劑
Disodium 2-Sulfolaurate	38841-48-4	0.16	界面活性劑
Caprylyl Glycol	122-99-6	0.10	保濕劑
Glyceryl Oleate	25496-72-4	0.09	界面活性劑
Glyceryl Stearate	31566-31-1	0.09	肌膚調理劑
Citric Acid	77-92-9	0.03	緩衝劑
Butylene Glycol	107-88-0	0.03	肌膚調理劑
Avena Sativa (Oat) Kernel Extract	-	0.02	肌膚調理劑
Benzoic Acid	65-85-0	0.015	防腐劑
Total		100	

(4) 產品標籤、仿單、外包裝或容器

項目	資料
包裝/容器 (正反面)	 
標籤/仿單	品名：嫩膚沐浴乳 用途：清潔肌膚。 用法：取適量於手部後，沾水搓揉至起泡沫後用於身體皮膚清潔，並以大量清水沖洗至無殘留泡沫。 全成分：Aqua、Cocamidopropyl Betaine、Sodium Methyl Cocoyl Taurate、Sodium Lauroyl Sarcosinate、Sodium Methyl 2-Sulfolaurate、Glycerin、PEG-150 Pentaerythrityl Tetrastearate、Potassium Cocoyl Glycinate、Phenoxyethanol、Glycol Distearate、PPG-2 Hydroxyethyl Cocamide、Fragrance、Potassium Cocoate、Sodium Sulfate、Coco-Glucoside、Disodium 2-Sulfolaurate、Caprylyl Glycol、Glyceryl Oleate、Glyceryl Stearate、Citric Acid、Butylene Glycol、Avena Sativa (Oat) Kernel Extract、Benzoic Acid。 保存方法：請放置於陰涼避光處。 製造業者/地址/電話： AJP化粧品股份有限公司 / oo市oo路oo段XX號 / 02-2xxx-xxxx 製造日期：2022.08.05　有效期間：3年 批號：IT22080E　　容量：500 mL 使用注意事項：使用時避免接觸眼部，若不慎接觸請以大量清水沖洗。

(5) 製造場所符合化粧品優良製造準則之證明文件或聲明書

衛 生 福 利 部

化 粧 品 優 良 製 造 證 明 書

證號：(C)GMPOOOO-OOO

製造廠（場所）名稱：

製造廠（場所）地址：

核定劑型及作業項目：

本證明書依據化粧品衛生安全管理法第 29 條規定發給。
本部係依據「化粧品優良製造準則」之規定進行查核，該優良製造準則之要求符合國際標準化組織(ISO)發布之 ISO 22716：2007。

衛生福利部

發 證 日 期：　　年　　月　　日
有 效 日 期：　　年　　月　　日

XXXX(流水號)

符合化粧品優良製造準則聲明書

Declaration of Conformity

本業者/本廠生產之化粧品符合中華民國之化粧品優良製造準則，產品資料如下：

I hereby declare that the products described below manufactured in conformity with Cosmetic Good Manufacturing Practice

一、製造廠名稱：

Manufacturer's Name

二、製造廠地址：

Manufacturer's Address

三、製造劑型：

Product forms

四、作業項目：

The process of operations

以上聲明書所保證之內容，如有造假不實或違背相關法規等情事，本業者/本人願自行負擔法律上一切責任。

Where violations of this declaration occur, I agree to take the legal responsibilities.

立聲明書人：　　(Signature)

Applicant

申請廠商蓋公司章

負責人/代表人：　　(Signature)

Person in charge

負責人或代表人章

統一編號或身分證字號：

Company Tax ID No. / ID Number

地址：

Address:

中 華 民 國　　年　　月　　日

Date　　year　　month　　day

(6) 製造方法、流程

序號	Trade Name (Product Name)	INCI Name	Cas No.	w/w%	功能
1	-	Aqua	7732-18-5	42.7	溶劑
2	SP CRODASINIC LS30 MIT MBAL-LQ-(RB)	Aqua(70%)	7732-18-5	15.0	界面活性劑
		Sodium Lauroyl Sarcosinate (30%)	137-16-6		
3	Dehyton® KE T IS	Aqua (63%)	7732-18-5	15.0	界面活性劑
		Cocamidopropyl Betaine (37%)	4016-21-1		
4.	Alpha-Step® PC-48	Aqua (56%)	7732-18-5	8.0	起泡劑
		Sodium Methyl 2-Sulfolaurate (38%)	4016-21-1		
		Sodium Sulfate (4%)	7757-82-6		
		Disodium 2-Sulfolaurate (2%)	38841-48-4		
5.	Amilite GCK-12H	Aqua (70%)	7732-18-5	5.0	界面活性劑
		Potassium Cocoyl Glycinate (21%)	301341-58-2		
		Potassium Cocoate (9%)	61789-30-8		
6.	HOSTAPON®CT PASTE	Sodium Methyl Cocoyl Taurate	12765-39-8	5.0	界面活性劑
7.	Lamesoft® TM Benz	Aqua (60.5%)	7732-18-5	3.0	珠光調理劑
		Glycol Distearate (22%)	627-83-8		
		Coco-Glucoside (10%)	110615-47-9		
		Glyceryl Oleate (3%)	25496-72-4		
		Glyceryl Stearate (3%)	31566-31-1		
		Citric Acid (1%)	77-92-9		
		Benzoic Acid (0.5%)	65-85-0		
8	Versathix™	PEG-150 Pentaerythrityl Tetrastearate (50%)	130249-48-8	2.6	流變調節劑
		Aqua (30%)	7732-18-5		

		PPG-2 Hydroxyethyl Cocamide (20%)	201363-52-2		
9.	-	Glycerin	56-81-5	2.0	保濕劑
10.	VERSTATIL PC	Phenoxyethanol (90%)	122-99-6	1.0	防腐劑
		Caprylyl Glycol (10%)	1117-86-8		
11.	-	Fragrance	-	0.5	香精
12.	Phytexcell OAT	Glycerin (60%)	56-81-5	0.2	肌膚調理劑
		Butylene Glycol (15%)	107-88-0		
		Aqua (15%)	7732-18-5		
		Avena Sativa (Oat) Kernel Extract (10%)	-		
Total				100.0	

製程簡述：

1.依序將編號 1、2、3、4、5、6、8、9 投入攪拌槽，升溫至 80℃攪拌 15 分鐘確認完全溶解後，冷卻至 40℃。

2.依序將編號 7、11 投入攪拌槽攪拌 5 分鐘。

3.將編號 12 投入攪拌槽攪拌 5 分鐘。

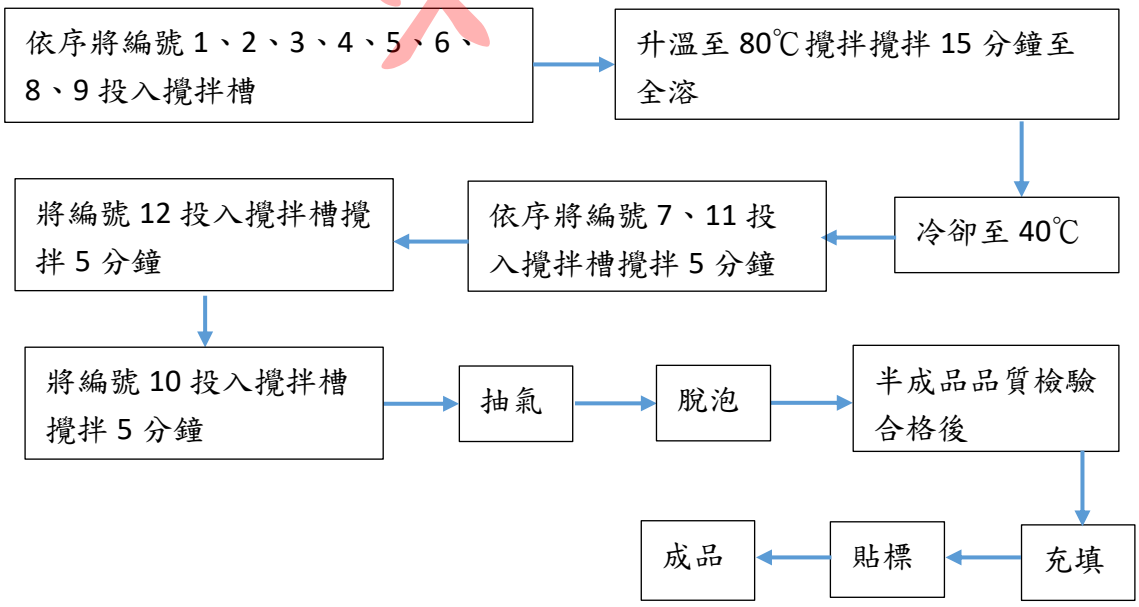
4.將編號 10 投入攪拌槽攪拌 5 分鐘。

5.抽氣。

6.脫泡。

7.完成半成品，品質檢驗合格後進行後續充填及貼標。

製程流程圖：



(7) 使用方法、部位、用量、頻率及族群

使用方法、部位及用量：取適量於手部後，沾水搓揉至起泡沫後用於身體皮膚清潔，並以大量清水沖洗至無殘留泡沫。

使用族群：消費大眾皆適用，無特定使用族群。

使用頻率：每天一次。

(8) 產品使用不良反應資料

目前本產品尚未有任何不良反應事件報告。如有不良反應和嚴重不良反應的資料時會及時提供給安全資料簽署人員進行確認與評估，並更新於本產品資訊檔案中

II. 品質資料

(9) 產品及各別成分之物理及化學特性

成品規格檢驗報告

嫩膚沐浴乳成品 CoA			
檢測項目	**規格**	**實際檢驗結果**	**檢驗方法**
外觀	流動液體	流動液體	目視
顏色	白色不透明帶有珠光	白色不透明帶有珠光	目視
氣味	橙花香	橙花香	嗅覺
pH **(at 25 °C)**	6.5±0.5	6.6	使用已校正之 pH meter 依 pH meter 檢測方法測定
黏度**(at 25 °C)**	20,000~30,000 mPa·s	24,650 mPa·s	使用已校正之黏度計依黏度計檢測方法測定
密度**(at 25 °C)**	1.0±0.05 g/cm^3	0.96 g/cm^3	定量瓶
微生物規格	生菌數 < 1000 cfu/g 不得檢出： 大腸桿菌 金黃色葡萄球菌 綠膿桿菌 白色念珠菌	生菌數 未檢出 (<10 cfu/g)； 大腸桿菌 陰性； 金黃色葡萄球菌 陰性； 綠膿桿菌 陰性； 白色念珠菌 陰性	參考衛生福利部食品藥物管理署 109.07.28 及 111.04.21 公告建議檢驗方法-化粧品中微生物檢驗方法及化粧品中白色念珠菌之檢驗方法。
檢測人員/日期		(請簽名並加上日期)	
複核人員/日期		(請簽名並加上日期)	

各成分物理化學特性

- 由 AJP 化粧品股份有限公司及安全資料簽署人員彙整各成分之安全資料表、檢驗成績書或技術資料表，另存放於成分物理化學特性檔案夾(附錄 1)。
- 安全資料簽署人員依據上述資料內容摘錄各成分物理化學特性如下：

1. INCI name：Aqua

Aqua CoA			
檢測項目	**規格**	**實際檢驗結果**	**檢驗方法**
pH (at 25 °C)	6.5~8.5	7.8	使用已校正之線上(on line) pH meter 測定
導電度(at 25 °C)	<10 µS/cm	5.2 µS/cm	使用已校正之線上(on line)導電度計測定
微生物規格	生菌數< 100 cfu/ml	生菌數 未檢出 (<10 cfu/ml)；	參考環境保護署環境檢驗所公告之水中總菌落數檢測方法測定
檢測人員/日期		(請簽名並加上日期)	
複核人員/日期		(請簽名並加上日期)	

2. Trade name (Product name)：SP CRODASINIC LS30 MIT MBAL-LQ-(RB)

INCI name：Sodium Lauroyl Sarcosinate

Repeat printout /

Certificate of Analysis

A quality management system registered to the international standard ISO 9001 was used to manufacture and test this material.

Quantity. 16,000.000 KG

Batch Details

Product Name: SP CRODASINIC LS30 MIT MBAL-LQ-(RB)

Date of test: 14.07.2021
Date of manufacture: 11.07.2021
Retest date: 11.07.2023

Quality Control Results

Analytical Test Method No.	Characteristic	Specification Limit Lower	Upper	Value	Unit	Status
	Addendum 00	PASS OR FAIL		Pass	-	P
	REVISION NUMBER	1.0		Pass	-	P
G30001	APPEARANCE (CLARITY)	CLEAR		Pass	-	P
G30001	APPEARANCE (COLOUR)	COLOURLESS		Pass	-	P
G30001	APPEARANCE (FORM)	FOAMING LIQUID		Pass	-	P
G34300	ACTIVITY OF N-ACYL SARCOSINATE BY NIR	29	31	30	%	P
G01801	COLOUR	0	60	7	APHA	P
G04401	PH (10% SOLUTION)	7.5	8.5	7.9		P
G00901	SOAP CONTENT OF N-LAUROYL SARCOSINATE	0.00	2.00	0.63	%	P
	RSPO CERTIFICATION NUMBER	BMT-RSPO-000157		Pass	-	P

This Product has been manufactured and tested to GMP in accordance with EXCiPACT

Batch Status: Pass

The quality tests on this batch are reported above. The tests carried out are those necessary to demonstrate compliance with our product specification and are not intended to guarantee the product as suitable for any application beyond those contained in the specification. We recommend you perform your own quality and or identification checks on receipt

3. Trade name (Product name)：Dehyton® KE T IS

INCI name：Cocamidopropyl Betaine

Certificate of Analysis

Certificate of Analysis according to DIN 55350-18-4.2.2

Dehyton® KE T IS

200KG Plastic drums

Lot/Qty	9400.000 KG
Total	16000.000 KG
Transport	CMAU1153056

Characteristic Method	Unit	Value	Lower Limit	Upper Limit
Appearance Visual		PASS		
Odour Smell		Pass		
Washing active substance Calculation	%	31	29	31
Water content ISO 4317	%	63		64
Sodium chloride Method no.920017-01	%	5.1		5.5
Sodium sulfate Method no.920015-01	%	0.9		1.5
pH (5% solution) ISO 4316		5.7	4.5	6.5
Total colony count		<10		

4. Trade name (Product name)：Alpha-Step® PC-48

INCI name：Aqua (56%)、Sodium Methyl 2-Sulfolaurate (38%)、Sodium Sulfate (4%)、Disodium 2-Sulfolaurate (2%)

Certificate of Analysis

Material No. & Description:
Specification number:

Date of Manufacture: 10-MAR-2021
Certification Date: 11-MAR-2021
Recommended Retest Date: 09-MAR-2024

Description		Limits	In Out	Result	Units
110-0	APPEARANCE (@ 25C)	Clear, Yellow Liquid	IN	Passes	
058-0	PH (10% in Water)	5.0 - 7.0	IN	5.6	
C0014	TOTAL ACTIVE (%) (MW 338)	37 - 40	IN	38	%
125-0	FREE OIL	2.5 Max.	IN	1.6	%
119-0	SODIUM CHLORIDE	0.1 Max.	IN	0.0	%
098-G	SODIUM SULFATE	3.0 Max.	IN	2.3	%
149-E	METHANOL	500 Max.	IN	286	ppm
225-0	FREE PEROXIDE	30 Max.	IN	0	ppm
006-C	COLOR GARDNER	3 Max.	IN	2	
045-0	ODOR	Characteristic	IN	Passes	
057-0	SULFITE (As NaHSO3)	50 Max. (ppm)	IN	Passes	

INCI name： Sodium Methyl 2-Sulfolaurate

PubChem Sodium Methyl 2-Sulfolaurate (Compound)

Property Name	Property Value	Reference
Molecular Weight	316.39	Computed by PubChem 2.1 (PubChem release 2021.05.07)
Hydrogen Bond Donor Count	0	Computed by Cactvs 3.4.8.18 (PubChem release 2021.05.07)
Hydrogen Bond Acceptor Count	5	Computed by Cactvs 3.4.8.18 (PubChem release 2021.05.07)
Rotatable Bond Count	12	Computed by Cactvs 3.4.8.18 (PubChem release 2021.05.07)
Exact Mass	316.13203935	Computed by PubChem 2.1 (PubChem release 2021.05.07)
Monoisotopic Mass	316.13203935	Computed by PubChem 2.1 (PubChem release 2021.05.07)
Topological Polar Surface Area	91.9 Å²	Computed by Cactvs 3.4.8.18 (PubChem release 2021.05.07)
Heavy Atom Count	20	Computed by PubChem
Formal Charge	0	Computed by PubChem
Complexity	337	Computed by Cactvs 3.4.8.18 (PubChem release 2021.05.07)
Isotope Atom Count	0	Computed by PubChem
Defined Atom Stereocenter Count	0	Computed by PubChem
Undefined Atom Stereocenter Count	1	Computed by PubChem
Defined Bond Stereocenter Count	0	Computed by PubChem
Undefined Bond Stereocenter Count	0	Computed by PubChem
Covalently-Bonded Unit Count	2	Computed by PubChem
Compound Is Canonicalized	Yes	Computed by PubChem (release 2021.05.07)

INCI name：Sodium Sulfate

Sodium sulfate anhydrous for analysis EMSURE® ACS,ISO,Reag. Ph Eur

	Spec. Values	
Assay (alkalimetric)	≥ 99.0	%
Assay (alkalimetric, calculated on dried substance)	98.5 - 101.0	%
Identity	passes test	
Appearance of solution	passes test	
Insoluble matter	≤ 0.01	%
Acidity or alkalinity	passes test	
pH-value (5 %; water; 25 °C)	5.2 - 8.0	
Chloride (Cl)	≤ 0.001	%
Phosphate (PO_4)	≤ 0.001	%
Total nitrogen (N)	≤ 0.0005	%
Heavy metals (ACS)	≤ 0.0005	%
Heavy metals (as Pb)	≤ 0.0005	%
As (Arsenic)	≤ 0.0001	%
Ca (Calcium)	≤ 0.005	%
Fe (Iron)	≤ 0.0005	%
K (Potassium)	≤ 0.002	%
Mg (Magnesium)	≤ 0.001	%
Loss on drying (130 °C)	≤ 0.5	%
Loss on ignition (800 °C)	≤ 0.5	%

INCI name：Disodium 2-Sulfolaurate

PubChem Disodium 2-sulfolaurate (Compound)

Property Name	Property Value	Reference
Molecular Weight	324.35	Computed by PubChem 2.1 (PubChem release 2021.05.07)
Hydrogen Bond Donor Count	0	Computed by Cactvs 3.4.8.18 (PubChem release 2021.05.07)
Hydrogen Bond Acceptor Count	5	Computed by Cactvs 3.4.8.18 (PubChem release 2021.05.07)
Rotatable Bond Count	9	Computed by Cactvs 3.4.8.18 (PubChem release 2021.05.07)
Exact Mass	324.09833354	Computed by PubChem 2.1 (PubChem release 2021.05.07)
Monoisotopic Mass	324.09833354	Computed by PubChem 2.1 (PubChem release 2021.05.07)
Topological Polar Surface Area	106 Å²	Computed by Cactvs 3.4.8.18 (PubChem release 2021.05.07)
Heavy Atom Count	20	Computed by PubChem
Formal Charge	0	Computed by PubChem
Complexity	299	Computed by Cactvs 3.4.8.18 (PubChem release 2021.05.07)
Isotope Atom Count	0	Computed by PubChem
Defined Atom Stereocenter Count	0	Computed by PubChem
Undefined Atom Stereocenter Count	1	Computed by PubChem
Defined Bond Stereocenter Count	0	Computed by PubChem
Undefined Bond Stereocenter Count	0	Computed by PubChem
Covalently-Bonded Unit Count	3	Computed by PubChem
Compound Is Canonicalized	Yes	Computed by PubChem (release 2021.05.07)

5. Trade name (Product name)：Amilite GCK-12H

INCI name：Aqua (70%)、Potassium Cocoyl Glycinate (21%)、Potassium Cocoate (9%)

CERTIFICATE OF ANALYSIS

Product	:	AMILITE GCK-12H
Date of Production	:	November 30, 2020
Date of Expiration	:	November 30, 2024
Date of Analysis	:	December 14, 2020

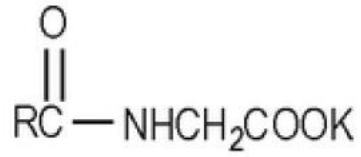
Item	Specification	Result
(1) Description	Refer "COMMENT"	Passed test
(2) Identification		
Infrared Spectrophotometry	Passed test	Passed test
Gas Chromatography	Passed test	Passed test
Potassium Salt	Passed test	Passed test
(3) Transmittance	NLT 60%	86%
(4) pH	8.0 ~ 9.0	8.1
(5) Heavy Metals (Pb)	NMT 20 ppm	NMT 20 ppm
(6) Arsenic (As_2O_3)	NMT 2 ppm	NMT 2 ppm
(7) Nitrogen Content	1.4 ~ 1.9%	1.7%
(8) Content	29 ~ 35%	30%
(9) Fatty acid Content of Residue on Evaporation	25 ~ 35%	31%
(10) Total Viable Counts	NMT 100 cfu/mL	NMT 100 cfu/mL

COMMENT: Pale yellow to yellow liquid, a slightly characteristic odor

INCI name：Potassium Cocoyl Glycinate

INCI NAME
Potassium Cocoyl Glycinate

STRUCTURE



where RCO- represents the cocoyl moiety.

CHARACTERISTICS

Appearance	Clear liquid
Odour	Typical

SPECIFICATIONS

Nitrogen content(%; Aq.)	1.1 - 1.6
Color (430 nm T%)	85.0 Min.
pH value	7.0 - 9.0
Solids (%)	30 - 35

INCI name：Potassium Cocoate

INCI-name:	Potassium Cocoate		
Characteristics:	Aspect:	Yellowish liquid	
	Preservative:	Preservative free	
Specifications:	Total solids (%):	42.0 – 44.0	EOC-method nr: 2101
	pH:	10.0 – 11.5	EOC-method nr: 3001
Storage:	15°C – 30°C		
Shelf-life:	1 year	In original closed packaging	

6. Trade name (Product name)：HOSTAPON®CT PASTE

INCI name：Sodium Methyl Cocoyl Taurate

Product Fact Sheet

Anionic surfactant for the cosmetic industry

Chemical name	Coconut fatty acid methyl tauride sodium salt R = C_8-C_{18}
INCI designation	Sodium Methyl Cocoyl Taurate

PRODUCT PROPERTIES[1]	
Appearance (20 °C)	white, pasty
Hazen colour (5 % water solution)	max. 100
pH-value (5 % tel quel in water)	7.0 – 9.0
Water	56.0 – 60.0 %
Active substance	28.5 – 31.5 %
Mean molecular weight	363 g/mol
Sodium chloride	5.5 – 8.5 %

7. Trade name (Product name)：Lamesoft® TM Benz

INCI name：Aqua (60.5%)、Glycol Distearate (22%)、Coco-Glucoside (10%)、Glyceryl Oleate (3%)、Glyceryl Stearate (3%)、Citric Acid (1%)、Benzoic Acid (0.5%)

Product Datasheet

Valid since 25.07.2014
Revision 1.1

Care Chemicals

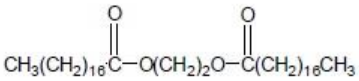
Characteristic values

The specifications stated in the paragraphs 'Quality control data' and 'Additional product descriptive data' finally and conclusively describe the properties of the product.

Quality control data
(Data which is used for quality release and is certified for each batch.)

Water content (Karl Fischer)	59.0 - 63.0 %	DGF C-III 13A
Dry residue (105 °C)	37.0 - 41.0 %	Internal method 96004901
Density (20 °C)	1.0200 - 1.0500 g/cm3	DIN 51757
Filling density	0.980 - 1.020 g/cm3	Internal method 94017101
Viscosity Brookfield (20 °C)	1000 - 10000 mPas	ASTM D 2196
pH value (20 °C; 10 %)	3.0 - 3.5	Internal method 92003901

INCI name：Glycol Distearate

INCI Name	Glycol distearate			
Description	Ester of ethylene glycol and stearic acid			
Composition	**Component Name**	**CAS No.**	**EINECS**	**Component**
	Glycol distearate	91031-31-1	292-932-1	100%
	* preservative : none			
Typical Properties	**Inspection**	**Specification**		**Method**
	Appearance	White flake		
	Color	80 max		APHA
	Acid value	1.50mgKOH/g max		
	Iodine value	1.00gI2/100g max		
	Melting point	60.0 - 63.0℃		
	Ash	0.50% max		780℃, 4hr

INCI name：Coco-Glucoside

Chemical Description

C8-C14 fatty alcohol glucoside

INCI name: Coco-Glucoside (pending)

Surfactant Type: Nonionic

Benefits

- Mild
- Produces moderate to high stable foam
- Compatible with broad range of surfactants and polymers, including cationic ingredients
- 100% vegetable origin
- Solvent-free
- Self-preserved
- Low eco-toxicity and toxicity
- Readily biodegradable

Applications

- Shampoo
- Body Wash
- Bubble Bath
- Hand and Facial Cleanser
- Liquid and Bar Soap
- Conditioner
- Baby Wipes

Typical Physical Properties

Actives % / Solvent	50 / Water
Cloud Point [1]	>100
HLB [2]	12-14
CMC[3] / Surface Tension[4]	67.2/28.7
Pour Point	-18°C
Form[5]	Hazy pale yellow liquid
pH, 10% aq solution	12
Viscosity at 40°C (104°F), cSt	1000
Density at 40°C (104°F), g/mL	1.11
Flash Pt, Closed Cup, ASTM D93	>100°C (est)

[1] Cloud point: °C, 1% Aqueous, [2] HLB Range: <10 w/o emulsifier, >10 o/w emulsifier, [3] Critical micellization concentration: ppm at 25°C, [4] Surface tension: dynes/cm at 0.1% actives, 25°C, [5] Form at 25°C

Solubility and Compatibility

- Soluble in water
- Soluble in concentrated electrolyte solutions
- Chemically stable in the presence of acids, bases and salts
- Compatible with anionic, amphoteric, cationic, and other nonionic surfactants

Storage

The product should not be stored at temperatures below 15°C, or above 40°C. If crystallization or sedimentation occurs when stored at temperatures below 15°C, the product should be heated and stirred until uniform before use.

INCI name：Glyceryl Oleate

Product Name: Glyceryl Oleate
INCI Name: Glyceryl Oleate
CAS Number: 25496-72-4

Expiration Date: 24 months from production date

Characteristic	Specifications	Result
Appearance @ 25°C	Pale yellow soft solid or liquid	Pass
Alpha Mono	42.0 - 60.0%	49.0%
% Free Glycerine	2.0% MAX	0.0%
Free Fatty Acid	2.0% MAX	0.0%
Moisture	1.0% MAX	0.2%
Color (Gardner)	6.0 MAX	1.0
Saponification Value	160.0 - 180.0	167.0
Iodine Value	73.0 - 115.0	78.0

INCI name：Glyceryl Stearate

Product Name: Glyceryl Stearate SE
INCI Name: Glyceryl Stearate
CAS Number: 123-94-4

Expiration Date: 24 months from production date

Characteristic	Specifications	Laboratory Values	Final Result
Melt Point (°C)	55 min	58	Pass
Acid Value (mg KOH/1g)	6 max	1.53	Pass
Iodine Value (g Iodine/10g)	3 max	0.47	Pass
Saponification Value (mg KOH/1g)	155-170	159.29	Pass
HLB Value	5-6	5.8	Pass

INCI name：Citric Acid

Certificate of Analysis

Certificate Of Analysis For Citric Acid

Sr No.	Characteristics	Unit	Specifications
1	Description		Colorless Crystals
2	Identification		Pass Test
3	Appearance Of Solution		Pass Test
4	Assay	%	99.5-101.0
5	Sulphate	PPM	<=150
6	Oxalate	PPM	<=100
7	Heavy Metal (as pb)	PPM	<=5
8	Barium		Pass Test
9	Calcium	PPM	<=200
10	Iron	PPM	<=10
11	Chloride	PPM	<=50
12	Sulphated Ash	%	<=0.05
13	Moisture	%	<=0.5
14	Readily Carbonisable		Not Darker than
15	Substances		Standard
16	Lead	PPM	<=0.5
17	As	PPM	<=1
18	Mercury	PPM	<=1
19	Aluminium	PPM	<=0.2
20	Bacteria Endotoxin	PPM	<=0.5
21	Organic Volatile Impurites		Pass Test
22	Tridodecylamine	PPM	<=0.1
23	Ultraviolet Absorbance		Pass Test

INCI name：Benzoic Acid

INCI Name: Benzoic acid

CAS No.: 65-85-0

EC No.: 200-618-2

Specification:

Items	Specification
Appearance	White to slightly yellowsih Powder
Odor	Faint balsam urine
Purity(GC) (%)	≥99.0
Melting point(℃)	121.0~123.0
Loss on drying(%)	≤0.5
Water(%)	≤0.5
Heavy Metals(Pb,ppm)	≤10
As(ppm)	≤3

8. Trade name (Product name)：Versathix™

INCI name：PEG-150 Pentaerythrityl Tetrastearate (50%)、Aqua (30%)、PPG-2 Hydroxyethyl Cocamide (20%)

Certificate of Analysis Repeat printout

Manufacturing site is certified according to ISO9001, ISO14001 and ISO45001 standards.

Quantity. 800.000 KG

Batch Details
Product Name: SP VERSATHIX MBAL-LQ-(SG)
Product Code: ES80743/0200/8S02

Date of test: 06.10.2021
Date of manufacture: 30.09.2021
Retest date: 30.09.2023

Specification: REV.00 12.06.2019

Quality Control Results

Analytical Test Method No.	Characteristic	Specification Limit Lower	Upper	Value	Unit	Status
	Addendum 00	PASS OR FAIL		Pass	-	P
AS039010	APPEARANCE @ 25°C (COLOUR)	LIGHT YELLOW		Pass	-	P
AS039010	APPEARANCE @ 25°C (STATE)	LIQUID		Pass	-	P
AS040010	ODOUR	CHARACTERISTIC		Pass	-	P
FS056010	SOLID CONTENT	69.0	71.0	70.0	%	P
LS007040	RESIDUAL ETHYLENE OXIDE	1 PPM MAX		Pass	-	P
LS055010	PROPYLENE OXIDE CONTENT	1 PPM MAX		Pass	-	P
LS007040	RESIDUAL 1,4 DIOXANE	5 PPM MAX		Pass	-	P

Product may exhibit phase separation at cold temperatures. To reconstitute, warm to 40°C and mix.

INCI name：PEG-150 Pentaerythrityl Tetrastearate

CHEMISTRY

Definition and Structure

PEG-150 pentaerythrityl tetrastearate (CAS No. 130249-48-8) is the tetraester of stearic acid and a polyethylene glycol ether of pentaerythritol with an average of 150 moles of ethylene oxide, and conforms to the molecular structure shown in figure 1:[1]

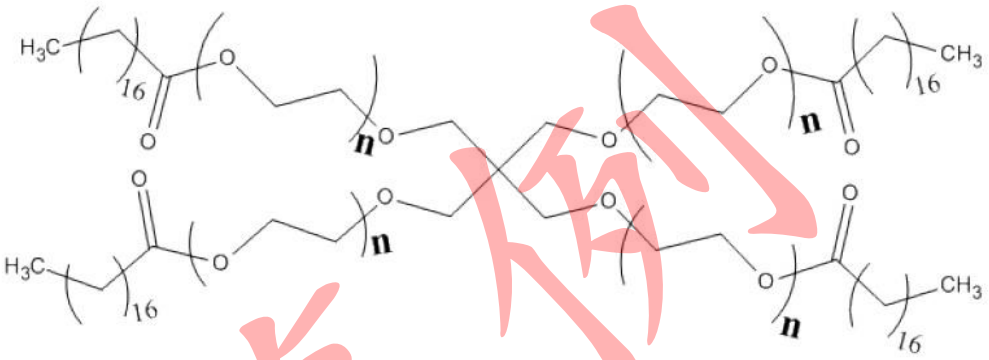


Figure 1. PEG-150 pentaerythrityl tetrastearate (wherein the sum of all instances of n is equal to 150)

Physical and Chemical Properties

PEG-150 pentaerythrityl tetrastearate (Crothix®) is slightly soluble in water, has a melting point of 45°C, and has a pH range of 5.5 to 7.5 (1% solutioin).

INCI name：PPG-2 Hydroxyethyl Cocamide

INCI Name: PPG-2 Hydroxyethyl Cocamide

Typical Properties:

Appearance (25℃)	Light Yellow Liquid
Color (Gardner)	6 Max.
Solid content (%, Halogen Moisture Analyzer)	98.0 Min.
pH (1% solution)	8.5-10.5
Amine Value (mg KOH/g):	20.0 Max.

9. INCI name：Glycerin

162/F01-QCD/II/2022

CERTIFICATE OF ANALYSIS

Date: 2022-02-17

Product Name	Glycerine	Model	USP997
Description of Goods	Glycerine	Manufacturer Date	2021-11-26
Invoice No.	DKCHKS 22/02/050	Batch No./Lot No.	2021.11.26.03
		Expire Date	2023-11-26
Container No.		Quantity	40 MTS

INSPECTION ITEM	Standard	Method	RESULT
Color,Hazen	10max	AOCS Td Ib-64	10
Water Content, %wt	0.3max	USP 39	0.12
Arsenic, ppm	1.5max	USP 39	＜1.5
Heavy metal, Lead, ppm	5max	USP 39	＜5
Fatty acid and esters (titrant:0.5N NaOH),ml	1max	USP 39	0.41
Specific Gravity at 25^0C	1.2612min	USP 39	1.2617
Assay, %wt	99.7min	USP 39	99.90
Chloride, ppm	10max	USP 39	＜10
Sulphate, ppm	20max	USP 39	＜20
Chlorinated Compound, ppm	20max	USP 39	＜20
Residue on Ignition, %wt	0.01max	USP 39	0.003
Ethylene Glycol content, %wt	0.1max	USP 39	＜0.1
Diethylene Glycol content, %wt	0.1max	USP 39	＜0.1
Identification by IR	Meet requirement	USP 39	Positive
Identification by GC	Meet requirement	USP 39	Positive
Conclusion	**PASS**		

10. Trade name (Product name)：VERSTATIL PC

INCI name：Phenoxyethanol (90%)、Caprylyl Glycol (10%)

Product	VERSTATIL PC 25,00 KG CAN:HDPE:25L:3H1:Y
Material	99119045
Customer material no.	A006.004.025
Quantity	4.550 KG = 182 EA
Manufacturing date	May 28, 2021
Expiration date	May 12, 2024
Spec.No.	K00:STANDARD

Property	Test method	Unit	Value	Min.	Max.
Appearance	GM_0170_00		Conforms	colourless clear liquid	
Odour	GM_0175_02		Conforms	Characteristic	
Density / 20°C	GM_0110_01	g/ml	1.0840	1.0700	1.0900
Refractive index 20% in Isopro	GM_0120_01		1.4017	1.4000	1.4050
Assay Octane-1,2-diol	GM_1516_02	%	10.0	9.0	11.0

Product Information

Verstatil® PC

The Product: Verstatil® PC

Verstatil® PC is a versatile and efficient preservative blend, which combines the reliable activity of Phenoxyethanol with the boosting performance of the wetting agent Caprylyl Glycol. The blend is water miscible and chemically stable with low impact on the stability of the final cosmetic product. The broad antimicrobial performance is pH independent. It is suitable for every type of emulsion and aqueous based product, with the help of a solubilizer.

CHARACTERISTICS

- INCI: Phenoxyethanol; Caprylyl Glycol
- Appearance: Clear, colorless liquid

- Economic and efficient preservative blend
- No isothiazolinone, parabens, no formaldehyde, no halogenorganic compounds
- No chemically acting preservatives with sensitizing potential

- Synergistic blend: High antimicrobial efficacy at low dosage
- Ideal in emulsions and oil based products
- Hardly any impact on emulsion stability
- Compatible with electrolytes
- pH range: unlimited

DOSAGE

Product Concept	Dosage *
O/W-emulsion	0.8 – 1.0 %
W/O-emulsion	1.0 %
Gels and Tonics	0.8 – 1.0 %

* Max. dosage 1.1% according to European Cosmetics Legislation. Please consider your national legislative restrictions.

ANTIMICROBIAL EFFICACY

Gram +	Gram –	Yeast	Mold
++	++	++	++

Legend: + = good, but needs a co-active | ++ = very good alone

INCI name：Phenoxyethanol

product benefits

- good bactericidal effect
- vapor phase activity
- stable to hydrolysis, temperature and pH
- fully effective in anionic, cationic and non-ionic systems
- cost effective

INCI declaration	CAS No
Phenoxyethanol	122-99-6

technical product properties

color	colorless
form	liquid
odor	characteristic
density (20 °C)	1.103 - 1.108 g/ml
boiling point/boiling range	245 °C
flash point	126 °C
viscosity (20 °C)	ca. 41 mPa*s
water solubility (20 °C)	24 g/l
foaming characteristics	non foaming
vapor pressure	< 0.01 hPa
natural ingredient acc. ISO 16128	0%

INCI name：Caprylyl Glycol

product benefits	INCI declaration	CAS No
o leading antimicrobial multifunctional o now 100% natural & COSMOS validated o known technology - easy drop-in o wide pH applicability (pH 2 – 12) o suitable for sensitive skin	Caprylyl Glycol	1117-86-8

technical product properties

color	colorless
form	clear liquid to white waxy solid
odor	slight characteristic
boiling point/boiling range	267°C
melting point	28 – 31°C
flash point	140.5°C
water solubility (20 °C)	< 1 g/l
natural ingredient acc. ISO 16128	100%

11. Fragrance

IFRA 50 CERTIFICATE

Product Name: Neroli Light Oil
INCI Name: Parfum

Amphora Aromatics hereby certify that the above named material is in compliance with the standards of the IFRA 50 Code of Practice and contains the following restricted components also listed in the 50th Amendment of the IFRA Code of Practice.

Restricted Component	CAS No:	% Level in Product	IFRA Standard Type	Year of publication
Limonene	5989-27-5	≤ 19.00	Specification	1995
Linalool	78-70-6	≤ 21.00	Specification	2004
Citral	5392-40-5	≤ 2.00	Restriction	2020
Citronellol	106-22-9	≤ 3.50	Restriction	2020
Citronellal	106-23-0	≤ 0.50	Restriction	2020
Geraniol	106-24-1	≤ 2.95	Restriction	2020
Hydroxycitronellal	107-75-5	≤ 3.00	Restriction	2020
Peroxides	-	≤ 20mmol/l	-	-

Additional Comments

Flavour use consideration - Due to the possible ingestion of small amounts of fragrance ingredients from their use in products in Categories 1 and 6, materials must not only comply with IFRA Standards but must also be recognized as safe as a flavouring ingredient as defined by the IOFI Code of Practice (www.iofi.org). For more details see chapter 1 of the Guidance for the use of IFRA Standards.

It is the ultimate responsibility of the customer to ensure the safety of the intended final product containing this material, by carrying out additional tests if necessary.

IFRA Category	% Maximum Use Level
Category 1	Not approved
Category 2	1.60
Category 3	5.00
Category 4	30.00
Category 5A	7.50
Category 5B	7.50
Category 5C	7.50
Category 5D	2.55
Category 6	Not approved
Category 7A	10.00
Category 7B	10.00
Category 8	2.55
Category 9	60.00
Category 10A	60.00
Category 10B	Not restricted
Category 11A	2.55
Category 11B	2.55
Category 12	Not restricted

IFRA Category	Product Type
IFRA Category 1	Products applied to the lips: Lip products e.g., lipstick, lip balm; Children's toys.
IFRA Category 2	Products applied to the axillae: Deodorant and antiperspirant products of all types; Body sprays/mists.
IFRA Category 3	Products applied to the face/body using fingertips: Eye products e.g., eye make-up, eye moisturizer; Facial make-up; Make-up remover; Nose pore strips; Wipes for face, neck, hands, body; Facial masks; Body and face paint.
IFRA Category 4	Products related to fine fragrance: Hydroalcoholic and non-hydroalcoholic fine fragrance of all types e.g.: Eau de Toilette, Parfum, Cologne, solid perfume, fragrancing cream, aftershaves of all types; Ingredients of perfume and fragrance mixtures for cosmetic kits; Scent pads; Scent strips.
IFRA Category 5A	Body lotion products applied to the body using the hands (palms), primarily leave on: Foot care products e.g., creams, powders; Insect repellent for application to the skin; All powders and talc (excluding baby powders and talc).
IFRA Category 5B	Face moisturizer products applied to the face using the hands (palms), primarily leave on: Facial toner; Facial moisturizers and creams.
IFRA Category 5C	Hand cream products applied to the hands using the hands (palms), primarily leave on: Hand cream; Nail care products including cuticle creams; Hand sanitizers.
IFRA Category 5D	Baby creams, baby oils and baby talc: Baby cream/lotion, baby oil, baby powders and talc.
IFRA Category 6	Products with oral and lip exposure: Toothpaste; Mouthwash, including breath sprays; Toothpowder, strips, mouthwash tablets.
IFRA Category 7A	Rinse-off products applied to the hair with some hand contact: Hair permanent or other hair chemical treatments (rinse-off) e.g., relaxers, including rinse-off hair dyes.
IFRA Category 7B	Leave-on products applied to the hair with some hand contact: Hair sprays of all types e.g., pumps, aerosol sprays; Hair styling aids non sprays e.g., mousse, leave- on conditioners; Hair permanent or other hair chemical treatments (leave-on) e.g., relaxers, including leave-on hair dyes; Shampoo - Dry (waterless shampoo); Hair deodorizer.
IFRA Category 8	Products with significant anogenital exposure: Intimate wipes; Tampons; Baby wipes; Toilet paper (wet).
IFRA Category 9	Products with body and hand exposure, primarily rinse off: Bar soap; Liquid soap; Shampoo of all type; Conditioner (rinse-off); Body washes and shower gels of all types; Baby wash, bath, shampoo; Bath gels, foams, mousses, salts, oils and other products added to bathwater; Cleanser for face (rinse-off); Shaving creams of all types e.g., stick, gels, foams; All depilatories (including facial) and waxes for mechanical hair removal; Foot care products (feet are placed in a bath for soaking); Shampoos for pets
IFRA Category 10A	Household care excluding aerosol / spray products: Hand wash laundry detergent; Laundry pre-treatment of all types e.g. paste, sprays, sticks; Machine laundry detergents with skin contact e.g. liquids, powders; Fabric softeners of all types including fabric softener sheets; Ironing water; Hand dishwashing detergent; Hard surface cleaners of all types e.g. bathroom, kitchen cleansers, furniture polish; Toilet seat wipes; Household cleaning products, other types including fabric cleaners, carpet cleaners, furniture polishes sprays and wipes, stain removers, treatment products for textiles e.g. starch sprays; Floor wax; Dry cleaning kits; Fragranced oil for lamp ring, reed diffusers, pot-pourri, liquid refills for air fresheners (non-cartridge systems), etc.
IFRA Category 10B	Household aerosol/spray products: Animal sprays applied to animals; Air freshener sprays, manual, including aerosol and pump; Aerosol/spray insecticides.
IFRA Category 11A	Products with intended skin contact but minimal transfer of fragrance to skin from inert substrate without UV exposure: Feminine hygiene conventional pads, liners, interlabial pads; Diapers (baby and adult); Adult incontinence pant, pad; Toilet paper (dry).
IFRA Category 11B	Products with intended skin contact but minimal transfer of fragrance to skin from inert substrate with potential UV exposure: Tights with moisturizers; Scented socks, gloves; Facial tissues (dry tissues); Napkins; Paper towels; Wheat bags; Facial masks (paper/protective) e.g., surgical masks not used as medical device; Fertilizers, solid (pellet or powder)
IFRA Category 12	Products not intended for direct skin contact, minimal or insignificant transfer to skin: Candles of all types ; Laundry detergents for machine wash with minimal skin contact (e.g., Liquid tabs, pods); Automated air fresheners and fragrancing of all types e.g. concentrated aerosol with metered doses, plug-ins, electrical, incense, liquid refills (cartridge); Air delivery systems; Cat litter; Cell phone cases; Deodorizers/maskers not intended for skin contact e.g. fabric drying machine deodorizers, carpet powders; Fuels; Insecticides e.g. mosquito coil, paper, electrical, for clothing, excluding aerosols/sprays; Joss sticks or incense sticks; Dishwash detergent and deodorizers - for machine wash; Olfactive board games; Paints; Plastic articles (excluding toys); Scratch and sniff; Scent pack; Scent delivery system (using dry air technology); Shoe polishes; Rim blocks (Toilet).

12. Trade name (Product name)：Phytexcell OAT

INCI name：Glycerin (60%)、Butylene Glycol (15%)、Aqua (15%)、*Avena Sativa* (Oat) Kernel Extract (10%)

Certificate of Analysis Repeat printout

Manufacturing site is certified according to ISO9001, ISO14001 and ISO45001 standards.

Certificate prepared at

Crodarom SAS
Parc d'Activités Les Plaines
48230 Chanac
France

Inspection Lot 040001125493
C of A Printed. 21.05.2021

Croda Del. No. 800109741
Quantity. 10.000 KG

Batch Details
Product Name: PHYTEXCELL OAT
Product Code: NA34678/0010/2P35
Batch No: 0001845076

Date of test: 20.04.2021
Date of manufacture: 08.04.2021
Retest date: 07.04.2024

Specification: 22/10/2004

Quality Control Results

Analytical Test Method No.	Characteristic	Specification Limit Lower	Upper	Value	Unit	Status
	Addendum 00	PASS OR FAIL		Pass	-	P
AC018000	ASPECT	CLEAR LIQUID		Pass	-	P
AC018000	COLOUR	PALE YELLOW TO PALE ORANGE BROWN		Pass	-	P
FC0031A0	SPECIFIC GRAVITY (20°C)	1.145	1.175	1.167		P
FC0032A0	REFRACTIVE INDEX (20°C)	1.425	1.455	1.444		P
FC0064C0	pH VALUE (20°C)(10% W/W IN DIST.WATER)	4.0	6.5	5.5		P
LC015800	L-VALINE CONTENT	260	99999	750	ppm	P
JC0054A0	TOTAL GERMS	100 MAX CFU/ML		<10 CFU/ml	-	P
JC0054A0	MOULDS/YEASTS	10 MAX CFU/ML		Pass	-	P

PRESERVATIVE FREE
Between 15-25°C, dark in closed containers
The performed analysis are guaranteed on original packaging
When stored accordingly, stable for 36 months
We hereby certify that the plants used for this production are originated from certified organic culture according to last version of EEC Council Regulation for organic agriculture.

INCI name：Butylene Glycol

Component & CAS Number：1,3-Butylene Glycol, 107-88-0

Weight %：99.5

Section 9 - Physical & Chemical Properties

Appearance: Clear, colorless, mobile, syrupy, liquid.

Odor: Essentially odorless

Vapor Pressure: 0.06mmHg at 20℃

Vapor density (Air =1@20 deg. C): 3.2

Boiling Point(760mm HgA): 207.5℃(405.5℉)

Freezing Point: -50℃(-58℉)

Specific Gravity:1.0059 at 20℃

Molecular Weight:90.12g/mol

INCI name：*Avena Sativa* (Oat) Kernel Extract

1. **INCI NAME:** Avena Sativa kernel extract
2. **BOTANICAL CLASSIFICATION:** *Avena sativa* (L.) **FAMILY:** Gramineae

ANALYSIS	TEST	SPECIFICATION	METHOD
ORGANOLEPTIC	Appearance	Homogeneous translucent liquid	Organoleptic
	Color	Colorless	Organoleptic
	Odor	Characteristic	Organoleptic
PHYSICOCHEMICAL	Density (g/mL)	1.0-1.1	USP
	Refraction index	1.380-1.400	USP
	Direct pH	5.0-7.0	USP
	Solubility in water (1/10)	Solvable	USP
	Solubility in Alcohol (1/10)	Solvable	USP
	Solubility in Mineral Oil (1/10)	Unsolvable	USP
MICROBIOLOGICAL	Mesophiles	< 100 UFC/mL	PETRIFILM 3M
	Fungi and Yeast	< 10 UFC/mL	PETRIFILM 3M
	Pathogens	Absent	PETRIFILM 3M

(10) 成分之毒理資料

- 由 AJP 化粧品股份有限公司及安全資料簽署人員查詢蒐集各成分之毒理資料，另存放於成分毒理資料檔案夾(附錄 2)。
- 安全資料簽署人員依據上述資料內容摘錄各成分相關毒理資料如下：

1. INCI name：Sodium Lauroyl Sarcosinate

- 不純物：分析 30%的月桂醯肌氨酸(Lauroyl Sarcosine)和月桂醯肌氨酸鈉(Sodium Lauroyl Sarcosinate)水溶液中的亞硝胺。月桂醯肌氨酸鈉和月桂醯肌氨酸中的 N-亞硝基肌氨酸(N-Nitrososarcosine)的檢測極限分別為 65 ppb 和 15 ppb；沒有檢測到亞硝胺(Nitrosamines)。[1]
- 急性毒性：月桂醯肌氨酸鈉、椰油醯肌氨酸(Cocoyl Sarcosine)和椰油醯肌氨酸鈉(Sodium Cocoyl Sarcosinate)在大鼠中的口服 LD_{50} 為 4.2 至 6.0 g/kg。雄性和雌性 Sprague-Dawley 大鼠以管飼法給予單劑量月桂醯肌氨酸鈉 5000 mg/kg bw 溶液。一隻雌性大鼠當天死亡；其餘動物均未觀察到臨床症狀，口服月桂醯肌氨酸鈉 LD_{50} >5000 mg/kg bw。[1,2]
- 重複劑量毒性：每組 15 隻雄性和 15 隻雌性 Sprague-Dawley 大鼠每天透過管飼法口服給藥溶解在蒸餾水中的月桂醯肌氨酸鈉 0、30、100 和 250 mg/kg bw，持續 91 或 92 天。100 和 250 mg/kg bw 組的雄性與對照組相比體重增加減少，中劑量組 13 週中有 5 週和高劑量組 13 週中有 8 週的體重下降具有統計學意義。在 100 和 250 mg/kg bw 劑量組中，絕對胃重（雄性）、胃體重比和胃腦重量比（雄性和雌性）在統計學上顯著增加，有一個胃壁厚度增加和非腺胃黏膜黃色變色，組織病理學顯示這些組的雌性和雄性非腺胃黏膜的鱗狀細胞增生、角化過度/角化不全、炎症和水腫的發生率和嚴重程度增加. 在統計學上與對照值有顯著差異的其他幾個器官的重量不被認為具有毒理學意義，血液學或臨床化學參數沒有毒理學上的顯著變化，沒有相關的死亡率報告。未觀察到不良反應劑量 (No Observable Adverse Effect Level, NOAEL)、可觀察到不良反應最低劑量(Lowest Observable Adverse Effect Level, LOAEL) 和未觀察到反應劑量 (No-Observed Effect Level, NOEL)分別為 30、100 和 250 mg/kg bw/day。[1,2]
- 皮膚腐蝕性/刺激性：在體外皮膚腐蝕人體皮膚模型試驗中使用重

建的人體表皮評估月桂醯肌氨酸鈉的刺激性(OECD Guideline 431)。將 20 mg 在 0.9%氯化鈉溶液測試材料施用於組織 3、60 或 240 分鐘，並使用 3-（4,5-二甲基噻唑-2-基）-2,5-二苯基四唑溴化銨 (MTT) 吸收量量測組織活力，月桂醯肌氨酸鈉對重建的人體表皮無腐蝕性。月桂醯肌氨酸鈉在以 20~30%溶液、2%的製劑濃度或純粉末形式給藥時對兔子的牙齦和口腔黏膜無刺激性。[1,2]

- 皮膚致敏性：0.01%月桂醯肌氨酸鈉水溶液對天竺鼠的皮膚不致敏。[1,2]
- 致突變性/遺傳毒性：以平板混合試驗法(Plate Incorporation)和斑點測試(spot test)對月桂醯肌氨酸鈉在五種鼠傷寒沙門氏菌菌株中進行測試，被認為未具有致突變性。此外，在使用人類白血球細胞和 V79 中國倉鼠細胞的彗星試驗中，結果顯示月桂醯肌氨酸鈉不會誘導雙股 DNA 斷裂，但該化合物具有細胞毒性。[1,2]
- 生殖與發育毒性：在 Sprague-Dawley 大鼠中對月桂醯肌氨酸鈉（純度 95%）進行一項產前發育毒性研究(OECD Guideline 414)。27 組 24 隻妊娠雌性大鼠第 5-10 天每天用 0、30、100 和 250mg/kgbw/day 蒸餾水中的試驗品管飼給藥，並在妊娠第 20 天犧牲動物。月桂醯肌氨酸鈉沒有胚胎毒性或致畸性。與對照組相比，中劑量組和高劑量組的妊娠期間懷孕雌鼠體重增加減少。在妊娠第 8-11 天和第 14-17 天之間，高劑量組的飼料消耗量減少，這種下降具有統計學意義。研究期間有兩隻高劑量測試組雌鼠死亡；一隻在妊娠第 10 天，另一隻在妊娠第 18 天一次。妊娠第 18 天死亡的雌鼠在胃的非腺體區域有脫皮，7 名死亡胎兒在右子宮角有脫皮，高劑量雌性在研究結束時被犧牲後發現都在胃的非腺體區域有脫皮；在低劑量或中劑量組中沒有觀察到這種現象。月桂醯肌氨酸鈉 NOAEL（母體毒性）、LOAEL（母體毒性）和 NOEL（發育毒性）分別為 30、100 和≥250 mg/kg bw/day。[1,2]
- 經皮吸收：研究人員將月桂醯肌氨酸鈉完全溶解在 PBS 中，使用人體屍體皮膚表皮檢測月桂醯肌氨酸鈉對螢光素經皮遞送的影響。僅觀察到“經皮通量非常小幅增加”(0.061 ± 0.013 µg)。[1]
- 毒物代謝動力學：月桂醯肌氨酸鈉施用於大鼠的牙齒、口腔黏膜和舌頭，給藥後放射性標記[^{14}C]的平均分佈分別為牙齒中的 1.12%、口腔黏膜中 2.22%和舌中 2.95%。經 24 小時，平均分佈為牙齒 0.79%、口腔黏膜 0.92%、舌 0.57%、肝臟 1.6%、腎臟 0.8%、糞便 1.8%和

尿中 42.2%。數據顯示月桂醯肌氨酸鈉不被口腔組織吸收，而是被吞嚥並吸收到血液中，大約 34%的放射性標記在 4 小時內從尿中排出，42%在 24 小時內排出。[1,2]

- 人體數據：一名女性患者的手、面部和頸部出現急性嚴重濕疹反應，該反應與使用洗手皂有關。在開放和未封閉的皮膚斑貼測試導致對產品產生+3 紅點起皰反應後，對一些單獨的成分進行皮膚斑貼測試。報告顯示對 30%月桂醯肌氨酸鈉在無菌水溶液產生+3 紅點起皰反應。在 2 名受試者中用肥皂和月桂醯肌氨酸鈉進行皮膚斑貼測試，得到陰性結果。在另一份報告中，一名患有復發性手部皮炎的女性患者對半開放式使用含有月桂醯肌氨酸鈉的液體清潔劑產生陽性反應。使用 0.1、0.5 和 1%月桂醯肌氨酸鈉水溶液的後續斑貼測試中觀察到陽性反應；在 98 小時時，這些濃度下的分數分別為“－”、“+/-”和“+”。[1,2]
- 其他安全資料：化粧品成分審查專家小組(Cosmetic Ingredient Review, CIR)評估科學數據並得出結論，椰油醯肌氨酸、月桂醯肌氨酸、肉荳蔻醯肌氨酸、油醯肌氨酸、硬脂醯肌氨酸、椰油醯肌氨酸鈉、月桂醯肌氨酸鈉、肉荳蔻醯肌氨酸鈉、椰油醯肌氨酸銨和月桂醯肌氨酸銨可安全用於沖洗型產品，免洗型產品於濃度低於 5%可安全使用。CIR 專家認為目前數據不足以確定用於可能吸入肌氨酸和肌氨酸鹽產品的安全性。CIR 專家小組警告說，這些成分可能容易形成亞硝胺。CIR 專家小組也提出，肌氨酸可能被亞硝化形成 N-亞硝基肌氨酸(N-Nitrososarcosine)，這是一種潛在的致癌化合物。因此，這些成分不應用於可能形成 N-亞硝基化合物(N-Nitroso compounds)的化粧品和個人護理產品中。[3]
- 參考資料：

1. Amended Safety Assessment of Fatty Acyl Sarcosines and Sarcosinate Salts as Used in Cosmetics. International Journal of Toxicology 2021, Vol. 40(Supplement 2) 117S–133S. CIR, 2021.
2. Amended Safety Assessment of Sarcosines and Sarcosinate Amides as Used in Cosmetics. CIR, 2016.
3. Cosmetics Info 網站：https://www.cosmeticsinfo.org/ingredients/sodium-lauroyl-sarcosinate/

2. INCI name：Cocamidopropyl Betaine

- 不純物：與椰油醯胺丙基甜菜鹼(Cocamidopropyl Betaine, CAPB)相關的雜質是生產過程中的反應物和中間體，包括醯氨基胺(Amidoamine)、一氯乙酸鈉(Sodium Monochloroacetate)和二甲基氨基丙胺(3,3-Dimethylaminopropylamine, DMAPA)。根據製造商的不同，殘留醯氨基胺和 3,3-二甲基氨基丙胺的範圍分別為 0.3%~3.0%和 0.0003% ~0.02%。[1]
- 急性毒性：通過管飼法對 10 隻（5 隻雌性、5 隻雄性）Wistar 大鼠組施用劑量分別為 5.00、6.30、7.94 和 10.00 mL/kg，pH 值為 5.5 未稀釋的 30%活性椰油醯胺丙基甜菜鹼。觀察大鼠 14 天，口服 LD_{50} 為 7.97 g/kg bw（根據 1.07 g/mL 的密度計算），可信賴範圍為 6.93 至 9.17 g/kg bw。所有劑量組的大鼠在給藥後約 20 分鐘開始活動減少、身體姿勢異常、出現協調障礙、發紺、腹瀉和體溫降低，持續 24 小時。所有組的存活大鼠體重增加 36 ~45 g，外觀和行為正常。屍檢時觀察到胃和腸粘膜發紅。美國化學委員會總結一項使用雄性和雌性 CD 大鼠（雌雄各 5 隻/；體重 200~232g）對 31% 活性椰油醯胺丙基甜菜鹼進行的急性皮膚毒性研究。在動物背腰區的表面上施用 2.0 g/kg bw， 封閉測試區域，24 小時後，除去敷料，用溫水清洗處理區域並擦乾。每天檢查處理區域的皮膚刺激跡象，持續 14 天。在第 1、8 和 15 天對大鼠進行稱重。在第 15 天，對大鼠進行屍檢。沒有發生計劃外死亡，也沒有觀察到全身毒性的臨床症狀，屍檢時未觀察到異常。在第 2 天觀察到輕微或明確的紅斑，第 3 天有 3 隻雄性和所有雌性的明確紅斑持續存在，並在第 6 天完全消退。僅在第 4 天和第 5 天有 6 隻大鼠出現蛻皮或過度角化。31% 椰油醯胺丙基甜菜鹼 LD_{50}>2.0 g/kg bw。[1]
- 重複劑量毒性：10 隻雄性和 10 隻雌性 Crl:CF(SD)BR Sprague-Dawley 大鼠組每天一次透過口服管飼 10 mL/kg 椰油醯胺丙基甜菜鹼蒸餾水（濃度未知），分別測試 0、250、500 或 1000 mg/kg bw/day 劑量，持續 92 天。每天記錄臨床症狀，每週記錄一次體重和飼料消耗。在給藥前以對照組和 1000 mg/kg bw/day 劑量組進行眼科檢查，並在治療的最後一週對所有組別進行眼科檢查。在治療的最後一週收集所有大鼠血液和尿液樣本，在研究終止時對犧牲存活的大鼠並進行完整的屍檢。對來自對照組和 1000 mg/kg bw/day 劑量組大鼠

的選定組織進行組織病理學檢查。因為在 1000 mg/kg bw/day 組的胃中觀察到相關的組織病理學變化，也對 250 和 500 mg/kg bw/day 組的胃進行顯微鏡檢查。在研究過程中未觀察到任何性別的劑量試驗相關死亡或影響。屍檢顯示高劑量組 1 隻雄性和 1 隻雌性的胃底和心臟區域有潰瘍。顯微鏡檢查發現非腺性胃炎發生於 1000 mg/kg bw/day 組 6 隻雄性和 3 隻雌性大鼠及 500 mg/kg bw/day 組 2 隻雄性和 2 隻雌性大鼠，在 250 mg/kg bw/day 劑量組中未觀察到這種現象。未觀察到其他與測試劑量相關的影響，該研究得出結論，該椰油醯胺丙基甜菜鹼大鼠亞慢性(90 天)研究的未觀察到反應劑量 NOEL 為 250 mg/kg bw/day。[1]

- 皮膚刺激性：根據各項研究表明，雖然全濃度(30%活性)椰油醯胺丙基甜菜鹼溶液是輕度刺激性的，但 50%的稀釋液是無刺激性的。[1]
- 皮膚致敏性：在對接觸性過敏文獻中，指出洗髮精、沐浴露、沐浴露和液體肥皂等沖洗產品中的椰油醯胺丙基甜菜鹼與化粧品過敏有關。由於對這些產品進行斑貼致敏測試可能會導致偽陽性和偽陰性反應，因此作者建議應單獨測試椰油醯胺丙基甜菜鹼。作者還建議將椰油醯胺丙基甜菜鹼納入美髮師和化粧師系列試驗，並瞭解到商業椰油醯胺丙基甜菜鹼使用濃度（1%在水中，約 0.3%活性）的是一種邊際刺激物，並非所有斑貼試驗陽性反應都顯示對椰油醯胺丙基甜菜鹼過敏。另一篇 Mowad 對接觸性過敏文獻評論將椰油醯胺丙基甜菜鹼描述為 2004 年的“年度接觸性過敏原”。由於椰油醯胺丙基甜菜鹼中的不純物可能導致過敏反應，作者建議在進行椰油醯胺丙基甜菜鹼的測試時，同時進行氨基胺和 DMAPA 的皮膚般貼試驗。作者進一步建議，對醯氨基胺(AMIDOAMINE)或 3,3-二甲基氨基丙胺(DMAPA)檢測呈陽性的患者應避免使用含有椰油醯胺丙基甜菜鹼的產品。[1]
- 致突變性/遺傳毒性：美國化學委員會總結使用鼠傷寒沙門氏菌菌株 TA1535、TA1537、TA1538、TA98 和 TA100 進行的椰油醯胺丙基甜菜鹼（未說明濃度）有和無代謝激活致突變性測試結果。測試濃度以 1、4、16、64 或 256 mg/plate（無 S-9 激活）和 4、16、64、256 和 1024 mg/plate（有 S-9 激活）進行測試。不論有或沒有代謝激活，椰油醯胺丙基甜菜鹼沒有增加突變頻率，不具致突變性。[1]
- 光毒性：30 名人類參與者測試 3.0%活性椰油醯胺丙基甜菜鹼水溶液誘發接觸性光致敏的可能性。在誘導試驗期間，11 名同時接受

UVA 和皮膚最低致紅斑劑量(minimal erythema dose，MED) UVB 照射（來源光譜未說明）參與者，受照射部位出現輕度至中度紅斑反應，這些反應僅來自暴露於 UVB 照射。在本研究中，椰油醯胺丙基甜菜鹼不是光致敏劑。[1]

- 其他安全資料：化粧品成分審查(CIR)專家小組已多次評估椰油醯胺丙基甜菜鹼和相關醯胺丙基甜菜鹼(Amidopropyl Betaine)成分的安全性。1991 年，CIR 專家小組審查現有已發表的科學文獻，並得出結論認為椰油醯胺丙基甜菜鹼在現有文獻報告的使用劑量下可安全用於沖洗型化粧品。由於在較高使用濃度下可能會刺激皮膚，但 CIR 專家小組建議，對於打算長時間駐留在皮膚上的化粧品（即免洗型產品），椰油醯胺丙基甜菜鹼的濃度不應超過 3 %。根據顯示椰油醯胺丙基甜菜鹼(Cocamidopropyl Betaine, CAPB)使用數量大幅增加的資訊，包括氣霧劑產品的新用途，以及使用沖洗型產品的患者出現過敏性皮膚反應的報告，2012 年 CIR 專家小組對椰油醯胺丙基甜菜鹼和其他相關醯胺丙基甜菜鹼進行審查，主要調查涉及椰油醯胺丙基甜菜鹼和其他相關醯胺丙基甜菜鹼中是否存在 3,3-二甲基氨基丙胺(DMAPA)和醯胺基胺，3,3-二甲基氨基丙胺和醯氨基胺有時會引起皮膚致敏反應。然而，CIR 專家小組審查的文獻表明，當 3,3-二甲基氨基丙胺和醯胺胺的劑量降低時，過敏反應的人數也會減少。基於對已發表的科學文獻的審查，CIR 專家小組得出結論，化粧品使用椰油醯胺丙基甜菜鹼和相關的醯胺丙基甜菜鹼是安全的，被配製成製劑不致敏。椰油醯胺丙基甜菜鹼和相關的醯胺丙基甜菜鹼成分有可能形成亞硝胺的副產物。亞硝胺是由胺（例如食品中的蛋白質或化粧品成分上的胺側基）與所謂的亞硝化劑（例如在食品中用作防腐劑的亞硝酸鹽）反應形成的有機物質。CIR 專家小組建議不要將椰油醯胺丙基甜菜鹼和相關的醯胺丙基甜菜鹼用於含有亞硝化劑的產品中。[2]
- 參考資料：

1. Final Report of the Cosmetic Ingredient Review Expert Panel on the Safety Assessment of Cocamidopropyl betaine (CAPB). International Journal of Toxicology 31(Supplement 1) 77S-111S. CIR, 2012.
2. Cosmetics Info 網站：https://www.cosmeticsinfo.org/ingredients/cocamidopropyl-betaine/

3. INCI name：Sodium Methyl 2-Sulfolaurate

2-磺基月桂酸甲酯鈉(Sodium Methyl 2-Sulfolaurate)查無相關毒理試驗相關數據，根據其結構式：$C_{13}H_{25}NaO_5S$，交互參照 Fatty acids, C12-18 (even numbered)-methyl esters, sulfonated, sodium salts ($C_{13}H_{25}NaO_5S$ - $C_{19}H_{37}NaO_5S$, mono sodium salts)相關毒理資訊。

- 急性毒性：根據 OECD 402 和歐盟方法 B.3 進行研究，以評估 Fatty Acids, C12-18 (even numbered)-methyl esters, sulfonated, sodium salts 在 Sprague-Dawley 大鼠中的急性皮膚毒性。一組 10 隻大鼠（5 隻雄性和 5 隻雌性）以 2000mg/kg bw 的劑量在完整皮膚上進行 24 小時半封閉皮膚斑貼試驗。試驗 14 天後觀察大鼠，然後犧牲動物進行大體病理檢查。研究期間沒有動物死亡，沒有發現全身毒性的現象，皮膚刺激的跡象是非常輕微到明確的紅斑、非常輕微的水腫、皮膚毛細血管輕微出血、脫皮和皮膚彈性喪失。給藥後 3 至 7 天，施用部位表現正常。在研究期間，所有大鼠都顯示出預期的體重增加，除了一隻雌性動物在第一週體重下降，第二週體重增加。屍檢時未發現異常現象。在 Sprague-Dawley 大鼠中，Fatty acids, C12-18 (even numbered)-methyl esters, sulfonated, sodium salts 急性皮膚致死劑量 LD_{50} 被確定為>2000 mg/kg bw。[1]
- 重複劑量毒性：通過管飼法以 15、150 和 1000 mg/kg bw/day 的劑量，連續 28 天向三組 Sprague-Dawley CD 系大鼠（每組 5 隻雄性和 5 隻雌性）口服 Fatty acids, C12-18 (even numbered)-methyl esters, sulfonated, sodium salts。5 隻雄性和 5 隻雌性對照組僅給予蒸餾水。在研究期間監測臨床體徵、體重以及食物和水的消耗。評估所有動物的血液學和血液化學，並進行大體屍檢及組織病理學評估。結果顯示非腺胃上皮的棘層肥厚和角化過度，但不表示對動物健康造成嚴重損害，並且確定未觀察到的不良反應劑量(NOAEL)為 150 mg/kg bw/day。[1]
- 皮膚刺激性：在根據 OECD 404 和 EU B.4 方法進行的研究中，將用水潤濕的 Fatty Acids, C12-18 (even numbered)-methyl esters, sulfonated, sodium salts 試驗品在半封閉條件下施用於三隻紐西蘭白兔的去毛背部 4 小時。4 小時後，用蒸餾水浸泡的棉花輕輕擦拭皮膚，去除任何剩餘的測試物。去除貼片後約 1 小時，以及 24、48 和 72 小時後，檢查試驗部位是否存在原發性刺激，並根據 Draize

評分表進行評分。在去除貼片後 1 小時、24 小時和 48 小時，在所在觀察測試皮膚部位時，在一隻白兔測試皮膚部位觀察到非常輕微的紅斑。在所有測試中，72 小時後均未發現任何影響。在去除貼片一小時後，在兩隻白兔測試皮膚部位發現非常輕微的水腫，但在 24 小時的觀察中沒有出現。根據本研究，Fatty Acids, C12-18 (even numbered)-methyl esters, sulfonated, sodium salts 未被歸類為皮膚刺激物。[1]

- 皮膚致敏性：在根據 OECD 406 和歐盟委員會指令 92/69/EEC（Magnusson & Kligman 最大化測試）B6 方法進行的一項研究中，研究 Fatty acids, C12-18 (even numbered)-methyl esters, sulfonated, sodium salts 在天竺鼠中的皮膚致敏潛力，20 隻測試天竺鼠和 10 隻對照天竺鼠用於主要研究。根據目測結果，誘導階段和激發階段的 Fatty acids, C12-18 (even numbered)-methyl esters, sulfonated, sodium salts 測試濃度選擇如下：蒸餾水中 0.1 %w/v 進行皮內誘導及局部誘導，結果顯示在 2/19 (11 %) 的測試動物中產生反應。因此得出結論，Fatty acids, C12-18 (even numbered)-methyl esters, sulfonated, sodium salts 未被歸類為致敏物。[1]
- 致突變性/遺傳毒性：根據體外細菌回復突變試驗(OECD 471 and EU Method B.14)，對於任何劑量的 Fatty acids, C12-18 (even numbered)-methyl esters, sulfonated, sodium salts，任何細菌菌株不論在有或沒有代謝激活的情況下都沒有記錄到回復菌落數量的顯著增加，是非誘變性的 Fatty acids, C12-18 (even numbered)-methyl esters, sulfonated, sodium salts。根據體外染色體畸變試驗(OECD 473 and EU Method B.10)，不論在存在或不存在肝酶代謝系統的情況下，Fatty acids, C12-18 (even numbered)-methyl esters, sulfonated, sodium salts 在毒理學上未誘導具有畸變的細胞或多倍體細胞的顯著頻率增加，並且在體外被證明對人體細胞沒有致 DNA 斷裂性，不具致突變性。[1]
- 生殖毒性：在以 Fatty acids, C12-18 (even numbered)-methyl esters, sulfonated, sodium salts 類似物以 OECD 422 進行研究中，通過管飼法對 Crj:CD (SD) IGS 大鼠（10 隻動物/性別/dose) 以 0、5、20、80 或 300 mg/kg bw/day 進行測試。在整個交配和妊娠期間，雄性從交配前第 14 天給藥 47 天，雌性從交配前 14 天到哺乳第 4 天給藥 42-45 天。對發情週期、交配指數、妊娠長度、黃體數量沒有化合物相

關的影響。在哺乳的第 0 天和第 4 天，在幼鼠中未檢測到化合物對數量、性別比、體重或生存力的影響。在哺乳期死亡的幼鼠和預定犧牲的幼鼠中沒有觀察到被認為可歸因於施用 Fatty acids, C12-18 (even numbered)-methyl esters, sulfonated, sodium salts 類似物的異常發現，在任何組的幼鼠中也沒有發現外部或內部畸形。基於這些發現，雄性和雌性大鼠的生殖/發育毒性的未觀察到不良反應劑量 NOAEL 被認為是 300 mg/kg bw/day（測試的最高劑量）。[1]

◆ 參考資料：

1. ECHA 註冊檔案網站：
   https://echa.europa.eu/registration-dossier/-/registered-dossier/23426/7/3/4

4. INCI name：Sodium Sulfate

◆ 急性毒性：遵循 OECD 423 方法，進行一項研究，以評估硫酸鈉(Sodium Sulfate)對 Wistar 大鼠的急性經口毒性。禁食(17-20 小時)後 1 組 3 隻雌性大鼠(無對照)，通過管飼法給予 1 劑含 2000 mg/kg 硫酸鈉的聚乙二醇(PEG 300)溶液。給藥後 48 小時未發現相關臨床症狀或硫酸鈉相關死亡，另一組 3 隻雌性大鼠（無對照）與第一組相同。觀察所有 6 隻大鼠 15 天，沒有觀察到對體重或總體病理學的影響。一隻大鼠在給藥後立即因管飼灌食程序而死亡，這與硫酸鈉處理無關，據此研究雌性大鼠試驗硫酸鈉 LD_{50} > 2000 mg/kg。[1,2]

◆ 重複劑量毒性：對口服 4 至 6 g/day 硫酸鈉的人類受試者（有結腸息肉病史）進行為期 14 天的研究，結果發現沒有產生不利影響。在一項為期 4 週的重複劑量研究中，對在水中隨意口服硫酸鈉的哺乳期仔豬進行觀察，結果顯示：增加 1800 mg/L 硫酸鈉的水攝入量，600、1200 和 1800 mg/L 硫酸鈉的腹瀉發生率增加，但在這些濃度下，對生長速度沒有負面影響，死亡率也沒有增加。在對兔進行 3 個月重複劑量皮膚毒性研究期間，經皮給藥硫酸鈉(2 mL/kg bw/day；16%w/w)對臨床症狀和死亡率、體重和體重增加、器官重量和大體病理學皆無影響。 血液學結果無生物學意義，組織病理學結果顯示，唯一與試驗相關的皮膚損傷是亞急性皮炎。[1,2]

◆ 皮膚刺激性/致敏性：在皮膚刺激和致敏實驗中，使用類似於 OECD 411-亞慢性皮膚毒性的方法進行為期 90 天的皮膚毒性研究，以確定硫酸鈉對紐西蘭白兔的影響。8 隻兔子在經皮暴露於 2 mL/kg

bw/day 的 16% (w/w)硫酸鈉時表現出輕度至中度亞急性皮炎，這被認為是 LOAEL 值。在本研究中，3 隻對照兔表現出輕度亞急性皮炎。在 4 小時的封閉斑貼覆蓋試驗中，確定 500 mg 硫酸鈉對家兔無刺激性。在使用 50%硫酸鈉（在 PEG 300 中）的激發劑量的天竺鼠最大化試驗(Guinea Pig Maximization Test, GPMT)中，硫酸鈉被認為是不易致敏的。[1,2]

- 致突變性/遺傳毒性：使用硫酸鈉對鼠傷寒沙門氏菌(5000 mg/plate [4 次稀釋])、中國倉鼠肺纖維細胞 V79 (1420.0 mg/mL)和小鼠淋巴瘤 L5178Y 細胞 (1420 mg/mL)進行研究，對基因毒性和細胞毒性呈陰性。對中國倉鼠肺纖維細胞的檢測對多倍體細胞也呈陰性。硫酸鈉不具致突變性及遺傳毒性。[1,2]
- 生殖/發育毒性：在雄性和雌性大鼠中以高達 1000 mg/kg bw/day 硫酸鈉的劑量透過管飼法給藥，除軟便外沒有異常結果。另一項對大鼠進行的透過管飼法給予高達 1000 mg/kg bw/day 的硫酸鈉的研究沒有發現異常結果，並報告生殖/發育毒性終點的 NOEL 為 1000 mg/kg bw/day。[1,2]
- 毒物代謝動力學：在人類受試者中，進行實驗以量測口服硫酸鈉後尿液中游離硫酸鹽的回收率。以 18.1 g 十水硫酸鈉單劑量或 4 等分分次給藥，給藥後 24 和 72 小時尿液中檢測到的硫酸鹽，分別為 36.4%和 53.4（單次給藥）和 43.5%和 61.8%（分次給藥），給予單劑量 18.1 g 硫酸鈉的受試者在給藥後 2 至 24 小時出現嚴重腹瀉。[1,2]
- 人體數據：人類受試者（5 名健康人、5 名哮喘患者）暴露於硫酸鈉氣霧劑（質量中值空氣動力學直徑為 0.5 mm），濃度為 3 mg/m^3，持續 10 分鐘。結果顯示，與對照組氯化鈉相比，暴露於硫酸鈉後 1 小時內的肺功能無差異，但 2 例哮喘患者的強制呼氣量(forced exhalation volume, FEV1)減少 15%至 20%。在一隨後對暴露於硫酸鈉氣霧劑(3 mg/m^3，持續 10 分鐘；暴露後 3 小時量測記錄肺功能)進行的人類受試者（6 名健康人、 6 名哮喘患者）試驗中，與對照組氯化鈉相比，對肺功能沒有不利影響。兩名哮喘患者暴露於硫酸鈉或氯化鈉後，強制呼氣量 FEV1 下降 15%至 20%。對於職業暴露於濃度高達 150 mg/m^3 硫酸鈉粉塵的工人，測量心肺、胃腸道或肝腎參數時，與一般情況相比，未發現與長期暴露（2 個月至 31 年）相關的異常。此外，肺功能、血清硫酸鹽、鈣和電解質均正常。[1,2]

- 其他安全資料：在評估硫酸鈉的安全性時，CIR 專家小組依靠其普遍被認為是安全的(Generally Recognized As Safe, GRAS)狀態排除對許多研究的需要。此外，提交的皮膚刺激和致敏數據解決 CIR 專家小組對已發表文獻中缺乏此類研究的擔憂。CIR 專家小組認為，這些數據足以得出結論，硫酸鈉在沖洗型配方中是安全的。然而，由於其中一些配方在皮膚斑貼測試條件下會產生刺激，因此 CIR 專家小組將硫酸鈉在駐留型產品中的使用量限制在 1%。[3]
- 參考資料：

1. Final Amended Safety Assessment of Sodium Sulfate as Used in Cosmetics. International Journal of Toxicology 2021, Vol. 40(Supplement 1) 86S –94S. CIR, 2021.
2. Final Amended Safety Assessment of Sodium Sulfate as Used in Cosmetics. CIR, 2016.
3. Cosmetics Info 網站：https://www.cosmeticsinfo.org/ingredients/sodium-sulfate/

5. INCI name：Disodium 2-Sulfolaurate

2-磺基月桂酸二鈉(Disodium 2-Sulfolaurate)查無相關毒理試驗數據，根據其結構式：$C_{12}H_{22}Na_2O_5S$，交互參照 Fatty acids, C12-18 (even numbered)-methyl esters, sulfonated, sodium salts ($C_{12}H_{22}Na_2O_5S$ - $C_{18}H_{34}Na_2O_5S$ disodium salts)相關毒理資訊。

- 急性毒性：根據 OECD 402 和歐盟方法 B.3 進行研究，以評估 Fatty acids, C12-18 (even numbered)-methyl esters, sulfonated, sodium salts 在 Sprague-Dawley 大鼠中的急性皮膚毒性。一組 10 隻大鼠（5 隻雄性和 5 隻雌性）以 2000mg/kg bw 的劑量在完整皮膚上進行 24 小時半封閉皮膚斑貼試驗。試驗 14 天後觀察大鼠，然後犧牲動物進行大體病理檢查。研究期間沒有動物死亡，沒有發現全身毒性的現象，皮膚刺激的跡象是非常輕微到明確的紅斑、非常輕微的水腫、皮膚毛細血管輕微出血、脫皮和皮膚彈性喪失。給藥後 3 至 7 天，施用部位表現正常。在研究期間，所有大鼠都顯示出預期的體重增加，除了一隻雌性動物在第一週體重下降，第二週體重增加。屍檢時未發現異常。在 Sprague-Dawley 大鼠中，Fatty acids, C12-18 (even numbered)-methyl esters, sulfonated, sodium salts 急性皮膚致死劑量 LD_{50} 被確定為>2000 mg/kg bw。[1]

- 重複劑量毒性：通過管飼法以 15、150 和 1000 mg/kg bw/day 的劑量，連續 28 天向三組 Sprague-Dawley CD 系大鼠（每組 5 隻雄性和 5 隻雌性）口服 Fatty acids, C12-18 (even numbered)-methyl esters, sulfonated, sodium salts。5 隻雄性和 5 隻雌性對照組僅給予蒸餾水。在研究期間監測臨床體徵、體重以及食物和水的消耗。在研究結束時評估所有動物的血液學和血液化學，並進行大體屍檢及組織病理學評估。結果顯示非腺胃上皮的棘層肥厚和角化過度，但不表示對動物健康造成嚴重損害，並且確定未觀察到不良反應劑量(NOAEL)為 150 mg/kg bw/day。[1]
- 皮膚刺激性：在根據 OECD 404 和 EU B.4 方法進行的研究中，將用水潤濕的 Fatty acids, C12-18 (even numbered)-methyl esters, sulfonated, sodium salts 試驗品在半封閉條件下施用於三隻紐西蘭白兔的去毛背部 4 小時。4 小時後，用蒸餾水浸泡的棉花輕輕擦拭皮膚，去除任何剩餘的測試物。去除貼片後約 1 小時，以及 24、48 和 72 小時後，檢查試驗部位是否存在原發性刺激，並根據 Draize 評分表進行評分。在去除貼片後 1 小時、24 小時和 48 小時，在所在觀察測試皮膚部位時，在一隻白兔測試皮膚部位觀察到非常輕微的紅斑。在所有測試中，72 小時後均未發現任何影響。在去除貼片一小時後，在兩隻白兔測試皮膚部位發現非常輕微的水腫，但在 24 小時的觀察中沒有出現。根據本研究，Fatty acids, C12-18 (even numbered)-methyl esters, sulfonated, sodium salts 未被歸類為皮膚刺激物。[1]
- 皮膚致敏性：在根據 OECD 406 和歐盟委員會指令 92/69/EEC（Magnusson & Kligman 最大化測試）B6 方法進行的一項研究中，研究 Fatty acids, C12-18 (even numbered)-methyl esters, sulfonated, sodium salts 在天竺鼠中的皮膚致敏潛力，20 隻測試天竺鼠和 10 隻對照天竺鼠用於主要研究。根據目測結果，誘導階段和激發階段的 Fatty acids, C12-18 (even numbered)-methyl esters, sulfonated, sodium salts 測試濃度選擇如下：蒸餾水中 0.1 %w/v 進行皮內誘導及局部誘導，結果顯示在 2/19 (11 %) 的測試動物中產生反應。因此得出結論，Fatty acids, C12-18 (even numbered)-methyl esters, sulfonated, sodium salts 未被歸類為致敏物。[1]
- 致突變性/遺傳毒性：根據體外細菌回復突變試驗(OECD 471 and EU Method B.14)，對於任何劑量的 Fatty acids, C12-18 (even numbered)-

methyl esters, sulfonated, sodium salts，任何細菌菌株不論在有或沒有代謝激活的情況下都沒有記錄到回復菌落數量的顯著增加，是非誘變性的 Fatty acids, C12-18 (even numbered)-methyl esters, sulfonated, sodium salts。根據體外染色體畸變試驗(OECD 473 and EU Method B.10)，不論在存在或不存在肝酶代謝系統的情況下，Fatty acids, C12-18 (even numbered)-methyl esters, sulfonated, sodium salts 在毒理學上未誘導具有畸變的細胞或多倍體細胞的顯著頻率增加，並且在體外被證明對人體細胞沒有致 DNA 斷裂性，不具致突變性。[1]

- 生殖毒性：在以 Fatty acids, C12-18 (even numbered)-methyl esters, sulfonated, sodium salts 類似物以 OECD 422 進行研究中，通過管飼法對 Crj:CD (SD) IGS 大鼠（10 隻動物/性別/dose）以 0、5、20、80 或 300 mg/kg bw/day 進行測試。在整個交配和妊娠期間，雄性從交配前第 14 天給藥 47 天，雌性從交配前 14 天到哺乳第 4 天給藥 42-45 天。對發情週期、交配指數、妊娠長度、黃體數量沒有化合物相關的影響。在哺乳的第 0 天和第 4 天，在幼鼠中未檢測到化合物對數量、性別比、體重或生存力的影響。在哺乳期死亡的幼鼠和預定犧牲的幼鼠中沒有觀察到被認為可歸因於施用 Fatty acids, C12-18 (even numbered)-methyl esters, sulfonated, sodium salts 類似物的異常發現，在任何組的幼鼠中也沒有發現外部或內部畸形。基於這些發現，雄性和雌性大鼠的生殖/發育毒性的未觀察到不良反應劑量 NOAEL 被認為是 300 mg/kg bw/day（測試的最高劑量）。[1]
- 參考資料：

1. ECHA 註冊檔案網站：
https://echa.europa.eu/registration-dossier/-/registered-dossier/23426/7/3/4

6. INCI name：Potassium Cocoyl Glycinate

椰油醯甘氨酸鉀(Potassium Cocoyl Glycinate)是由椰子醯氯(coconut acid chloride)和甘胺酸(Glycine)反應形成的醯胺鉀鹽。[2]

- 急性毒性：通過皮膚施用 2000mg/kg bw 的測試物質(脂肪酸、可可衍生物、與甘氨酸、鉀鹽的反應產物；Fatty acids, coco derivs., reaction products with glycine, potassium salts)處理五隻雄性和五隻雌性 Wistar 大鼠。測試物質以聚乙二醇 300 (Polyethylene Glycol 300)為賦型劑配製，施用期限為 24 小時。在 14 天的觀察期後，犧牲所有動物進行屍檢並進行肉眼檢查，在整個觀察期間沒有死亡發生，也沒有記錄到臨床症狀。唯一與物質相關的影響包括觀察期間一隻雄性和兩隻雌性出現非常輕微至輕微的紅斑和/或水腫形式皮膚刺激反應。屍檢時未觀察到肉眼可見的發現，根據研究結果，對兩性大鼠單次皮膚給藥後乾燥的測試物質 LD_{50} >2000 mg/kg bw。[1]
- 重複劑量毒性：在一項為期 28 天的研究中，測試物質(脂肪酸、可可衍生物、與甘氨酸、鉀鹽的反應產物；Fatty acids, coco derivs., reaction products with glycine, potassium salts)透過管飼法以 0 (10 隻雄性和 10 隻雌性)、62.5 (5 隻雄性和 5 隻雌性)、250 (5 隻雄性和 5 隻雌性)和 1000 (10 隻雄性和 10 隻雌性) mg/kg bw/day 的劑量對 Wistar 大鼠進行測試。即使在最高劑量下，也沒有任何不良反應發生，因此全身毒性的 NOAEL 確定為 1000 mg/kg bw/day。[2]
- 皮膚腐蝕性/刺激性：在一項根據 OECD 404 指引體內研究中，通過局部半封閉施用 0.5 mL 椰油醯甘氨酸鉀結構類似物或替代物應用於三隻紐西蘭白兔的完整左腹，施用時間為 4 小時。在去除敷料後 1、24、48 和 72 小時以及 7、10 和 14 天進行皮膚反應評分。在任何測量時間間隔內，對任何動物的處理過的皮膚都沒有發現腐蝕作用，也沒有觀察到臨床症狀。根據結果，該物質不被視為皮膚刺激物。[1]
- 眼睛刺激性：根據 OECD 405 指引對椰油醯甘氨酸鉀結構類似物或替代物進行初級眼刺激測試。將 0.1 mL 測試品塗於 3 隻紐西蘭白兔的左眼結膜中，右眼作為對照。在施用後 1、24、48 和 72 小時以及 7 天進行評估。在研究期間，在動物中沒有觀察到全身毒性的臨床症狀，也沒有發生死亡。滴注後 24、48 和 72 小時分別計算每隻動物的角膜混濁、虹膜紅腫和結膜水腫的平均評分。所有三隻動

物的角膜混濁和虹膜的個體平均得分均為 0.00。結膜的個體平均評分對於發紅分別為 1.67、2.00 和 1.67，對於結膜水腫分別為 2.00、1.33 和 2.00。滴注後 1 至 72 小時，所有動物的結膜均出現輕度至中度變紅，且在所有動物中觀察到結膜輕度至顯著腫脹（眼瞼半閉），一隻動物的瞬膜出現中度變紅，在所有動物中記錄到輕微至中度的眼部分泌物。滴注後 7 天，在任何動物的治療眼中均未觀察到異常發現。不論在任何觀察時間都沒有觀察到角膜腐蝕。[1]

- 皮膚致敏性：在一項依據 OECD 429 進行的研究中，雌性小鼠在雙耳背側局部暴露於丙酮/橄欖油(Acetone/Olive Oil, AOO)中濃度為 1%、10%和 25%的測試物質(脂肪酸、可可衍生物、與甘氨酸、鉀鹽的反應產物；Fatty acids, coco derivs., reaction products with glycine, potassium salts)連續三天，對照小鼠用 AOO（賦形劑對照）或以參考物質（陽性對照）AOO 中含 10%和 30%的濃度己基肉桂醛(Hexyl Cinnamic Aldehyde, HCA)處理。三天後犧牲小鼠，從每隻小鼠塗藥耳朵上切下小塊並稱重。切除耳下引流淋巴結，稱重，並製備單細胞懸浮液，測量淋巴結細胞懸浮液的細胞計數，並根據耳朵腫脹的顯著反應和淋巴結細胞計數的增加，計算測試物質和參考物質的分化指數(Differentiation index, DI)。DI 說明皮膚引流淋巴結細胞活化（淋巴結細胞計數指數）和皮膚炎症（耳重指數）之間的關係，DI > 1 表示化學誘導的過敏反應（皮膚致敏），而 0< DI <1 顯示受試物質的刺激效力。由於沒有劑量反應，因此不應將測試物質評估為皮膚致敏劑。[1]
- 致突變性/遺傳毒性：測試物質(脂肪酸、可可衍生物、與甘氨酸、鉀鹽的反應產物；Fatty acids, coco derivs., reaction products with glycine, potassium salts)的遺傳毒性在細菌基因突變試驗、體外哺乳動物染色體畸變試驗和小鼠體內微核試驗三項研究中進行試驗。整體而言，沒有跡象表明測試物質具有誘導突變/遺傳毒性潛力。[1]
- 生殖毒性：測試物質(脂肪酸、可可衍生物、與甘氨酸、鉀鹽的反應產物；Fatty acids, coco derivs., reaction products with glycine, potassium salts)以 62.5、250 和 1000 mg/kg bw/day 的劑量溶解於水中管飼給藥 Wistar 大鼠，對照組僅接受水。測試物質在配對前對雄性大鼠給藥 28 天，對雌性大鼠給藥 14 天，直至 F1 代達到產後第 4 天。在任何劑量下均未觀察到對交配性能、生育能力、黃體計數或妊娠持續時間的影響。[1]

◆ 參考資料：

1. ECHA 註冊檔案網站：
https://echa.europa.eu/registration-dossier/-/registered-dossier/27867/7/5/1
2. Safety Assessment of Amino Acid Alkyl Amides as Used in Cosmetics. International Journal of Toxicology 2017, Vol. 36(Supplement 1) 17S-56S. CIR, 2017.

7. INCI name：Potassium Cocoate

◆ 急性毒性：透過口胃管將未稀釋的椰子油以 5 g/kg bw 的單劑量給予 10 隻大鼠。在 7 天的觀察期內沒有死亡發生。[3]

◆ 重複劑量毒性：椰油酸鉀(Potassium Cocoate)交叉參照二十二烷酸(Docosanoic Acid, CAS No. 112-85-6)哺乳動物毒性試驗數據。在 OECD 422 研究中，大鼠（13 隻/性別/劑量）透過口服管飼法暴露於 0、100、300 或 1000 mg /kg bw /day 的二十二烷酸。雄性的暴露期為 42 天，對於雌性暴露期為從交配前 14 天到泌乳第 3 天（最少暴露 39 天）。大鼠沒有發生死亡或一般生理狀況變化，沒有體重增加或食物消耗變化，也沒有不利的組織病理學、血液學或生化影響。NOAEL 為 1000 mg /kg bw /day (測試的最高劑量)。[4]

◆ 皮膚刺激性：評估椰油酸鉀對已患有皮膚炎的參與者皮膚刺激潛力。用 15 mL 的 5% 椰油酸鉀水溶液對 40 名健康志願者和 480 名患有皮膚病的參與者皮膚進行斑貼測試。在 5 名(2 名參與者患有銀屑病，3 名患有濕疹)參與者(0.9%)中觀察到陽性反應，沒有說明陽性反應的強度。[1]

◆ 皮膚致敏性：在一項雙盲隨機對照試驗研究中，12 名已知對椰油醯胺丙基甜菜鹼(Cocamidopropyl Betaine, CAPB)有過敏反應之參與者以 100%濃度的椰子油和幾種椰子油衍生物進行斑貼測試，證實不是過敏原。[1]

◆ 致突變性/遺傳毒性：在幾個原核生物系統中評估皂化椰子油(saponified coconut oil, SCO) 的遺傳毒性潛力。用 SCO 處理的質體沒有 DNA 鏈斷裂。在未進行代謝激活的 Ames 試驗中，SCO 對鼠傷寒沙門氏菌菌株 TA98 沒有致突變性，但對菌株 TA100 和 TA104 顯示出誘變潛力。[1]

◆ 生殖毒性：在 OECD 422 研究中，大鼠（13 隻/性別/劑量）透過口

服管飼法暴露於 0、100、300 或 1000 mg /kg bw /day 的二十二烷酸(Docosanoic Acid, CAS No. 112-85-6)。雄性的暴露期為 42 天，對於雌性暴露期為從交配前 14 天到泌乳第 3 天（最少暴露 39 天）。對性腺功能、交配行為、受孕或分娩的發育沒有影響。生殖毒性 NOAEL ≥1000 mg /kg bw /day (測試的最高劑量)。[4]

- 其他安全資料：椰油酸鉀已通過化粧品成分 (CIR)專家小組審查，CIR 專家小組評估科學數據並得出結論，椰子油和椰子酸以及由椰子油和椰子酸製成的其他成分可安全用作化粧品成分。CIR 專家小組審查急性、慢性和亞慢性口服毒性研究，認為椰子油和氫化椰子油都不會產生明顯的皮膚或眼睛刺激，沒有過敏相關報告，含有椰子油和其他椰子油衍生成分的化粧品和個人護理產品的臨床評估產生的皮膚刺激反應非常小。在人體測試後，沒有跡象說明這些成分是主要刺激物、致敏劑或光毒性化合物。基於之前審查過的椰子油和其他成分的安全性，CIR 專家小組認為審查的所有椰子油衍生成分都可安全用於化粧品和個人護理產品。[2]
- 參考資料：

1. Final Report on the Safety Assessment of Cocos nucifera (Coconut) Oil and Related Ingredients. International Journal of Toxicology 30(Supplement 1) 5S-16S. CIR, 2011.
2. Cosmetics Info 網站：https://www.cosmeticsinfo.org/ingredients/potassium-cocoate/
3. Amended Safety Assessment of Cocos Nucifera (Coconut) Oil, Coconut Acid, Hydrogenated Coconut Acid, Hydrogenated Coconut Oil, Ammonium Cocomonoglyceride Sulfate, Butylene Glycol Cocoate, Caprylic/Capric/Coco Glycerides, Cocoglycerides, Coconut Alcohol, Coconut Oil Decyl Esters, Decyl Cocoate, Ethylhexyl Cocoate, Hydrogenated Coco-Glycerides, Isodecyl Cocoate, Lauryl Cocoate, Magnesium Cocoate, Methyl Cocoate, Octyldodecyl Cocoate, Pentaerythrityl Cocoate, Potassium Cocoate, Potassium Hydrogenated Cocoate, Sodium Cocoate, Sodium Cocomonoglyceride Sulfate, Sodium Hydrogenated Cocoate, and Tridecyl Cocoate. CIR, 2008.
4. SIDS Initial Assessment Profiles Agreed In The Course Of The Oecd Cooperative Chemicals Assessment Programme In 2014. OECD, 23 November 2017.

8. INCI name：Sodium Methyl Cocoyl Taurate

- 不純物：據報導甲基牛磺酸鈉(Sodium Methyltaurate)的純度為87.0%~96.0% (w/w)。不純物是氫氧化鈉(Sodium Hydroxide)和 2-羥基乙磺酸鈉(Sodium 2-Hydroxyethanesulfonate.)。[1]
- 急性毒性：甲基椰油醯基牛磺酸鈉(Sodium Methyl Cocoyl Taurate)的大鼠皮膚 LD_{50} 為>2000 mg/kg bw，大鼠口服 LD_{50} 為>2000 mg/kg bw。[1]
- 重複劑量毒性：在大鼠 14 天口服毒性研究中，甲基椰油醯基牛磺酸鈉和甲基油醯牛磺酸鈉(Sodium Methyl Oleoyl Taurate)的未觀察到不良反應劑量(NOAEL)均為≥1000 mg/kg bw/day。在大鼠高達 1000 mg/kg bw/day 甲基椰油醯基牛磺酸鈉的 28 天口服毒性研究中沒有出現臨床症狀。[1]
- 皮膚腐蝕性/刺激性：對 11 名受試者（n = 8 名女性，3 名男性）進行甲基椰油醯基牛磺酸鈉（溶解在蒸餾水中 40%；pH 7）封閉斑貼試驗。將 50 mm^2 的貼片施用於上背部 24 小時。在移除後 30 分鐘、24 和 48 小時觀察測試部位。2 名受試者在 24 小時出現輕微至明確的紅斑，1 名受試者在 48 小時出現，9 名受試者未觀察到反應。[1]
- 皮膚致敏性：在根據 OECD 406 在雌性 Pirbright-White 天竺鼠（n = 20；對照= 10）中進行的 Buehler 致敏試驗中，以 100%甲基椰油醯基牛磺酸鈉在封閉下進行表皮誘導，在 20%水溶液中進行激發，也在封閉下進行。在給藥後 24 和 48 小時觀察激發部位。在誘導期間或激發之後沒有觀察到反應，得出的結論是甲基椰油醯基牛磺酸鈉不致敏。[1]
- 致突變性/遺傳毒性：甲基椰油醯基牛磺酸鈉最高 320 µg/mL 沒有代謝激活，和最高 240 µg/mL 有代謝激活時，在哺乳動物細胞微核試驗中沒有基因毒性。甲基椰油醯基牛磺酸鈉最高 100 µg/mL 沒有代謝激活，和最高 120 µg/mL 有代謝激活時，在哺乳動物細胞沒有基因毒性。[1]
- 參考資料：

1. Safety Assessment of Alkyl Taurate Amides and Taurate Salts as Used in Cosmetics. CIR, 2015.

9. INCI name：Glycol Distearate

- 不純物：乙二醇(Ethylene glycol)和/或環氧乙烷(Ethylene oxide)用於合成硬脂酸乙二醇酯（Glycol stearate）的起始原料，這些原料預計也將用作相關成分乙二醇二硬脂酸酯(Glycol Distearate)的原料。已知前者被不純物痕量的 1,4-二惡烷污染，所以這種痕量也可能出現在最終合成的原料中。含有乙二醇二硬脂酸酯產品混合物的安全資料表表明，未檢測到 1,4-二惡烷。[1]
- 急性毒性：乙二醇二硬脂酸酯已在四項研究中對大鼠急性經口毒性進行測試。在各種研究中，玉米油中 13g/kg bw (13000mg/kg bw)或更高劑量產生的影響包括腹瀉、濕油性皮毛和鼻出血，症狀在給藥後 4 天內出現，但在接下來的 6 天內消失。沒有動物單獨服用高劑量的玉米油。一項關於乙二醇二硬脂酸酯的研究報告指出 14 天的大體屍檢中，胃中含有測試物質殘留物。5000 mg/kg（2.5%溶解於羧甲基纖維素中）在 24 小時內以 2.2~2.3 mL 的劑量管飼 Sprague-Dawley 大鼠 (n = 5/sex)兩次，觀察 14 天，沒有發現死亡或臨床毒性跡象， LD_{50} > 5000 mg/kg。依據 OECD 401 方式在大鼠(未說明品種及數量)進行口服急毒性試驗，得出 LD_{50} > 2000 mg/kg。[1]
- 重複劑量毒性：兩種含有乙二醇二硬脂酸酯濃度範圍為 0.05%~0.5%配方在大鼠上測試，測試時間為 28 天。在包括血液學在內完整的肉眼和顯微鏡檢查後，沒有證據顯示全身毒性作用。測試 91 天，也沒有觀察到施用測試物質所誘導的全身毒性作用。一項單獨但類似的 28 天研究報告兩種配方，其中乙二醇二硬脂酸酯的濃度範圍為 0.05~0.4%，報告指出，與測試相關的組織中沒有“大體屍檢或顯微鏡下的改變”。以 0.05%和 0.3%的濃度向 10 隻兔子（5 隻雄性和 5 隻雌性）施用含有 1~3%乙二醇二硬脂酸酯的洗髮乳，四週後，施用試驗化合物未出現全身性影響或死亡。[1]
- 皮膚腐蝕性/刺激性：兩種含乙二醇二硬脂酸濃度範圍為 0.05%~0.5%配方在兔子體內試驗 28 天，根據報告、由表面活性劑引起的皮膚刺激從輕微到嚴重不等。將含有 1~3%乙二醇二硬脂酸酯的洗髮水以 0.05%和 0.3%的濃度分別施用於 10 隻兔子（5 隻雄性和 5 隻雌性）。在 0.05% 濃度的一隻兔子和 0.3%濃度下大多數兔子觀察到輕微的短暫皮膚刺激。以 Draize 測試乙二醇二硬脂酸酯對白化兔子皮膚的主要刺激，發現這些成分是無刺激性到輕微刺激性。

此外，當對乙二醇二硬脂酸酯進行腐蝕性測試時，發現它對兔子皮膚沒有腐蝕性。[1]

- 皮膚致敏性：在天竺鼠中對硬脂酸乙二醇酯和乙二醇二硬脂酸酯進行致敏研究。將 0.1%二種成分皮內注射到兩隻雄性白色天竺鼠鼠的剃毛背部。在最初的 0.05 mL 注射後，每週進行 3 次 0.1 mL 注射，總共注射 10 次。兩週後給予激發注射，並在 24 小時後讀取讀數。發現這兩種成分都不會引起過敏。對 125 名年齡在 19~76 歲之間的受試者使用 50% w/v 在礦物油中乙二醇二硬脂酸酯的進行重複損傷皮膚斑貼試驗。將含有 0.25g 樣品的貼片塗抹在每個人的上臂背面 24 小時，在每週一、週三和週五將貼片施用於同一部位進行為期三週的誘導。每個部位的刺激評分共 9 次。在最後的皮膚損傷斑貼後 14 天，將誘導貼片應用於每個受試者的雙臂；在 48 和 96 小時後對這些部位的致敏反應進行分級。在任何受試者中均未觀察到具有刺激或致敏特徵的可見皮膚變化。[1]
- 生殖毒性：根據 OECD 414（產前發育毒性研究）和 EU B.31 方法（產前發展毒性研究）進行的研究中，Sprague-Dawley CD 大鼠（n=24）於妊娠期 6 至 15.5 天透過管飼法給藥乙二醇二硬脂酸酯（0、100、300 或 900 mg/kg bw/day；C16-18 混合物）。對照組接受 0.5%羧甲基纖維素鈉(sodium carboxymethylcellulose)和 0.25%Cremophor® 蒸餾水溶液。在妊娠期 20 天犧牲雌鼠並進行屍檢。檢查產仔數和體重、存活率、性別比和明顯異常。還檢查幼鼠的外部、內臟和骨骼異常，在研究期間無死亡病例。與對照組相比，試驗組未觀察到乙二醇二硬脂酸酯相關症狀。體重、體重增加和校正體重均在預期範圍內。與對照組相比，試驗組的平均生殖數據沒有觀察到差異。 屍檢顯示，試驗組的母體沒有宏觀變化，在試驗組中未觀察到與試驗物質相關的影響。屍檢時未發現與治療相關的胎兒異常。根據此結果，大鼠母體致畸性毒性 NOAEL> 900 mg/kg bw/day。[1]
- 人體數據：兩家生產硬脂酸乙二醇酯和乙二醇二硬脂酸酯已有 20 至 30 年的歷史製造商報告指出，沒有員工報告說他或她的健康可能因接觸這些化合物而受到不利影響。該結論基於：(a)30 名員工在 10 年內可能在 1%的工作時間內接觸過硬脂酸乙二醇酯；(b)70 名員工 20 年來可能在 20%的工作時間中接觸過乙二醇二硬脂酸酯；(c)50 名員工在 30 年內可能在 5% 工作時間內接觸過硬脂酸乙二醇酯。一家製造商指出，其員工流動率非常低，因此一些人在公司生

產的許多年裡一直接觸這些成分。[1]

- 其他安全資料：CIR 安全審查指出使用 50%乙二醇二硬脂酸酯進行的重複損傷斑貼試驗沒有發現皮膚刺激或過敏的跡象。[2]
- 參考資料：

1. Safety Assessment of Monoalkylglycol Dialkyl Acid Esters as Used in Cosmetics. CIR, 2017.
2. Cosmetics Info 網站：https://www.cosmeticsinfo.org/ingredients/glycol-distearate/

10. INCI name：Coco-Glucoside

- 急性毒性：參考其他類似之烷基糖苷(Alkyl Glucosides)成分試驗數據。在使用兔子進行的辛基/辛基葡萄糖苷(caprylyl/capryl glucoside)和 C10-16 烷基葡萄糖苷的單劑量皮膚研究中，LD_{50} 大於給予的 2 g/kg 劑量。在使用辛基/辛基葡萄糖苷的口服研究中，小鼠給藥 2 g/kg 的和大鼠給藥 C10-16 烷基糖苷(C10-16 alkyl glucoside) 5 g/kg，均未發生在研究期間動物死亡現象。[1]
- 重複劑量毒性：參考其他類似之烷基糖苷(Alkyl Glucosides)成分試驗數據。在使用兔子進行的為期 2 週重複劑量皮膚研究中，封閉施用辛基/辛基葡萄糖苷會產生睾丸效應，而非封閉施用則不會。無法確定睾丸效應的 NOEL，但附睾、攝護腺和膀胱腺的微觀效應 NOEL 為 0.14 g/kg。在非閉塞性研究中，全身毒性的 NOEL 為 0.18 g /kg 辛基/辛基葡萄糖苷，但尚不清楚其影響是否與測試品有關。封閉性研究中觀察到嚴重的皮膚刺激，而非封閉性研究呈現輕微至中度刺激。[1]
- 皮膚刺激性：在臨床研究中，以 2.0%椰油烷基糖苷電離物質水溶液在貼片上對表皮進行皮膚的刺激性評估，另外 1.0%椰油烷基糖苷電離物質水溶液以肥皂刺激性腔室法(soap chamber tests)進行測試，椰油烷基糖苷具輕微刺激性。[1]
- 皮膚致敏性：以人體重複性封閉型斑貼試驗(Human Repeat Insult Patch Test, HRIPT) 測試 1%椰油烷基糖苷電離物質水溶液對 213 名患者的致敏潛力，以 0.2 mL 待測物質於封閉貼片 24 小時，持續 3 週，9 個施用部位，結果顯示沒有刺激性或致敏性。[1]
- 毒物代謝動力學：參考其他類似之烷基糖苷(Alkyl Glucosides)成分試驗數據。在使用人體皮膚樣本進行的體外皮膚吸收研究中，10%辛

基/辛基葡萄糖苷(Caprylyl/Capryl Glucoside)的平均吸收劑量為0.01%。在管飼給藥的雌性小鼠中，辛基葡萄糖苷在胃、腸、肝臟（僅有微量未發生變化）和腎臟中最高。在大鼠的餵養研究中，大部分攝入的乙基葡萄糖苷(Ethyl Glucoside)在尿液中回收。[1]

- 其他安全資料：尚未發現烷基葡萄糖苷成分具有遺傳毒性。含有烷基葡糖苷成分的產品臨床試驗發現，這些產品不是皮膚刺激物或致敏劑。根據審查的數據，CIR 專家小組得出結論，烷基糖苷成分（包括癸基葡萄糖苷、月桂烷基糖苷、花生烷基葡萄糖苷、辛基/辛基葡萄糖苷和椰油烷基糖苷）在配製為無刺激性的情況下可安全用於化粧品中。[2]
- 參考資料：

1. Safety Assessment of Decyl Glucoside and Other Alkyl Glucosides as Used in Cosmetics. International Journal of Toxicology 32(Supplement 3) 22S-48S. CIR, 2013.
2. Cosmetics Info 網站：https://www.cosmeticsinfo.org/ingredients/coco-glucoside/

11. INCI name：Glyceryl Oleate

- 急性毒性：大鼠口服單劑量含有 5%油酸甘油酯(Glyceryl Oleate)的防曬製劑 13 mL/kg 沒有產生毒性跡象和致死性。[1]
- 重複劑量毒性/生殖發育毒性：在雄性和雌性 Sprague-Dawley 大鼠中對油酸甘油酯進行生殖/發育毒性篩選試驗。雄性和雌性均在交配前每天一次通過管飼法給予 0、100、300 或 1000 mg/kg bw/day 的油酸甘油酯玉米油，持續 14 天；雄性再給藥 28 天，雌性給藥持續到泌乳第 4 天。對照組和 3 個試驗組各 12 隻雌性，對照組和高劑量組各 7 隻雄性，低劑量和中劑量組各 12 隻雄性。試驗組 5 隻雄性和 5 隻雌性給藥 42 天，給藥後觀察期為 14 天。全身毒性（雄性和雌性）、生育能力（雄性和雌性）和發育力（F1 代）的 NOAEL 為 1000 mg/kg bw/day。[1]
- 皮膚刺激性：玉米油中未稀釋和 50%濃度的油酸甘油酯用於兔子皮膚研究刺激性試驗中，發現具有輕微刺激性。0.5 mL 含有 5%油酸甘油酯的防曬劑配方在兔子身上產生紅斑和輕微水腫。每天使用 2.0 mL/kg 的含有油酸甘油酯的 25.0%玉米油溶液配方 20 天，會對兔子產生嚴重的皮膚刺激。在為期 4 週的皮膚毒性/光毒性研究中，

含有 5%油酸甘油酯不同濃度的 2 種防曬產品配方產生輕微的、可逆的皮膚刺激。兩種油酸甘油酯水性製劑（濃度分別為 15% 和 30%）和一種含有 19.0% 油酸甘油酯的香料製劑在使用人體皮膚單次損傷封閉斑貼試驗時，經測試對皮膚刺激呈陰性。[1]

- 皮膚致敏性：使用 107 名健康受試者，其中 93 人完成研究，在 以 Finn Chambers 中評估油酸甘油酯的皮膚刺激和致敏潛力。在石蠟油中以 50%的濃度測試油酸甘油酯，發現不會引起刺激或過敏。[1]
- 致癌性：在 TM 品系小鼠的 2 代研究中，該小鼠的飼料每天補充 50~100 毫克油酸甘油酯，油酸甘油酯給藥與少數腦瘤（63 隻小鼠中有 3 個腫瘤）的發生有關。在 TM 品系小鼠中發現消化道腫瘤，該小鼠每天餵食含 200 mg 油酸甘油酯飼料補充劑，持續 4 至 7 代，研究認為消化道腫瘤是由於游離脂肪酸不純物所致。[1]
- 其他安全資料：CIR 安全審查指出油酸甘油酯的代謝產物是甘油和油酸。甘油酯、甘油、油酸和油酸鈉的安全性數據支持油酸甘油酯的安全性。在皮膚刺激研究中，單次接觸未稀釋的油酸甘油酯只會產生輕微刺激。在為期 4 週的皮膚毒性/光毒性研究中，含有高達 5%的油酸甘油酯的產品配方產生輕微的可逆皮膚刺激。未稀釋的油酸甘油酯會產生輕微至中度的眼睛刺激。長期口服大劑量油酸甘油酯與腫瘤形成沒有明顯關聯。人體暴露於含有油酸甘油酯的配方中未觀察到刺激、致敏或光毒性作用。根據報告中包含的資訊，CIR 專家小組得出結論，油酸甘油酯作為化粧品成分是安全的。[2]
- 參考資料：

1. Safety Assessment of Monoglyceryl Monoesters as Used in Cosmetics. International Journal of Toxicology 2020, Vol. 39(Supplement 3) 93S-126S. CIR, 2020.
2. Cosmetics Info 網站：https://www.cosmeticsinfo.org/ingredients/glyceryl-oleate/

12. INCI name：Glyceryl Stearate

- 不純物：硬脂酸甘油酯可能含有甘油單酯、二酯和三酯(tri-Glyceride)雜質和脂肪酸雜質。[1]
- 急性毒性：在口服研究中，硬脂酸甘油酯的 LD_{50} > 5 g/kg bw。在亞慢性和慢性皮膚毒性試驗中，4%~5%硬脂酸甘油酯對兔子無毒，但確實會引起中度刺激（輕度至中度紅斑、水腫、肌張力乏力、脫屑

和/或龜裂）。在連續 3 代大鼠飲食中添加 15% ~ 25%的硬脂酸甘油酯沒有發現不良反應。餵食含 25%硬脂酸甘油酯 2 年的大鼠出現腎鈣化。[1]

- 重複劑量毒性/生殖毒性：在為期 28 天的口服毒性研究中，大鼠分別服用 0、100、300 和 1000 mg/kg/day 甘油酯、C8-18 和 C18-不飽和單-和二-乙酸酯，聚乙二醇(PEG)重複劑量毒性研究中，每組另外包括 10 隻雌性 Wistar Han 大鼠，以評估生殖和發育毒性。在給藥至少 14 天後，生殖研究組的雌性與來自同一試驗組的雄性同住。對受試雌性給藥總共 41 至 49 天，即在交配前 2 週、交配期間、交配後和至少 4 天的哺乳期。未觀察到與試驗相關的影響，雌雄生育力的 NOAEL 為 1000 mg/kg bw/day。[1]
- 皮膚刺激性：在人體重複性封閉型斑貼試驗(Human Repeat Insult Patch Test, HRIPT)臨床測試中，5%硬脂酸甘油酯沒有刺激性。[1]
- 皮膚致敏性：據報導，濃度高達 100%的硬脂酸甘油酯和硬脂酸甘油酯/SE 對兔子皮膚有輕微刺激性或無刺激性。在 7 項天竺鼠致敏研究中，得出的結論是 0.1%硬脂酸甘油酯和 0.1%硬脂酸甘油酯 SE 均不能誘發致敏。[1]
- 致癌性：以 50~100 mg/day 或 1.5%的劑量餵食小鼠直至死亡，硬脂酸甘油酯不會分別誘導顯著的腦瘤或胃腫瘤形成。5%的硬脂酸甘油酯不會促進 9,10 二甲基苯並[α]蒽在小鼠皮膚中的致癌性。[1]
- 光毒性：含有 2%硬脂酸甘油酯的產品無光毒性和光敏性。[1]
- 其他安全資料：CIR 專家小組審查硬脂酸甘油酯的長期研究，這些研究表明對生殖沒有不利影響，也沒有致癌作用。對含有硬脂酸甘油酯和硬脂酸甘油酯 SE 產品的人體暴露研究以及臨床經驗說明，這些化合物是非致敏性、非光毒性和非光敏性的。[2]
- 參考資料：

1. Safety Assessment of Monoglyceryl Monoesters as Used in Cosmetics. International Journal of Toxicology 2020, Vol. 39(Supplement 3) 93S-126S. CIR, 2020.
2. Cosmetics Info 網站：https://www.cosmeticsinfo.org/ingredients/glyceryl-stearate/

13. INCI name：Citric Acid

- 急性毒性：檸檬酸(Citric Acid)在 10 隻兔子施用 5 g/kg bw 皮膚急性試驗中，無症狀發生，LD_{50} 為>5 g/kg。[1]
- 重複劑量毒性：已經進行許多檸檬酸重複劑量研究，儘管可能不符合當前的測試要求，但它們仍然表明在所使用的測試條件下缺乏任何顯著的毒理學影響。在大鼠中進行的 5 天餵養研究得出的 NOAEL 值為 4000 mg/kg (Bachtold, 1976a)；在小鼠和大鼠中進行的為期 10 天的餵養研究得出的 NOAEL 值分別為 1000 mg/kg 和 4000 mg/kg（Bachtold, 1978a）。[2]
- 皮膚刺激性：在兔子的刺激性研究中，30%的檸檬酸不是主要刺激物，60%的檸檬酸會產生一些隨時間消退的紅斑和水腫，未稀釋的檸檬酸會產生輕度至重度的紅斑和輕度至中度的水腫。[1]
- 眼睛刺激性：在體外研究中，檸檬酸被預測為中度/重度至重度/極度眼部刺激物，濃度為 10%時對兔眼睛的刺激性最小，濃度為 30%時對兔眼有輕微刺激性。[1]
- 皮膚致敏性：在致敏性測試中，含有 4%檸檬酸的去角質霜對人體沒有刺激性或致敏性。以 2.5%檸檬酸水溶液在 91 名蕁麻疹或血管性水腫患者皮膚以檸檬酸點刺激試驗，有 3 名產生陽性結果。[1]
- 致突變性/遺傳毒性：檸檬酸及其鹽和酯在體外和體內遺傳毒性試驗中大多為陰性，不具致突變性。[1]
- 毒物代謝動力學：口服檸檬酸吸收佳和大量代謝，外源性和內源性檸檬酸可以被完全代謝並作為能量來源。檸檬酸是 Krebs（或三羧酸）循環的中間體，檸檬酸完成由葡萄糖經由糖解形成丙酮酸的分解，並釋放二氧化碳。人體每天會形成和代謝約 2 kg 的檸檬酸，檸檬酸鹽被認為可在腎臟的腎小球自由過濾，65%~ 90%的過濾檸檬酸鹽在人體中被重新吸收。經過濾的 10%~35%的檸檬酸鹽隨尿液排出，人體正常的血液檸檬酸鹽劑量約為 25 mg/L。[1]
- 人體數據：透過將人類精子懸浮在檸檬酸溶液中來確定檸檬酸的殺精作用。向人類精子中添加 0.1%的檸檬酸會降低 pH 值，並在 30 分鐘內使精子無法活動，而 1%的檸檬酸幾乎可以立即殺精。經由將酸添加到毛細管中的人宮頸粘液中來評估對宮頸粘液的精子穿透力影響。添加 0.01%的檸檬酸時降低精子的穿透力，添加 0.1%完全消除精子的穿透力。一名婦女在使用含有 10%檸檬酸（和其他未鑑定的化合物）的產品進行專業美容換膚手術 4 小時後，出現呼吸困難和嚴重的面部疼痛。患者的面部和頸部前部也有一級和二級燒

傷，造成永久性的面部和頸部疤痕，但沒有氣管病變。[1]

- 其他安全資料：含有檸檬酸及其一些鹽和酯可以安全地配製應用於嬰兒皮膚或眼部附近或黏膜的產品。此外，還可用於化粧品噴霧劑，包括頭髮、除臭劑、身體和其他推進劑和泵噴霧產品。檸檬酸也是一組稱為α羥基酸(Alpha Hydroxy Acids)的成分之一，可用作化學皮膚換膚中的活性成分。檸檬酸及其二銨鹽、鉀鹽和鈉鹽都用於透過螯合來幫助保存化粧品和個人護理產品。檸檬酸及其鹽也被添加到化粧品中，幫助調節酸鹼平衡。[3]
- 參考資料：

1. Safety Assessment of Citric Acid, Inorganic Citrate Salts, and Alkyl Citrate Esters as Used in Cosmetics. International Journal of Toxicology 2014, Vol. 33(Supplement 2) 16S-46S. CIR, 2014.
2. ECHA 註冊檔案網站：https://echa.europa.eu/registration-dossier/-/registered-dossier/15451/7/6/1
3. Cosmetics Info 網站：https://www.cosmeticsinfo.org/ingredients/citric-acid/

14. INCI name：Benzoic Acid

- 不純物：在食品中，苯甲酸(Benzoic Acid)和苯甲酸鹽具有釋放苯的潛力，包括在長波紫外線 (UVA) 存在的情況下。檢查包含在紫外線穩定和非紫外線穩定包裝中樣品的苯形成。選擇用 UVA 測試的一些樣品包括在無緩衝水中用 0.04%苯甲酸鹽 0.025%抗壞血酸製備的溶液。 24 小時 UV 研究的結果顯示，在強紫外線下，儲存在非紫外線穩定瓶中的溶液中，苯含量新增 53%（與暴露在可見光下溶液的苯[206 ng/g]相比，達到 315 ng/g）。 然而，使用紫外線穩定的聚對苯二甲酸乙二醇酯(polyethylene terephthalate)瓶，與非紫外線穩定瓶相比，苯的生成減少 13%，照射 7 天後觀察到類似的趨勢。[1]
- 急性毒性：根據 OECD SIDS 關於苯甲酸鹽的初步評估報告指出，苯甲酸及其鈉鹽和鉀鹽有關低急性經口毒性 LD_{50}>2,000 mg/kg bw。[1]
- 重複劑量毒性：根據 OECD SIDS 關於苯甲酸鹽的初步評估報告，重複劑量口服苯甲酸毒性研究得出的未觀察到的不良反應劑量(NOAEL)為 800 mg/kgb w/day。在較高劑量下，觀察到死亡率增加、

體重增加減少以及對肝臟和腎臟的影響。在與苯甲醇、苯甲酸、苯甲酸鈉和苯甲酸鉀一起給藥後，觀察到類似性質的全身毒性作用（例如，肝臟和腎臟）。[1]

- 皮膚刺激性：根據 OECD SIDS 關於苯甲酸鹽的初步評估報告，苯甲酸和苯甲醇對皮膚有輕微刺激性，而苯甲酸鈉無刺激性。[1]
- 皮膚致敏性：根據 OECD SIDS 關於苯甲酸的初步評估報告，苯甲酸在動物研究中沒有引起過敏，在皮膚病患者貼片測試中觀察到陽性反應的發生率較低。幾十年來，職業性接觸苯甲醇、苯甲酸或苯甲酸鈉並未導致皮膚過敏。[1]
- 致癌性：使用一組 120 隻 Eppley 瑞士小鼠（每一性別各 60 隻）進行皮膚彩繪研究。將含有 2.0%苯甲醇和 0.016%苯甲酸的非氧化性染髮劑以 0.05 mL 劑量塗在皮膚上，每週 3 次，持續 20 個月。每次使用前 24 小時將部位剃光，每週使用一瓶新染料。研究九個月後，10 隻小鼠/性別/組被犧牲。試驗組和對照組之間的體重和存活率差異不大，在包括對照組在內的所有組中都發現不同程度的慢性皮膚炎症。在接受試驗的雌性(23/60)中注意到惡性淋巴瘤的顯著增加 ($P < 0.01$)。然而，研究人員指出，一個對照組的該腫瘤類型的發病率非常低（7/60 或 12%）。另一個對照組的發病率為 22%，在之前的研究中，3 個對照組的平均發病率為 33%。因此，惡性淋巴瘤研究結果不被認為與試驗物質有關。這種小鼠品系中常見的肺腺瘤和肝血管瘤的發病率在試驗組和對照組之間相似。未觀察到異常腫瘤。[1]
- 致突變性/遺傳毒性：根據 OECD SIDS Johnson 等人對苯甲醇、苯甲酸及其鈉鹽和鉀鹽的 15S 初步評估報告顯示，在體外 Ames 測試中均沒有致突變性。使用 L5178Y TK +克隆 3.7.2C 小鼠淋巴瘤細胞，在 250 到 1,000 mg/mL（有和沒有代謝活化）的微核試驗中評估苯甲酸（在二甲基亞碸中）。不含苯甲酸的培養物作為陰性對照，絲裂黴素 C (Mitomycin-C)作為陽性對照。苯甲酸在測試的濃度範圍內無論是否有代謝激活都沒有遺傳毒性。[1]
- 生殖毒性：根據 OECD SIDS 關於苯甲醇、苯甲酸及其鈉鹽和鉀鹽的初步評估報告，在一項 4 代生殖毒性研究中，每組每性別各 20 隻大鼠組在飲食中連續接受 375 或 750 mg/kg bw/day 的苯甲酸劑量。第三代動物在 16 週後被犧牲，結果發現苯甲酸不會對生殖造成影響，NOAEL 為>750 mg/kgbw/day。[1]

- 經皮吸收：透過天竺鼠切除背側皮膚（全層並去除角質層）的測試苯甲酸滲透。皮膚製劑置於 2 擴散槽(chamber diffusion cell)中，將過量苯甲酸在鹽水中的懸浮液添加到供藥腔室中。在全層皮膚中，滲透的延遲時間很短。苯甲酸的溶解度（Cd, 單位 mM）和滲透性（Kp, 單位 X $10^{-2}cm^2/h$）係數分別為 32.7+1.6 和 9.01+ 1.51。透過膠帶剝離去除角質層並使用有機溶劑混合物將其脫脂增強苯甲酸的皮膚滲透性。[1]
- 毒物代謝動力學：苯甲酸和苯甲酸鈉(Sodium Benzoate)都能迅速從哺乳動物的胃腸道吸收，並在肝臟中與甘氨酸(Glycine)結合，產生的馬尿酸(Hippuric Acid)會迅速從尿中排出。[1]
- 人體數據：在一名有紅斑和搔癢症病史 46 歲女性，使用含 5%苯甲酸凡士林，出現過敏陽性反應。[1]
- 參考資料：

1. Safety Assessment of Benzyl Alcohol, Benzoic Acid and its Salts, and Benzyl Benzoate. International Journal of Toxicology 2017, Vol. 36(Supplement 3) 5S-30S. CIR, 2017.

15. INCI name：PEG-150 Pentaerythrityl Tetrastearate

- 急性毒性：使用 10 隻 Wistar 白化大鼠（5 隻雄性，5 隻雌性；6~9 週齡）評估 25% PEG-150 季戊四醇四硬脂酸酯(PEG-150 Pentaerythrityl Tetrastearate)水懸浮液的急性經口毒性。每隻動物接受 5 g/kg bw 的單次口服劑量。給藥後觀察 14 天，並進行大體屍檢。 沒有一隻動物死亡，LD_{50} >5 g/kg。[1]
- 重複劑量毒性：在已發表的文獻中未發現關於 PEG-150 季戊四醇四硬脂酸酯重複給藥毒性的數據，也未提供未發表的數據。[1]
- 皮膚刺激性：使用 6 隻紐西蘭白兔（3 個月大）研究未稀釋的 PEG-150 季戊四醇四硬脂酸酯的皮膚刺激潛力。將測試物質(0.5 mL) 施用於脊柱兩側的 2 個部位（1 個損傷，1 個完整）。施用部位封閉 24 小時，然後在施用後 24 和 72 小時評估紅斑、水腫和其他影響。 測試物質不會引起原發性皮膚刺激（原發性刺激指數 2.65）。[1]
- 皮膚致敏性：在受試者使用未稀釋的 PEG-150 季戊四醇四硬脂酸酯（53 名受試者）或該成分的 25%水溶液（52 名受試者）進行人體重複性封閉型斑貼試驗(Human Repeat Insult Patch Test, HRIPT)，未觀察到皮膚刺激或致敏作用。[1]

- 致癌性：已發表的文獻中未發現有關 PEG-150 季戊四醇四硬脂酸酯的致癌性數據，也未提供未發表的數據。[1]
- 致突變性/遺傳毒性：PEG-150 季戊四醇四硬脂酸酯在使用以下鼠傷寒沙門氏菌菌株 TA98、TA100、TA1535、TA1537 和 TA1538 進行的 Ames 試驗中，無論是否有代謝活化皆沒有遺傳毒性。[1]
- 生殖毒性：在已發表的文獻中未發現有關 PEG-150 季戊四醇四硬脂酸酯的生殖或發育毒性的數據，也未提供未發表的數據。[1]
- 參考資料：

1. Safety Assessment of PEG-150 Pentaerythrityl Tetrastearate as Used in Cosmetics. International Journal of Toxicology 2018, Vol. 37(Supplement 2) 5S-9S. CIR, 2018.

16. INCI name：PPG-2 Hydroxyethyl Cocamide

- 不純物：據報導 PPG-2 羥乙基椰油醯胺的純度> 90%，甲醇含量通常<300 ppm，重金屬含量<0.5 ppm。[1]
- 急性毒性：PPG-2 羥乙基椰油醯胺在 Sprague-Dawley 大鼠中的皮膚 LD_{50} > 2000 mg/kg。在大鼠中，PPG-2 羥乙基椰油醯胺的口服 LD_{50} >2000 mg/kg。[1]
- 重複劑量毒性：根據 OECD 407，3 隻雄性和 3 隻雌性白化大鼠組透過管飼法給予 0、100、500 或 1000 mg/kg/day PPG-2 羥乙基椰油醯胺 7 天，所有動物都存活到研究終止。用最高劑量觀察到的短暫流涎被認為是不顯著的，對腎臟、肝臟或脾臟的重量沒有影響。屍檢時未觀察到明顯的損傷。未進行臨床化學、血液學和顯微鏡檢查，沒有觀察到毒性的證據。在根據 OECD 407 進行的為期 28 天的研究中，5 隻雄性和 5 隻雌性白化大鼠組通過管飼法給予 0、100、500 或 1000 mg/kg/day PPG-2 羥乙基椰油醯胺 28 天。沒有死亡發生，在所有測試組的一些動物中觀察到短暫的給藥後流涎。沒有臨床化學或血液學參數與試驗相關的變化。尿液參數的變化包括高劑量組雄性尿量和尿磷減少以及尿液 pH 值升高，以及高劑量組雄性和高、中劑量組雌性尿鉀降低，病理變化不支持這些變化。絕對和相對胸腺重量的輕微降低不被認為具有毒理學意義。在三隻高劑量組雄性大鼠中觀察到的局灶性嗜鹼性皮質小管不被認為與試驗物質相關。NOEL 為 15 mg/kg bw/day，NOAEL 為 1000 mg/kg bw/day。[1]

- 皮膚刺激性：將未稀釋的 PPG-2 羥乙基椰油醯胺塗抹在兔皮膚上 4 小時（2.5 cm^2 的貼片，含有 0.5 ml 測試物質）被歸類為有刺激性、產生皮膚增厚、脫屑和明顯紅斑，但暴露 3 分鐘和 1 小時沒有刺激性。[1]
- 皮膚致敏性：在天竺鼠 Magnusson-Kligman 最大化研究中，PPG-2 羥乙基椰油醯胺（皮內誘導:0.5%、局部誘導:50%、局部激發: 5%和 10%；在水中）不是致敏劑。[1]
- 致癌性：已發表的文獻中未發現有關致癌性研究。[1]
- 致突變性/遺傳毒性：PPG-2 羥乙基椰油醯胺在濃度高達 5000 µg/plate 的 Ames 測試中，無論有或沒有代謝激活沒有致突變性。在哺乳動物染色體畸變研究中，PPG-2 羥乙基椰油醯胺在高達 250 µg/ml 的濃度，無致畸突變性。[1]
- 參考資料：

1. Safety Assessment of Alkoxylated Fatty Amides as Used in Cosmetics. CIR, 2019.

17. INCI name：Glycerin

- 不純物：美國藥典國民處方集(USP-NF)標準規定甘油中任何單體雜質的含量不得超過 0.1%，所有雜質（包括二甘醇 Diethylene Glycol 和乙二醇 Ethylene Glycol）的總量不得超過 1%。[1]
- 急性毒性：大鼠口服 LD_{50} 2530~58400 mg/kg。大鼠皮膚 LD_{50}>21900 mg/kg bw。據研究顯示，針對人類甘油的口服 LD_{50} 為 1428 mg/kg。當人類口服 30 ml 甘油時，沒有毒性跡象。當作為藥物口服給藥時，對人類的不良反應包括輕度頭痛、頭暈、噁心、嘔吐、口渴和腹瀉。[1]
- 重複劑量毒性：當雜種犬口服給藥 3 天時的 NOAEL 為 950 mg/kg bw/day，在劑量 3800 mg/kg bw/day 時，胃粘膜嚴重充血並伴有點狀出血。當雜種狗在飼料中加入 35%甘油時，在 36 週後體重減輕。天竺鼠口服 6300 mg/kg bw/day 甘油 30 至 40 天未見病理變化。當人類患者口服大約 1300 至 2200 mg/kg bw/day 甘油 50 天時，沒有出現毒性或對血液或尿液產生影響的跡象，NOAEL 為 2200 mg/kg bw/day。當 100%甘油每天局部施用於兔子 30%的體表 45 週時，沒有任何效應。[1]
- 皮膚腐蝕性/刺激性：刺激眼睛和皮膚的可能性極小。[1]

- 皮膚致敏性：非皮膚致敏物。[1]
- 致癌性：非致癌性物質。[1]。
- 致突變性/遺傳毒性：既沒有致突變性也沒有遺傳毒性。[1]
- 生殖毒性：非生殖毒性物質。[1]。
- 毒物代謝動力學：來自人類和動物研究的數據顯示，甘油在腸道和胃中迅速被吸收，並分佈在細胞外。由於甘油的 Log Pow(-2.66 至-1.76)較低且缺乏其他研究數據，甘油的皮膚吸收率設定為 80%。[2]
- 人體數據：一名 29 歲女性因眼瞼、面部、頸部、頭皮和腋窩出現斑片狀濕疹 7 個月就診。根據歐洲化粧品和美髮系列標準，對她自己的化粧品和洗漱用品進行 Patch Test，她在第 4 天對二甲氨基丙胺（1%水溶液）和她自己的手部保濕霜有 a+陽性反應。對該保濕霜成分的進一步測試在第 4 天對甘油（1%水溶液）有 a+陽性反應，當她避免使用含甘油的化粧品時，她的濕疹得到緩解。[1]。
- 其他安全資料：2014 年化粧品成分審查專家小組對支持用於化粧品和個人護理產品的甘油安全性科學數據進行徹底審查，並根據現有文獻和數據，專家小組得出結論： 甘油在目前的使用和濃度實驗中是安全的（即在免沖洗類產品中高達 79%，在沖洗類產品中高達 99%）。美國食品和藥物管理局承認甘油在食品包裝中的使用是一般公認安全的(GRAS)，並且在按照優良製造規範使用時，它是一種多用途的 GRAS 食品物質。此外，甘油已獲得美國食品和藥物管理局批准用於 OTC 藥物，例如肛門直腸藥物產品、皮膚保護劑、眼科藥物和口腔保健產品。可用的甘油科學數據顯示，單次和重複劑量使用後，口服和皮膚不良反應較低。此外，數據顯示在人體臨床研究中沒有報告過敏性皮膚反應。在多項實驗室繁殖和發育安全性研究中，甘油不會對親代繁殖能力或其後代的生長發育、生育力或繁殖性能產生任何不利影響。在對製造合成甘油的男性員工進行的一項人類生育研究中，與使用化粧品的消費者相比，他們預期會接觸到更高暴露量，與使用化粧品的組別相比，在精子數量或正常形狀精子的百分比方面沒有觀察到差異。此外，多項實驗室研究顯示，在口服天然和合成甘油長達兩年的情況下，甘油不會導致基因突變，也沒有證據顯示腫瘤發生率會增加（即甘油不會導致癌症）。[3]。
- 參考資料：

1. Safety Assessment of Glycerin as Used in Cosmetics, International Journal of Toxicology, Vol.38(Supplement 3), 6S-22S, CIR, 2019.

2. SIDS Initial Assessment Report For SIAM 14 . Glycerol CAS N°: 56-81-5, 2002.
3. Cosmetics Info 網站：https://cosmeticsinfo.org/ingredient/glycerin-0

18. INCI name：Phenoxyethanol

- 不純物：潛在雜質苯酚(Phenol)<10 ppm、環氧乙烷(Ethylene oxide)<2 ppm。[1]
- 急性毒性：所有給藥 681 mg/kg bw Wistar 大鼠在 14 天的觀察期內皆存活。所有雄性大鼠在 1470 mg/kg bw 的劑量施用後存活，而 5 隻雌性大鼠中有 2 隻死亡。在 3160 mg/kg bw 的劑量下，分別有 2 隻雄性和 4 隻雌性死亡。在最高劑量下，3 隻雄性和所有雌性死亡。通常，雌性比雄性更容易受到苯氧乙醇(Phenoxyethanol)的影響。臨床症狀包括呼吸困難、發冷、姿勢異常、蹣跚、乏力、疼痛和角膜反射不足、昏迷狀態、痙攣性步態、毛皮粗糙、乾燥、眼球突出和一般不良狀況。在研究過程中死亡的動物在屍檢時顯示出以下跡象：充血性充血、輕微膨脹的肺部和偶爾變紅的胃腺。根據以上試驗得出結論，雌性和雄性的 LD_{50} 分別為 1840 mg/kg bw 和 4070 mg/kg bw。整體雄性和雌性的 LD_{50} 為 2740 mg/kg bw。皮膚急性毒性研究中，2 mL/kg bw 苯氧乙醇施用於 4 隻紐西蘭白兔，14 天後犧牲動物進行大體屍檢，結果顯示在評估的任何主要器官中沒有大體病理學發現，包括心臟、肺、腦、胃腸道、肝臟和脾臟。在兩隻兔子中觀察到施用部位的局部紅斑，並且在給藥天內是可逆的。在給藥後第 3~14 天，在一隻兔子的施用部位觀察到脫屑。本研究中苯氧乙醇急性皮膚毒性的 LD_{50} >2214 mg/kg bw。[1]
- 重複劑量毒性：根據一份已發表的報告，每組 3 隻體重為 3~4.5 kg 的紐西蘭白兔連續 10 天分別以 100、300、600 或 1000 mg/kg bw/day 的劑量管飼苯氧乙醇。此外，6 隻雌性兔子在類似的時間內被給予蒸餾水（溶劑對照）。所有兔子每天接受一次劑量。在試驗的第 1、5 和 10 天記錄體重。屍檢時，採集血液樣本用於血液學量測、尿液分析和組織病理學分析的代表性器官切片並保存。在 600 和 1000 mg/kg bw/day 劑量組中，沒有一隻動物存活。在 300mg/kg bw/day 劑量組中，發現 1 隻動物在給藥後第 10 天死亡。毒性跡象的特徵是厭食、嗜睡和暗紅色尿液排泄。在第 5 天，每天服用 100、300 或 600 mg/kg bw/day 的兔子的平均體重較其暴露前體重下降約 8%，

較對照動物下降 10~14%。在第 10 天，100 和 300 mg/kg bw/day 劑量組的兔子繼續表現出類似的體重下降。對照組兔子在 10 天給藥期間表現出平均體重略有增加。從 1000、600 和 300 mg/kg bw/day 劑量組的兔子身上採集的尿液樣本表現出 pH 值降低，同時蛋白質、膽紅素、尿膽紅素和血紅蛋白水平升高。在 100 mg/kg bw/day 劑量組中至少 1 隻兔子觀察到尿液 pH 值降低和尿液膽紅素和紅血球增加。大多數兔子每天服用 1000 或 600mg/kg bw/day，表現出與溶血性貧血一致的嚴重病理改變，包括腎臟和脾臟腫大和發黑、膀胱尿色變深，會陰區域尿色變深。相反，用 100 或 300 mg/kg bw/day 管飼的兔子沒有與試驗相關的嚴重損傷。在所有劑量的兔子中都觀察到與試驗相關的微觀變化。在兩個高劑量組的大多數動物中，脾臟鏡下變化包括紅髓充血和巨噬細胞吞噬紅血球作用。兩個高劑量組的腎臟和胃也發生與試驗相關的微觀變化。在 300 mg/kg bw/day 劑量組中，1 隻兔子的脾臟在靜脈竇中出現血栓，導致全身性脾壞死，給予 100 mg/kg bw/day 的兩隻兔子有脾髓外造血。總結在這項研究中，兔子經口管飼苯氧乙醇 10 天，LOAEL 為 100 mg/kg bw/day。每組紐西蘭白兔雄性和雌性各 10 隻在開始給藥之前，並在研究過程中根據需要定期剪掉每隻動物背部的一個區域（大約 10 x 15cm）以去除毛髮。每組分別施用苯氧乙醇 0、50、 150、500 mg/kg bw/day 均勻地分佈在剪裁區域上。將吸水紗布和非吸水的封閉繃帶包紮於給藥區域背面，並固定在適當的位置。每次給藥後約 6 小時取下繃帶和護套，連續 13 週每週 5 天，對照組兔子每天接受 0.5 ml/kg bw/day 的蒸餾水。SCCS 認為這項研究是苯氧乙醇安全性評估的關鍵研究，因為應用於皮膚途徑是苯氧乙醇作為化粧品成分的相關途徑，並且兔子已被證明是對暴露於苯氧乙醇全身性血液毒性作用最敏感的物種。考慮到本研究中使用的給藥方案，NOAEL 應乘以 5/7 的係數，得出調整後的 NOAEL 為 357 mg/kg bw/day。[1]

- 皮膚刺激性：將 0.5 ml 苯氧乙醇施用於 3 隻維也納白兔的完整皮膚上，暴露 4 小時，面積為 2.5 cm^2 。封閉暴露後，去除貼片並用水/Lutrol (1:1) 清洗施用部位。觀察動物 72 小時，在去除貼片後 30~60 分鐘以及開始暴露後 24、48 和 72 小時對皮膚部位進行評分。3 隻動物中的 2 隻在 4 小時時間點的紅斑評分為 1。紅斑在 24 小時內是可逆的，所有 3 隻動物的紅斑評分在 24、48 和 72 小時均為 0，3 隻動物的水腫評分在所有時間點均為 0。在本研究的條件下，未

稀釋的苯氧乙醇對兔子皮膚沒有刺激性。[1]

- 眼睛刺激性：將 0.1 ml 未稀釋的苯氧乙醇滴注於 3 隻維也納白兔的右眼結膜囊中，測試物質沒有被洗掉，處理的眼睛作為對照。在滴注測試物質後的 1、24、48 和 72 小時以及 8 和 15 天進行評估。未稀釋的苯氧乙醇在 3 隻動物中都產生明顯的眼睛刺激跡象。在 1 小時內觀察到所有 3 隻動物的結膜發紅（評分 2）和腫脹（評分 2）以及分泌物（評分 1 或 2）；在 72 小時，2 隻動物仍觀察到發紅（評分 2）和 1 隻動物腫脹（評分 1）。所有動物的虹膜在 24 和 48 小時（評分 1）、兩隻動物在 72 小時（評分 1 和 2）和 1 隻動物在 8 天（評分 1）時受到影響。在 24、48、72 小時和 8 天（評分 1 或 2）和 1 隻動物在 15 天（評分 1）觀察到角膜混濁，整個角膜區域在 24、48 和 72 小時受到影響。刺激在施用後 48 至 72 小時之間最嚴重。此後，刺激消退，並且在 15 天後，只有 1 隻動物仍然表現出輕微的角膜混濁，影響不到 1/4 的受試驗眼睛角膜區域。在該測試條件下，苯氧乙醇對眼睛有刺激性。[1]
- 皮膚致敏性：用未稀釋的苯氧乙醇進行的表皮誘導導致所有測試組 Hsd Poc:DH 天竺鼠的結痂和中度和融合的紅斑和腫脹。在對照組或測試組動物中用未稀釋的測試物質在側腹進行激發試驗都沒有引起任何皮膚反應。在本研究的實驗條件下，苯氧乙醇不是皮膚致敏劑。[1]
- 致癌性：兩份來自大鼠和小鼠研究的總結報告，未檢測到腫瘤病變。[1]
- 致突變性：苯氧乙醇在一系列具有各種終點的體外和體內試驗中進行誘變/遺傳毒性潛力測試。苯氧乙醇在 Ames 試驗中在濃度高達 5000 µg/Plate 時，無論是否有代謝激活沒有致突變性。對哺乳動物細胞中 Hprt 基因座基因突變的進一步測試，無論有或沒有代謝激活都沒有發現誘變潛力。體外染色體畸變試驗未顯示有致染色體斷裂作用的證據。體內試驗也顯示苯氧乙醇沒有誘變/遺傳毒性潛力。在小鼠和大鼠中進行的體內微核和染色體畸變試驗顯示沒有證據說明存在致突變作用。在大鼠中測試 DNA 損傷也沒有顯示基因毒性的證據。因此，根據目前的報告，可以認為苯氧乙醇沒有體內基因毒性潛力，對人類沒有基因毒性危害，不需要額外的測試。[1]
- 生殖毒性：在小鼠中進行 0、0.25、1.25 和 2.5%苯氧乙醇的兩代生殖毒性研究。在最高劑量下，生育能力受到的影響很小，但在中等

和高劑量施用苯氧乙醇時，觀察到對後代有顯著毒性的證據。 在中等和高劑量下顯示父母毒性。對於雄性和雌性，父母毒性和生殖毒性的 NOAEL 被認為是飲食中的 0.25%。對於雄性，計算得出的 NOAEL 為 400 mg/kg bw/day，雌性的 NOAEL 約為 950mg/kg bw/day。有兩項關於發育毒性的研究，一項是大鼠口服研究，一項是兔子皮膚研究。在這兩項研究中，發育毒性的 NOAEL 均高於母體毒性的 NOAEL（兩項研究中均為 300 mg/kg bw/day）。[1]

- 經皮吸收：使用靜態和流通擴散細胞（大鼠皮膚）或流通擴散細胞（人體皮膚）評估皮膚吸收。將放射性標記的苯氧乙醇在 10 µl 甲醇中的擴散槽中施用於皮膚表面。對於大鼠皮膚研究，靜態細胞實驗的計算量為 272 µg/cm^2，流通細胞實驗的計算量為 1140 µg/cm^2。對於人體皮膚的研究，在流通池實驗中計算的應用量為 552 µg/cm^2。對於 MoS 計算，可以使用平均值± 1 SD：37% ± 10%，即 47%皮膚吸收率，用於沖洗型配方中的 1% 苯氧乙醇可以使用 78%±7%，即 85%皮膚吸收率用於 1%苯氧乙醇在免洗配方評估。[1]
- 人體數據：人體生物監測數據在毒物動力學部分進行討論。由於 苯氧乙酸是苯氧乙醇在人體中的主要代謝物，人體尿液樣本中苯氧乙酸的背景劑量數據說明，化粧品是消費者接觸苯氧乙醇的主要來源，已經有人類接觸致敏記錄，但從現有研究可以得出結論，這種情況很少見，致敏的風險非常低。[1]
- 其他安全資料：化粧品成分審查(CIR)專家小組於 1990 年透過審查可用的科學文獻和數據審查苯氧乙醇。認為苯氧乙醇不是皮膚刺激物，暨不屬於皮膚致敏劑，也不屬於光毒性物質。測試數據顯示，苯氧乙醇沒有基因毒性，也沒有全身毒性問題。因此，得出的結論是“在目前的使用和濃度中(通常< 1%)作為化粧品成分是安全的”。考慮到可用的新數據，在 2007 年對苯氧乙醇的審查中，CIR 重申最初的“使用安全”結論。[2]
- 參考資料：

1. SCCS OPINION ON Phenoxyethanol. SCCS/1575/16 Final version of 6 October 2016.
2. Cosmetics Info 網站：https://www.cosmeticsinfo.org/ingredients/phenoxyethanol/

19. INCI name：Caprylyl Glycol

- 急性毒性：辛甘醇(Caprylyl Glycol)和其他 1,2-乙二醇的急性經口毒性數據表明，在相對較高的劑量（LD_{50} 範圍：2200 至>20000 mg/kg bw）下會發生死亡。[1,2] 使用雄性和雌性大鼠（未說明數量和品系）評估辛甘醇的急性經口毒性。劑量≥ 464mg/kg 引起鎮靜和共濟失調。 具體而言，在 1000 mg/kg 劑量下觀察到肌肉張力喪失和呼吸困難，在 1470 mg/kg 劑量時觀察到側位、昏迷和死亡。給藥 2 小時內死亡，屍檢時，3160 和 4640mg/kgbw 劑量組觀察到灰白的實質器官。 存活動物 24 小時內恢復，215 mg/kg bw 是本研究中的無毒劑量，結果推估雄性大鼠 LD_{50} 為 2240 mg/kg bw 和雌性大鼠 LD_{50} 為 2200 mg/kg bw。在另一項涉及大鼠的研究（依據 OECD 423 測試）中，辛甘醇的 LD_{50}>2500 mg/kg。[2]
- 重複劑量毒性：在對>98%辛甘醇(Dermosoft Octiol)進行為期 28 天的口服毒性研究中，報告大鼠全身毒性的 NOEL 為 50 mg/kg bw/day 和 NOAEL 為 300 mg/kg bw/day。NOAEL 是基於發現對大鼠非腺體和限制性胃嵴刺激性；類似的結構在人類中不存在。[1]
- 皮膚刺激性：105 名受試者用含有 0.5%辛甘醇的口紅進行貼片測試在皮膚重複封閉型斑貼試驗(Repeat Insult Patch Test, RIPT test)中，皮膚刺激和致敏潛力的結果為陰性。[1,2]
- 眼睛刺激性：在體外眼刺激試驗(HET-CAM)中，中性油 1%的 SymClariol 和中性油中的辛甘醇（1%或 3%）被歸類為非刺激性物質。然而，在同一測定中以 1%的水溶液濃度（每種成分的有效濃度 0.5%）進行評估時，辛甘醇和 1,2-己二醇(1,2-Hexanediol)的 50:50 (w/w)混合物被歸類為嚴重的眼部刺激物。[1]
- 皮膚致敏性：在天竺鼠最大化試驗中，在凡士林中 50%辛甘醇的激發濃度下，結果為陰性。在 56 名受試者用 50:50 (w/w) 1,2-己二醇(1,2-Hexanediol)和辛甘醇混合物（Symdiol 68；每種成分的有效濃度 10%）進行 RIPT 中測試也未觀察到皮膚過敏。[1,2]
- 致突變性/遺傳毒性：辛甘醇>98% (Dermosoft Octiol)不會在中國倉鼠 V79 細胞中誘導基因突變（濃度高達 1480 mg/mL），而>98%辛甘醇 (ADEKA NOL OG)不會在體外誘導中國倉鼠肺細胞染色體畸變（濃度高達 700 mg/mL）。[1]
- 經皮吸收：在體外將 5%辛甘醇溶於 70%乙醇/30%PG（5%Dermosoft Octiol 多元醇防腐劑替代方案溶於酒精溶液）局部應用於雌性豬皮膚後，約 97%的測試溶液在施用後 24 小時內被皮膚吸收。基於辛

甘醇、1,2-己二醇、癸二醇和十二烷基二醇的皮膚滲透模組資訊，每 24 小時吸收的百分比劑量預設值為 80% 1,2-己醇和 1,2-辛二醇，40% 1,2-癸二醇與 1,2-十二烷二醇。己二醇、癸二醇、戊二醇、1,2-丁二醇和 1,2-己二醇的皮膚滲透增強作用已在體外得到證實。[1]

- 其他安全資料：戊二醇(Pentylene Glycol)、1,2-己二醇和辛甘醇是 1,2-乙二醇(1,2-glycol)化合物，僅因碳數而異。這些化合物中的每一個在第一個和第二個碳上都有一個羥基(-OH)。在碳鏈中，戊二醇有 5 個碳，1,2-己二醇有 6 個碳，辛二醇有 8 個碳。這些成分可用於嬰兒產品、沐浴產品、眼粧、清潔產品、護膚產品和護髮產品化粧品和個人護理產品中。[3]
- 參考資料：

1. Safety Assessment of 1,2-Glycols as Used in Cosmetics. International Journal of Toxicology 31(Supplement 2) 147S-168S. CIR, 2012.
2. Caprylyl Glycol as used in Cosmetics. CIR, 2010.
3. Cosmetics Info 網站：https://www.cosmeticsinfo.org/ingredients/caprylyl-glycol/

20. INCI name：Butylene Glycol

- 急性毒性：基於幾個物種的口服 LD_{50}> 10000 mg/kg bw，且大鼠在飽和蒸氣濃度下暴露 8 小時沒有致死效應，皮膚 LD_{50}>20000 mg/kg bw 以及腸胃外施用後的低毒性，認為丁二醇(Butylene Glycol)的急性毒性低。[1] 丁二醇的急性口服 LD_{50} 在大鼠中為 23 g/kg bw，在天竺鼠中為 11 g/kg bw。含有 5.0%丁二醇的指甲油在大鼠體內的 LD_{50} 大於 5 g/kg，而含有 21.35%丁二醇的產品在以 15 g/kg bw 的劑量餵食大鼠時，不會導致死亡。[2]
- 重複劑量毒性：在一項為期 2 年的大鼠餵養研究（高達 5000 mg/kg bw/day）和 2 年對狗進行的餵養研究(攝入劑量最高為 750 mg/kg bw/day)。這兩項研究中，即使是最高劑量，也沒有觀察到與丁二醇相關的影響。在另一項狗的亞慢性 13 週餵養研究中，兩個丁二醇最高劑量組（9000 和 12000 mg/kg bw/day）的狗表現出毒性作用，例如行為變化（癲癇樣癲癇發作）、血液學、血液生化、器官重量和生長速度發生變化。但在 6000 mg/kg bw/day 時沒有發生與試驗相關的影響，推估 NOAEL 為 6000 mg/kg bw/day，LOAEL 為 9000

mg/kg bw/day。[1]

- 皮膚刺激性：在一項人體研究中，200 名志願者在 5 週內（週一、週三和週五暴露）通過上臂封閉貼片暴露於 50%的丁二醇水溶液中 15 次（每次 24 小時），2 名受試者報告有輕度皮膚刺激。改變施用部位後，在受試者身上沒有觀察到進一步的刺激跡象。此外，在對兔子進行的一項動物研究中，兔子在完整的皮膚上暴露 24 小時，並在暴露結束後立即或在暴露結束後 48 小時進行評估，沒有觀察到皮膚刺激。來自人類和動物的各種數據提供一致的資訊，顯示丁二醇對皮膚沒有刺激性或僅輕微刺激性。[1]
- 眼睛刺激性：將一滴丁二醇滴在人眼上會立即引起類似於丙二醇(Propylene Glycol)引起的刺痛，用水沖洗後立即獲得緩解。未稀釋的丁二醇只會對兔子的眼睛造成輕微刺激。[1,2]
- 皮膚致敏性：丁二醇在 200 名受試者的其中 2 名產生輕微的皮膚老化，但沒有皮膚過敏的證據。許多含有濃度高達 21.4%的丁二醇產品配方已在各種人體皮膚刺激和致敏試驗中進行測試。產生的刺激程度取決於特定的劑型，與製劑中存在的乙二醇濃度之間沒有相關性。在皮膚過敏試驗的 1087 名受試者中，沒有任何反應顯示皮膚對乙二醇(Glycol)過敏。[2]
- 生殖毒性：在一項採用嵌入式連續育種研究的五代研究中，在 1~4 代中未觀察到對生育力的影響，直至第五代測試的最高濃度（飲食中的 24%；12000 mg/kg bw/day 丁二醇），發現 F1A 大鼠的妊娠率在連續 5 個交配週期中下降。在丁二醇存在下未觀察到致畸作用。[1]
- 光毒性：在對產品配方進行的一些皮膚致敏試驗中，暴露於紫外線下沒有發現光毒性或光敏性的反應。[2]
- 其他安全資料：丁二醇和相關成分的安全性已經過化妝品成分審查(CIR)專家小組的評估。CIR 專家小組審查科學數據並得出結論，丁二醇、己二醇(Hexylene Glycol)、乙氧基二甘醇(Ethoxydiglycol)和二丙二醇(Dipropylene Glycol)可安全用於化粧品和個人護理產品。2004 年，CIR 專家小組審議有關丁二醇及相關成分的現有新數據，並重申上述結論。CIR 專家小組指出，丁二醇可以被代謝並用作卡路里的來源。急性、亞慢性和慢性口服毒性研究的結果顯示這些乙二醇(Glycol)的毒性較低。腸胃外注射、吸入以及急性和亞慢性皮膚毒性研究的結果同樣支持其低毒性。丁二醇引起輕微至輕微的皮膚

刺激，但沒有致敏跡象。在任何皮膚致敏試驗中，沒有反應表明皮膚對這些乙二醇過敏，也沒有光毒性或光敏作用的跡象。[3]

- 參考資料：

1. ECHA 註冊檔案網站：https://echa.europa.eu/registration-dossier/-/registered-dossier/14962/7/1
2. Final Report on the Safety Assessment of Butylene Glycol, Hexylene Glycol, Ethoxydiglycol, and Dipropylene Glycol. CIR, 1985.
3. Cosmetics Info 網站：https://www.cosmeticsinfo.org/ingredients/butylene-glycol/

21. INCI name：*Avena Sativa* (Oat) Kernel Extract

- 成分特質：據報導，燕麥（燕麥）葉/莖提取物(*Avena Sativa* (Oat) Leaf/Stem Extract)的成分 60%糖；7%～10%黃酮類化合物(flavonoids)及約 1%皂甙(saponins)。燕麥仁油(*Avena Sativa* (Oat) Kernel Oil)的成分是 22.8%~3.1%亞油酸(Linoleic Acid)；31.4%~51.26%油酸(Oleic Acid)及 13.9%~18.82%棕櫚酸(Palmitic Acid)。[1]
- 皮膚刺激性：在一系列累積刺激測試中，得出的結論是，含有各種 *A.sativa* 燕麥衍生成分濃度範圍為 0.00002% ~ 1%的多種產品沒有刺激性。[1]
- 眼睛刺激性：在一系列人類眼部測試中，得出的結論是，含有各種 A.*sativa* 燕麥衍生成分的多種產品不是眼部刺激物。[1]
- 皮膚致敏性：含 25%燕麥仁提取物(*Avena Sativa* (Oat) Kernel Extract)的糊狀面膜產品(150mL)，在雙盲 HRIPT 半封閉狀態下給藥，3 天/週，持續 3 週，24 小時後移除，在研究的任何階段均未觀察到任何致敏反應。[1]
- 致癌性：已發表的文獻中未發現有關 *A.sativa* 燕麥衍生成分致癌性的數據，也未提供未發表的數據。[1]
- 生殖毒性：已發表的文獻中未發現有關 *A.sativa* 燕麥衍生成分的生殖和發育毒性的數據，也未提供未發表的數據。[1]
- 光毒性：據報導，牛、山羊、豬和綿羊食用燕麥(*Avena sativa*)會引起光敏，但沒有提供進一步的數據資訊。[1]
- 人體數據：CIR 專家組討論含有高達 0.0025%燕麥仁提取物(*Avena Sativa* (Oat) Kernel Extract)的面部和頸部噴霧產品和含有高達

0.001% 燕麥仁提取物的髮膠噴霧偶然吸入暴露的問題，發現沒有可用的吸入毒性數據。[1]。

◆ 參考資料：

1. Safety Assessment of *Avena sativa* (Oat)-Derived Ingredients As Used in Cosmetics. International Journal of Toxicology 2019, Vol. 38(Supplement 3) 23S-47S. CIR, 2019.

(11) 產品安定性試驗報告

試驗結果評估：針對外觀、顏色、氣味、pH、黏度、密度、微生物、包材外觀項目進行 6 個月產品安定性試驗，結果判定均合格，將持續執行達宣稱效期之長期安定性試驗。

產品名稱	嫩膚沐浴乳			
包裝材質	瓶身：PET、瓶蓋：PP、吸管：LDPE			
試驗時間 / 試驗項目	第 0 個月	第 1 個月	第 3 個月	第 6 個月
	40 ℃ 75 %RH	40 ℃ 75 %RH	40 ℃ 75 %RH	40 ℃ 75 %RH
外觀	流動液體	流動液體	流動液體	流動液體
顏色	白色不透明帶有珠光	白色不透明帶有珠光	白色不透明帶有珠光	白色不透明帶有珠光
氣味	橙花香	橙花香	橙花香	橙花香
pH (at 25 °C)	6.6	6.5	6.7	6.6
黏度(at 25 °C)	24650 mPa·s	26490 mPa·s	25735 mPa·s	27120 mPa·s
密度(at 25 °C)	0.96 g/cm^3	0.92 g/cm3	0.99g/cm3	1.01 g/cm3
微生物檢測結果	未檢出	未檢出	未檢出	未檢出
包材外觀	無膨脹、變色、腐蝕及脆裂之現象	無膨脹、變色、腐蝕及脆裂之現象	無膨脹、變色、腐蝕及脆裂之現象	無膨脹、變色、腐蝕及脆裂之現象
結果判定	■合格 □不合格	■合格 □不合格	■合格 □不合格	■合格 □不合格
參考試驗方法	ISO/TR 18811 Cosmetics-Guidelines on the stability testing of cosmetics products,2018. 參考 5.3.2 建議之溫度及濕度進行加速安定性試驗			
檢測人員/日期	(請簽名並加上日期)	(請簽名並加上日期)	(請簽名並加上日期)	(請簽名並加上日期)
複核人員/日期	(請簽名並加上日期)	(請簽名並加上日期)	(請簽名並加上日期)	(請簽名並加上日期)

(12)微生物檢測報告

產品名稱	**嫩膚沐浴乳**		
產品批號	IT22080E		
產品製造日期	2022.08.05		
包裝材質	瓶身：PET、瓶蓋：PP、吸管：LDPE	**試驗日期**	111.08.29
檢測項目	**規 格**	**檢測結果**	**參考測試方法**
生菌數	<1000 cfu/g	未檢出 (<10 cfu/g)	參考衛生福利部食品藥物管理署 109.07.28 及 111.04.21 公布建議檢驗方法-化粧品中微生物檢驗方法及化粧品中白色念珠菌之檢驗方法。
大腸桿菌	不得檢出	未檢出	
綠膿桿菌	不得檢出	未檢出	
金黃色葡萄球菌	不得檢出	未檢出	
白色念珠菌	不得檢出	未檢出	
結果判定	■合格 □不合格		
檢測人員/日期	(請簽名並加上日期)		
複核人員/日期	(請簽名並加上日期)		

(13) 防腐效能試驗報告

樣品名稱 (Sample Name)	嫩膚沐浴乳				
測試日期(Date Tested): 111.07.01~08.12					
試驗參考方法(Method Code): 衛福部食藥署 110.05.13 公告之化粧品防腐效能試驗指引					
測試菌種 (Microbial strains)					
分析時間點 (Assay Time)	大腸桿菌 *Escherichia coli* (ATCC 8739) (CFU/g or ml)	金黃色葡萄球菌 *Staphylococcus aureus* (ATCC 6538) (CFU/g or ml)	綠膿桿菌 *Pseudomonas aeruginosa* (ATCC 9027) (CFU/g or ml)	白色念珠菌 *Candida albicans* (ATCC 10231) (CFU/g or ml)	黑麴菌 *Aspergillus brasiliensis* (ATCC 16404) (CFU/g or ml)
第 0 天	9.3×10^5	8.8×10^5	9.1×10^5	8.7×10^4	9.2×10^4
第 7 天	<10	<10	<10	3.6×10^2	6.9×10^2
第 14 天	<10	<10	<10	<10	<10
第 28 天	<10	<10	<10	<10	<10
檢測人員/日期	(請簽名並加上日期)				
複核人員/日期	(請簽名並加上日期)				

(14) 功能評估佐證資料

相關功能性測定，依產品宣稱之功能提供相關佐證資料。

(15) 與產品接觸之包裝材質資料

產品容量 ：500 ml

包裝材料	包裝材質
瓶身	PET
瓶蓋	PP
吸管	LDPE

III. 安全評估資料

(16) 產品安全資料

嫩膚沐浴乳每日皮膚暴露量計算

參考 2023 年 5 月發布之歐盟消費者安全科學委員會(Scientific Committee on Consumer Safety, SCCS)化粧品成分測試及其安全性評估指引第 12 版(SCCS/1647/22)，並依用途、部位、頻率進行皮膚暴露量計算。

基本數據	
平均體重	60 kg
接觸部位	身體表面
接觸種類	沖洗類產品
每日使用頻率	1 次
使用表面積(cm^2)	17500
駐留因子	0.01

每日皮膚暴露量($E_{product}$)

對於此嫩膚沐浴乳，參考 2023 年 5 月發布之 SCCS 化粧品成分測試及其安全性評估指引第 12 版(SCCS/1647/22)表 3A，查表得知每日皮膚暴露量：

Product type	Estimated daily amount applied q_a (g/d)	Relative daily amount applied[1] q_a/bw (mg/kg bw/d)	Retention factor[2] f_{ret}	Calculated daily exposure $E_{product}$ (g/d)	Calculated relative daily exposure[1] $E_{product}$/bw (mg/kg bw/d)
Bathing, showering					
Shower gel	18.67	279.20	0.01	**0.19**	**2.79**

在 MoS 計算中使用的每日皮膚暴露量為 2.79 mg/kg bw/day。

嫩膚沐浴乳各成分 MoS 值計算

計算各個成分之 Margin of Safety (MoS) 安全邊際值如下表：

SED= $E_{product}$ (每日皮膚暴露量)×C/100(配方百分比)×DAp/100(皮膚吸收率)

MoS = POD_{sys}/SED

SED (mg /kg bw/day)為全身暴露劑量；Eproduct (mg /kg bw/day)為每日皮膚暴露量；

C(%)為配方百分比；DAp(%)為皮膚吸收率；PODsys 一般常用 NOAEL 估算。

SCCS 化粧品成分測試及其安全性評估指引第 12 版(SCCS/1647/22) 提及 90 天口服毒性試驗是化粧品成分最常用的重複劑量毒性試驗，當有科學合理的 90 天研究確認明確的每日使用的劑量反應點(Point of Departure, PoD)時 SCCS 會考慮以該研究計算 MoS，當對亞慢性毒性研究的品質存疑或缺乏支持 90 天研究的 PoD 時，則建議應用不確定性因子來推估，為了保守嚴謹評估，故亦將各成分之 NOAEL 在考慮各別的毒理試驗條件後將不確定因子進行校正。以校正後之 NOAEL 值計算結果如下:

INCI name	配方百分比 C(%)	皮膚吸收率 DA_P(%)	NOAEL (mg /kg bw/day)	SED (mg /kg bw/day)	MoS
Aqua	73.255	-	-	-	>100
Sodium Lauroyl Sarcosinate	4.5	100	15	0.1256	119.474
Cocamidopropyl Betaine	5.55	100	125	0.1548	807.259
Sodium Methyl 2-Sulfolaurate	3.04	100	23.3333	0.0848	275.105
Sodium Sulfate	0.32	100	500	0.0089	56003.584
Disodium 2-Sulfolaurate	0.16	100	23.3333	0.0045	5226.994
Potassium Cocoyl Glycinate	1.05	100	155.5556	0.0293	5309.971
Potassium Cocoate	0.45	100	233.3333	0.0126	18584.890
Sodium Methyl Cocoyl Taurate	5	100	77.7778	0.1395	557.547
Glycol Distearate	0.66	100	100	0.0184	5430.651
Coco-Glucoside	0.3	100	28	0.0084	3345.281
Glyceryl Oleate	0.09	100	233.3333	0.0025	92924.452
Glyceryl Stearate	0.09	100	227.7778	0.0025	90711.987

Citric Acid	0.03	100	55.5556	0.0008	66374.671
Benzoic Acid	0.015	100	375	0.0004	896057.35
PEG-150 Pentaerythrityl Tetrastearate	1.3	100	-	0.0363	-
PPG-2 Hydroxyethyl Cocamide	0.52	100	155.5556	0.0145	10722.057
Glycerin	2.12	100	611.1111	0.0591	10331.898
Phenoxyethanol	0.9	78	357	0.0196	18227.491
Caprylyl Glycol	0.1	100	46.6667	0.0028	16726.416
Fragrance	0.5	-	-	-	- (附 IFRA 符合性聲明)
Butylene Glycol	0.03	100	3000	0.0008	3584229.4
Avena Sativa (Oat) Kernel Extract	0.02	100	-	0.0006	-

INCI name	**NOAEL 校正說明**
Sodium Lauroyl Sarcosinate	由大鼠口服試驗 91~92 天試驗得出 NOAEL 為 30 mg/kg bw/day，考慮口服生物可用率 50%之不確定因子，將 30 *50% =15 mg/kg bw/day。
Cocamidopropyl Betaine	由大鼠口服試驗持續 92 天試驗得出未觀察到反應劑量 NOEL 為 250 mg/kg bw/day，考慮口服生物可用率 50%之不確定因子，將 250 *50% =125 mg/kg bw/day。
Sodium Methyl 2-Sulfolaurate	交叉參照大鼠口服 Fatty acids, C12-18 (even numbered)-methyl esters, sulfonated, sodium salts 28 天試驗，NOAEL 為 150 mg/kg bw/day，考慮口服生物可用率 50%及試驗天數(28 天)之不確定因子，將 150*50%*28/90=23.3333 mg/kg bw/day。
Sodium Sulfate	由大鼠口服試驗得出 NOEL 為 1000 mg/kg bw/day，考慮口服生物可用率 50%之不確定因子，將 1000 *50% =500 mg/kg bw/day。
Disodium 2-Sulfolaurate	交叉參照大鼠口服 Fatty acids, C12-18 (even numbered)-methyl esters, sulfonated, sodium salts 28 天試驗，NOAEL 為 150 mg/kg bw/day，考慮口服生物可用率 50%及試驗天數(28 天)之不確定因子，將 150*50%*28/90=23.3333 mg/kg bw/day。
Potassium Cocoyl Glycinate	大鼠口服 28 天試驗，NOAEL 為 1000 mg/kg bw/day，考慮口服

	生物可用率 50%及試驗天數(28 天)之不確定因子，將 1000*50%*28/90=155.5556 mg/kg bw/day。
Potassium Cocoate	交叉參照二十二烷酸(Docosanoic Acid, CAS No. 112-85-6)大鼠口服 42 天試驗，NOAEL 為 1000 mg/kg bw/day，考慮口服生物可用率 50%及試驗天數(42 天)之不確定因子，將 1000*50%*42/90=233.3333 mg/kg bw/day。
Sodium Methyl Cocoyl Taurate	大鼠口服 14 天試驗，NOAEL 為 1000 mg/kg bw/day，考慮口服生物可用率 50%及試驗天數(14 天)之不確定因子，將 1000*50%*14/90=77.7778 mg/kg bw/day。
Glycol Distearate	大鼠口服 20 天試驗，得出大鼠母體致畸性毒性 NOAEL> 900 mg/kg bw/day，考慮口服生物可用率 50%及試驗天數(20 天)之不確定因子，將 900*50%*20/90=100 mg/kg bw/day。
Coco-Glucoside	兔子皮膚為期 2 週試驗，得出 NOEL 為 0.18 g /kg bw/day=180 mg/kg bw/day，考慮試驗天數(14 天)之不確定因子，將 180*14/90=28 mg/kg bw/day。
Glyceryl Oleate	大鼠口服 42 天試驗，NOAEL 為 1000 mg/kg bw/day，考慮口服生物可用率 50%及試驗天數(42 天)之不確定因子，將 1000*50%*42/90=233.3333 mg/kg bw/day。
Glyceryl Stearate	大鼠口服 41~49 天試驗，NOAEL 為 1000 mg/kg bw/day，考慮口服生物可用率 50%及試驗天數(41 天)之不確定因子，將 1000*50%*41/90=227.7778 mg/kg bw/day。
Citric Acid	小鼠口服 10 天試驗，NOAEL 為 1000 mg/kg bw/day，考慮口服生物可用率 50%及試驗天數(10 天)之不確定因子，將 1000*50%*10/90=55.5556 mg/kg bw/day。
Benzoic Acid	大鼠口服 16 週試驗，NOAEL 為>750 mg/kg bw/day，考慮口服生物可用率 50%之不確定因子，將 750*50%=375 mg/kg bw/day。
PPG-2 Hydroxyethyl Cocamide	大鼠口服 28 天試驗，NOAEL 為 1000 mg/kg bw/day，考慮口服生物可用率 50%及試驗天數(28 天)之不確定因子，將 1000*50%*28/90=155.5556 mg/kg bw/day。
Glycerin	人類患者口服大約 1300 至 2200 mg/kg bw/day 甘油 50 天時，沒有出現毒性或對血液或尿液產生影響的跡象，NOAEL 為 2200 mg/kg bw/day，考慮口服生物可用率 50%及試驗天數(50 天)之不確定因子，將 2200*50%*50/90=611.1111mg/kg bw/day。
Phenoxyethanol	兔子皮膚為期 13 週試驗，連續 13 週每週 5 天，NOAEL 乘以 5/7

	的係數，得出調整後的 NOAEL 為 357 mg/kg bw/day。
Caprylyl Glycol	大鼠口服 28 天試驗，NOAEL 為 300 mg/kg bw/day，考慮口服生物可用率 50%及試驗天數(28 天)之不確定因子，將 300*50%*28/90=46.6667mg/kg bw/day。
Butylene Glycol	大鼠口服 2 年試驗，NOAEL 為 6000 mg/kg bw/day，考慮口服生物可用率 50%之不確定因子，將 6000*50%=3000 mg/kg bw/day。

嫩膚沐浴乳安全評估結論

安全評估結論簡述

經分析所有可取得之安全性資料，根據上述評估計算結果並根據當前科學知識，推定嫩膚沐浴乳在預期正常合理使用條件下，本產品為可安全使用之產品，對人體健康傷害風險低。

標籤警語和使用說明

嫩膚沐浴乳的包裝材料/標籤上提到以下警告和使用說明：

使用方式：取適量於手部後，沾水搓揉至起泡沫後用於身體皮膚清潔，並以大量清水沖洗至無殘留泡沫。

使用注意事項：使用時避免接觸眼部，若不慎接觸請以大量清水沖洗。

供消費者使用時參考，避免誤用。

安全評估理由

嫩膚沐浴乳的安全性評估基於每種成分的毒理學特徵並評估所收集之產品數據。

1. 該產品在符合化粧品優良製造規範之場所和生產設施中生產，並進行微生物品質管理以及倉儲管理作業。
2. 根據本產品「嫩膚沐浴乳」之化粧品的物理/化學特性、安定性試驗報告、微生物檢測報告及防腐效能試驗報告，結果由數據顯示產品符合規格特性，證實「嫩膚沐浴乳」產品配方具有足夠安定性及微生物安全性。由六個月之加速安定性試驗推測本產品於架儲期間品質穩定，上市後將同時進行長期安定性試驗確認之。
3. 微生物檢測報告結果符合我國化粧品微生物容許量基準之要求。防腐效能試驗報告顯示通過衛福部食藥署 110.05.13 公告之化粧品防腐效能試驗指引標準 A 之標準要求。
4. 本產品使用之包裝材質為 PET 、PP 及 LDPE，根據過去類似配方及此包材之使用經驗，評估此包裝材料適宜。
5. 根據 SCCS 化粧品成分測試及其安全性評估指引第 12 版，計算化粧品中產品和每種成分的暴露程度。對於產品使用暴露量，採用國際間常用 SCCS 用於嫩膚沐浴乳產品之標準暴露值以計算安全邊際值(MoS)。
6. 使用之香精符合國際香料協會標準(IFRA 50th Amendment)，應用嫩膚沐浴乳之最大濃度為 60%，此嫩膚沐浴乳添加 0.5%香精，推測致敏風險低。
7. 此嫩膚沐浴乳中的所有原材料和成分均可使用於化粧品中，而針對所有

成分計算的安全邊際值(MoS)皆高於 100，支持此產品的安全性。PEG-150 Pentaerythrityl Tetrastearate 及 *Avena Sativa* (Oat) Kernel Extrac 目前未能取得相關之重複劑量毒性試驗數據，由收集此二成分獲取之毒理數據資料可得知，此二成分對皮膚引起刺激性及致敏性風險低。

8. 目前此產品尚未出現不良反應和嚴重不良反應，如有不良反應和嚴重不良反應的相關資料時，會及時提供給安全資料簽署人員重新評估此產品之安全性，並更新於本產品資訊檔案。

（請簽名並加上日期）

安全資料簽署人員簽名及日期

*請檢附安全資料簽署人員之符合之學歷及資格證明文件

附錄 1：產品及各別成分之物理及化學特性資料

註：本範例僅提供其中一成分之物理化學特性資料為示範，實際執行時應包含所有蒐集到之產品及內含各成分之品質規格或各成分之檢驗報告(Certificate of Analysis, COA)、安全資料表(Safety Data Sheet, SDS)、檢驗標準或試驗方法等分析規格書，且內容如有變更應隨時更新。

INCI name：Sodium Lauroyl Sarcosinate

SP CRODASINIC LS30 MIT MBAL-LQ-(RB)

Version 2.0 Revision Date 18.12.2015 Print Date 07.01.2016

SECTION 1: Identification of the substance/mixture and of the company/undertaking

1.1 Product identifier

Trade name : SP CRODASINIC LS30 MIT MBAL-LQ-(RB)

INCI : Aqua and Sodium Lauroyl Sarcosinate
Substance name : Sodium N-Lauroylsarcosinate

CAS-No. : 137-16-6

1.2 Relevant identified uses of the substance or mixture and uses advised against

Use of the Substance/Mixture : Surfactant

1.3 Details of the supplier of the safety data sheet

1.4 Emergency telephone number

USA: 24 Hour Emergency Response Information CHEMTREC toll free: 1-800-424-9300; direct/international: 1-703-527-3887. CANADA: Quantum Murray (spill response)1-877-378-7745. CANADA: CANUTEC(collect) 1-613-996-6666. EUROPE: 00 32 3575 5555. ASIA PACIFIC - excl. China: +65 6542-9595. CHINA: +86 816-635 2206. AUSTRALIA: +61 2 9616 5890. SOUTH AFRICA: +32 3 575 55 55. LATAM: 0800 720 8000. 1-613-996-6666. INDIA: +91 22 30948601/2. JAPAN: +65 6542 9595 (24時間 日本語対応無料通話、シンガポール) TÜRKİYE: Sağlık Bakanlığı Ulusal Zehir Merkezi - 114

SECTION 2: Hazards identification

2.1 Classification of the substance or mixture

Classification (REGULATION (EC) No 1272/2008)

Acute toxicity, Category 4	H332: Harmful if inhaled.
Eye irritation, Category 2	H319: Causes serious eye irritation.

Classification (67/548/EEC, 1999/45/EC)

Harmful	R20: Harmful by inhalation.
Irritant	R36: Irritating to eyes.

2.2 Label elements

Labelling (REGULATION (EC) No 1272/2008)

Hazard pictograms :

Signal word : Warning

Hazard statements	: H332	Harmful if inhaled.
	H319	Causes serious eye irritation.
Precautionary statements	: **Prevention:**	
	P280	Wear protective gloves/ eye protection/ face protection.
	P261	Avoid breathing dust/ fume/ gas/ mist/ vapours/ spray.
	P271	Use only outdoors or in a well-ventilated area.
	Response:	
	P305 + P351 + P338	IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
	P304 + P340	IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing.
	P312	Call a POISON CENTER or doctor/ physician if you feel unwell.

Hazardous components which must be listed on the label:
Sodium N-lauroylsarcosinate

2.3 Other hazards

This substance/mixture contains no components considered to be either persistent, bioaccumulative and toxic (PBT), or very persistent and very bioaccumulative (vPvB) at levels of 0.1% or higher.

SECTION 3: Composition/information on ingredients

3.2 Mixtures

Hazardous components

Chemical Name	CAS-No.	Classification	Classification	Concentration

	EC-No. Registration number	(67/548/EEC)	(REGULATION (EC) No 1272/2008)	(%)
Sodium N-lauroylsarcosinate	137-16-6 205-281-5 01-2119527780-39-0000	T; R23 Xi; R41 Xi; R38	Acute Tox. 2; H330 Skin Irrit. 2; H315 Eye Dam. 1; H318	>= 30 - < 35

For explanation of abbreviations see section 16.

SECTION 4: First aid measures

4.1 Description of first aid measures

If inhaled : If breathed in, move person into fresh air.
If symptoms persist, call a physician.

In case of skin contact : In case of contact, immediately flush skin with plenty of water for at least 15 minutes while removing contaminated clothing and shoes.
If symptoms persist, call a physician.

In case of eye contact : In the case of contact with eyes, rinse immediately with plenty of water and seek medical advice.

If swallowed : If swallowed, call a poison control centre or doctor immediately.

4.2 Most important symptoms and effects, both acute and delayed

Symptoms : None known.

4.3 Indication of any immediate medical attention and special treatment needed

Treatment : None known.

SECTION 5: Firefighting measures

5.1 Extinguishing media

Suitable extinguishing media : Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.
Use water spray, alcohol-resistant foam, dry chemical or carbon dioxide.

Unsuitable extinguishing media : High volume water jet

5.2 Special hazards arising from the substance or mixture

Specific hazards during fire-fighting : In case of fire hazardous decomposition products may be produced such as:
Carbon oxides

Do not use a solid water stream as it may scatter and spread fire.

5.3 Advice for firefighters

Special protective equipment for firefighters : In the event of fire, wear self-contained breathing apparatus.

Further information : Prevent fire extinguishing water from contaminating surface water or the ground water system.
Fire residues and contaminated fire extinguishing water must be disposed of in accordance with local regulations.

SECTION 6: Accidental release measures

6.1 Personal precautions, protective equipment and emergency procedures

Personal precautions : Ensure adequate ventilation.
Use personal protective equipment.
Contaminated surfaces will be extremely slippery.

6.2 Environmental precautions

Environmental precautions : Prevent product from entering drains.
If the product contaminates rivers and lakes or drains inform respective authorities.

6.3 Methods and material for containment and cleaning up

Methods for cleaning up : Soak up with inert absorbent material.
Sweep up and shovel into suitable containers for disposal.

6.4 Reference to other sections

None.

SECTION 7: Handling and storage

7.1 Precautions for safe handling

Advice on safe handling : Avoid contact with skin, eyes and clothing.
Handle in accordance with good industrial hygiene and safety practice.

Advice on protection against fire and explosion : Normal measures for preventive fire protection.

7.2 Conditions for safe storage, including any incompatibilities

Requirements for storage areas and containers	:	Store in original container. Containers which are opened must be carefully resealed and kept upright to prevent leakage. Keep container tightly closed in a dry and well-ventilated place.
Advice on common storage	:	No special restrictions on storage with other products.
Other data	:	Stable under recommended storage conditions.

7.3 Specific end use(s)

Specific use(s)	:	Surfactant

SECTION 8: Exposure controls/personal protection

8.1 Control parameters

Contains no substances with occupational exposure limit values.

8.2 Exposure controls

Personal protective equipment

Eye protection	:	Tightly fitting safety goggles
Hand protection Remarks	:	Impervious gloves
Skin and body protection	:	Impervious clothing
Respiratory protection	:	In the case of vapour formation use a respirator with an approved filter.

SECTION 9: Physical and chemical properties

9.1 Information on basic physical and chemical properties

Appearance	:	liquid
Colour	:	clear, colourless
Odour	:	characteristic
Odour Threshold	:	No data available
pH	:	7.5 - 8.5
Melting point	:	No data available
Boiling point	:	No data available
Flash point	:	Not applicable

Evaporation rate	:	No data available
Flammability (solid, gas)	:	No data available
Upper explosion limit	:	No data available
Lower explosion limit	:	No data available
Vapour pressure	:	No data available
Relative vapour density	:	No data available
Density	:	ca. 1.01 g/cm3 (25 °C)
Solubility(ies)		
Water solubility	:	completely soluble
Solubility in other solvents	:	not determined
Partition coefficient: n-octanol/water	:	No data available
Auto-ignition temperature	:	No data available
Thermal decomposition	:	No data available
Viscosity		
Viscosity, dynamic	:	No data available
Viscosity, kinematic	:	40 - 80 mm2/s (25 °C)
Explosive properties	:	Classification Code: No data available
Oxidizing properties	:	No data available

9.2 Other information

Oxidizing potential	:	No data available

SECTION 10: Stability and reactivity

10.1 Reactivity

No data available

10.2 Chemical stability

No data available

10.3 Possibility of hazardous reactions

Hazardous reactions	:	Stable under recommended storage conditions.

10.4 Conditions to avoid

Conditions to avoid : None known.

10.5 Incompatible materials

Materials to avoid : Strong oxidizing agents

10.6 Hazardous decomposition products

Hazardous decomposition products : No data available

SECTION 11: Toxicological information

11.1 Information on toxicological effects

Acute toxicity

Components:

Sodium N-lauroylsarcosinate:

Acute oral toxicity : LD50 Oral (Rat, male and female): > 5,000 mg/kg
Method: OECD Test Guideline 401
GLP: yes

Acute inhalation toxicity : LC50 (Rat, male and female): 1 - 5 mg/l
Exposure time: 4 h
Method: OECD Test Guideline 403
Test substance: 35%
GLP: yes
Remarks: Harmful by inhalation.

LC50 (Rat, male and female): 0.05 - 0.5 mg/l
Exposure time: 4 h
Method: OECD Test Guideline 403
Test substance: 100%
GLP: yes
Remarks: Toxic by inhalation.

Acute dermal toxicity : Remarks: Not applicable

Skin corrosion/irritation

Components:

Sodium N-lauroylsarcosinate:

Species: Rabbit
Exposure time: 4 h
Assessment: No skin irritation
Method: OECD Test Guideline 404
Result: No skin irritation
GLP: yes
Test substance: 30%

Assessment: Non-corrosive

Method: EPISKIN Human Skin Model Test
Result: Non-corrosive
GLP: yes

Serious eye damage/eye irritation

Components:

Sodium N-lauroylsarcosinate:
Species: Rabbit
Method: OECD Test Guideline 405
Result: irritating
Test substance: 30%

Respiratory or skin sensitisation

Components:

Sodium N-lauroylsarcosinate:
Test Type: Maximisation Test (GPMT)
Species: Guinea pig
Assessment: Does not cause skin sensitisation.
Method: Directive 67/548/EEC, Annex V, B.6.
Result: Did not cause sensitization.
GLP: yes
Test substance: 30%

Germ cell mutagenicity

Components:

Sodium N-lauroylsarcosinate:
Genotoxicity in vitro : Test Type: in vitro assay
Metabolic activation: with and without metabolic activation
Method: Mutagenicity (Salmonella typhimurium - reverse mutation assay)
Result: negative
GLP: yes

: Test Type: Chromosome aberration test in vitro
Test species: Human lymphocytes
Metabolic activation: with and without metabolic activation
Method: Directive 67/548/EEC, Annex V, B.10.
Result: negative
GLP: yes

: Test Type: in vitro assay
Metabolic activation: with and without metabolic activation
Result: negative
GLP: yes

Carcinogenicity

Components:

Sodium N-lauroylsarcosinate:

Test substance: No data available

Reproductive toxicity

Components:
Sodium N-lauroylsarcosinate:
Effects on fertility : Test substance: No data available

STOT - single exposure

Product:
Assessment: No data available

Components:
Sodium N-lauroylsarcosinate:
Assessment: No data available

STOT - repeated exposure

Repeated dose toxicity

Components:
Sodium N-lauroylsarcosinate:
Species: Rat, male and female
NOAEL: 30 mg/kg
Application Route: Oral
Exposure time: 90 days
Number of exposures: 1x /day
Method: Directive 67/548/EEC, Annex V, B.7.
GLP: yes

Aspiration toxicity

Product:
No data available

Further information

Product:
Remarks: No data available

SECTION 12: Ecological information

12.1 Toxicity

Components:
Sodium N-lauroylsarcosinate:
Toxicity to fish : LC50 (Danio rerio (zebra fish)): 107 mg/l

Exposure time: 96 h
Test Type: semi-static test
Test substance: 30%
Method: OECD Test Guideline 203
GLP: yes

Toxicity to daphnia and other aquatic invertebrates : EC50 (Daphnia magna (Water flea)): 29.7 mg/l
Exposure time: 48 h
Test Type: static test
Test substance: 30%
Method: OECD Test Guideline 202
GLP: yes

Toxicity to algae : ErC50 (Desmodesmus subspicatus (green algae)): 79 mg/l
Exposure time: 72 h
Test Type: static test
Test substance: 30%
Method: OECD Test Guideline 201
GLP: yes

EbC50 (Desmodesmus subspicatus (green algae)): 39 mg/l
Exposure time: 72 h
Test Type: static test
Test substance: 30%
Method: OECD Test Guideline 201
GLP: yes

12.2 Persistence and degradability

Components:

Sodium N-lauroylsarcosinate:

Biodegradability : Test Type: Biodegradability, ISO 14593
Result: Readily biodegradable
Biodegradation: 82 %
Exposure time: 28 d
Method: Directive 67/548/EEC Annex V, C.4.B.
GLP: yes

12.3 Bioaccumulative potential

Components:

Sodium N-lauroylsarcosinate:

Bioaccumulation : Remarks: No bioaccumulation is to be expected (log Pow <= 4).

Partition coefficient: n-octanol/water : log Pow: estimated 0.37

12.4 Mobility in soil

Product:

Distribution among environmental compartments : Remarks: No data available

Components:

Sodium N-lauroylsarcosinate:

Distribution among environmental compartments	:	Remarks: Not applicable

12.5 Results of PBT and vPvB assessment

Product:

Assessment	:	This substance/mixture contains no components considered to be either persistent, bioaccumulative and toxic (PBT), or very persistent and very bioaccumulative (vPvB) at levels of 0.1% or higher..

Components:

Sodium N-lauroylsarcosinate:

Assessment	:	This substance is not considered to be persistent, bioaccumulating and toxic (PBT)..

12.6 Other adverse effects

Product:

Environmental fate and pathways	:	No data available
Additional ecological information	:	Remarks: No data available

SECTION 13: Disposal considerations

13.1 Waste treatment methods

Product	:	Dispose of in accordance with local regulations.
Contaminated packaging	:	Empty remaining contents. Do not re-use empty containers. Empty containers should be taken to an approved waste handling site for recycling or disposal.

SECTION 14: Transport information

14.1 UN number

Not regulated as a dangerous good

14.2 Proper shipping name

Not regulated as a dangerous good

14.3 Transport hazard class

Not regulated as a dangerous good

14.4 Packing group

Not regulated as a dangerous good

14.5 Environmental hazards

Not regulated as a dangerous good

14.6 Special precautions for user

Remarks : Not classified as dangerous in the meaning of transport regulations.

14.7 Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code

Not applicable for product as supplied.

SECTION 15: Regulatory information

15.1 Safety, health and environmental regulations/legislation specific for the substance or mixture

The components of this product are reported in the following inventories:

REACH	:	On the inventory, or in compliance with the inventory
AICS	:	On the inventory, or in compliance with the inventory
DSL	:	All components of this product are on the Canadian DSL
NZIoC	:	On the inventory, or in compliance with the inventory
ENCS	:	On the inventory, or in compliance with the inventory
ISHL	:	On the inventory, or in compliance with the inventory
KECI	:	On the inventory, or in compliance with the inventory
PICCS	:	On the inventory, or in compliance with the inventory
IECSC	:	On the inventory, or in compliance with the inventory

For explanation of abbreviations see section 16.

15.2 Chemical Safety Assessment

This information is not available.

SECTION 16: Other information

Full text of R-Phrases

R23	:	Toxic by inhalation.
R38	:	Irritating to skin.
R41	:	Risk of serious damage to eyes.

Full text of H-Statements

H315	:	Causes skin irritation.
H318	:	Causes serious eye damage.
H330	:	Fatal if inhaled.

Full text of other abbreviations

Acute Tox.	:	Acute toxicity
Eye Dam.	:	Serious eye damage
Skin Irrit.	:	Skin irritation

Key or legend to abbreviations and acronyms used in the safety data sheet

AICS (Australia), DSL (Canada), IECSC (China), REACH (European Union), ENCS (Japan), ISHL (Japan), KECI (Korea), NZIoC (New Zealand), PICCS (Philippines), TCSI (Taiwan), TSCA (USA)

Further information

Other information	:	Additions, Deletions, Revisions Section 2

The information provided in this Safety Data Sheet is correct to the best of our knowledge, information and belief at the date of its publication. The information given is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal and release and is not to be considered a warranty or quality specification. The information relates only to the specific material designated and may not be valid for such material used in combination with any other materials or in any process, unless specified in the text.

附錄 2：各成分之毒理相關資料

註：本範例僅提供其中一成分之毒理資料為示範，實際執行時應包含所有蒐集之各個成分之毒理資料，且內容如有變更應隨時更新。

INCI name：Sodium Lauroyl Sarcosinate

1. Amended Safety Assessment of Fatty Acyl Sarcosines and Sarcosinate Salts as Used in Cosmetics. International Journal of Toxicology 2021, Vol. 40(Supplement 2) 117S–133S. CIR, 2021.

CIR Supplement Manuscript

Amended Safety Assessment of Fatty Acyl Sarcosines and Sarcosinate Salts as Used in Cosmetics

International Journal of Toxicology
2021, Vol. 40(Supplement 2) 117S–133S

DOI: 10.1177/10915818211023881
journals.sagepub.com/home/ijt
SAGE

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Abstract

The Expert Panel for Cosmetic Ingredient Safety (Panel) assessed the safety of 5 acyl sarcosines and 9 sarcosinate salts as used in cosmetics; all of these ingredients are reported to function in cosmetics as hair conditioning agents and most also can function as surfactants—cleansing agents. The ingredients reviewed in this assessment are composed of an amide comprising a fatty acyl residue and sarcosine and are either free acids or simple salts thereof. The Panel relied on relevant new data, including concentration of use, and considered data from the previous Panel report, such as the reaction of sarcosine with oxidizing materials possibly resulting in nitrosation and the formation of *N*-nitrososarcosine. The Panel concluded that these ingredients are safe as used in cosmetics when formulated to be non-irritating, but these ingredients should not be used in cosmetic products in which *N*-nitroso compounds may be formed.

Keywords

safety, cosmetics, fatty acyl sarcosines, sarcosinate salts

Introduction

In 2001, the Expert Panel for Cosmetic Ingredient Safety (Panel) published a safety assessment with the conclusion that the 5 fatty acyl sarcosines and 5 fatty acyl sarcosine salts listed below are safe as used in rinse-off products, safe for use in leave-on products at concentrations of ≤5%, and the data are insufficient to determine the safety for use in products where the fatty acyl sarcosines and their salts are likely to be inhaled.[1] These ingredients should not be used in cosmetic products in which *N*-nitroso compounds may be formed.

Cocoyl Sarcosine	Ammonium Cocoyl Sarcosinate
Lauroyl Sarcosine	Ammonium Lauroyl Sarcosinate
Myristoyl Sarcosine	Sodium Cocoyl Sarcosinate
Oleoyl Sarcosine	Sodium Lauroyl Sarcosinate
Stearoyl Sarcosine	Sodium Myristoyl Sarcosinate

Concentration of use data was not provided at the time of the original safety assessment; because those values were not available, the concentration limit of 5% was established for leave-on products based upon the highest concentration tested in human repeat-insult patch tests. Concentration of use data is now available, and additional new relevant data have been discovered; therefore, the Panel re-opened the 2001 safety assessment to reassess the original conclusion.

The Panel determined that the following four additional fatty acyl sarcosine salts are structurally similar to the ingredients named above, and that the data in the original safety assessment, together with the new data presented in this report, support the safety of these four additional fatty acyl sarcosine salts; therefore, these ingredients are included in this report:

Potassium Cocoyl Sarcosinate	Sodium Oleoyl Sarcosinate
Potassium Lauroyl Sarcosinate	Sodium Palmitoyl Sarcosinate

All of the ingredients included in this assessment are reported to function in cosmetics as hair conditioning agents, and most of these ingredients are reported to function as surfactants—cleansing agents[2] (Table 1).

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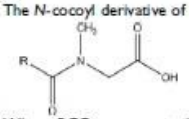
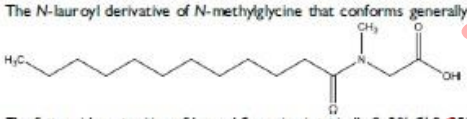
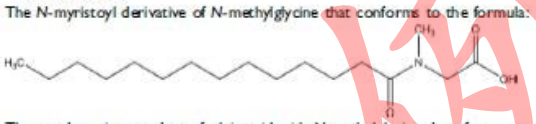
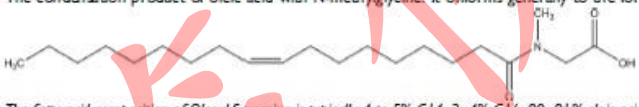
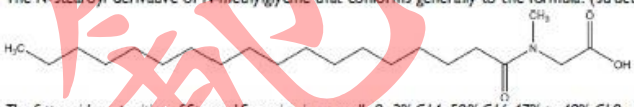
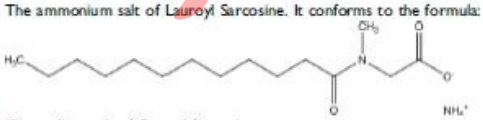
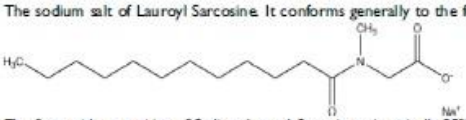
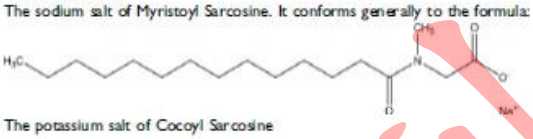
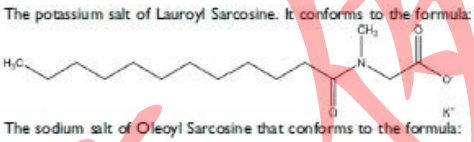
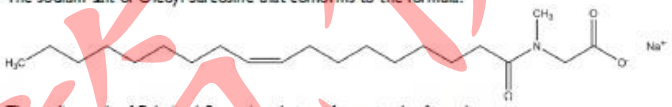
Table 1. Definitions, Idealized Structures, and Functions of the Ingredients in this Safety Assessment (Ref. 2, CIR Staff).

Ingredient CAS no.	Definition and structure	Function(s)
Fatty Acyl Sarcosines		
Cocoyl Sarcosine (68411-97-2)	The *N*-cocoyl derivative of sarcosine that conforms generally to the formula:  Where RCO- represents the fatty acids derived from coconut oil *The fatty acids in Cocoyl Sarcosine have the following composition: 2–4% C_{10}, 55% C_{12}, 19–22% C_{14}, 0–7% C_{16}, 4–21% C_{18}, 0–8% oleic acid, and 0–3% unsaturated fatty acid*[1]	Hair conditioning agent; surfactant—cleansing agent
Lauroyl Sarcosine (97-78-9)	The *N*-lauroyl derivative of *N*-methylglycine that conforms generally to the formula:  *The fatty acid composition of Lauroyl Sarcosine is typically 0–2% C10, 95% C12, 3% C14, 0–1% C16, and 0–1% oleic acid*[1]	Hair conditioning agent; surfactant—cleansing agent
Myristoyl Sarcosine (52558-73-3)	The *N*-myristoyl derivative of *N*-methylglycine that conforms to the formula: 	Hair conditioning agent; surfactant—cleansing agent
Oleoyl Sarcosine (110-25-8)	The condensation product of oleic acid with *N*-methylglycine. It conforms generally to the formula:  *The fatty acid composition of Oleoyl Sarcosine is typically 4 to 5% C14, 3–4% C16, 80–81% oleic acid, and 11–12% unsaturated fatty acids*[1]	Hair conditioning agent; surfactant—cleansing agent
Stearoyl Sarcosine (142-48-3)	The *N*-stearoyl derivative of *N*-methylglycine that conforms generally to the formula: (structure):  *The fatty acid composition of Stearoyl Sarcosine is generally 0–2% C14, 50% C16, 47% to 49% C18, and 1% oleic acid*[1]	Hair conditioning agent; surfactant—cleansing agent
Fatty Acyl Sarcosine salts		
Ammonium Cocoyl Sarcosinate	The ammonium salt of Cocoyl Sarcosine	Surfactant—cleansing agent
Ammonium Lauroyl Sarcosinate (68003-46-3)	The ammonium salt of Lauroyl Sarcosine. It conforms to the formula: 	Hair conditioning agent; surfactant—cleansing agent
Sodium Cocoyl Sarcosinate (61791-59-1)	The sodium salt of Cocoyl Sarcosine	Hair conditioning agent; surfactant—cleansing agent

(continued)

Table I. (continued)

Ingredient CAS no.	Definition and structure	Function(s)
Sodium Lauroyl Sarcosinate (137-16-6)	The sodium salt of Lauroyl Sarcosine. It conforms generally to the formula:  *The fatty acid composition of Sodium Lauroyl Sarcosinate is typically 95% C12, 3% C14, 0–1% C16, and 0–1% oleic acid*[1]	Hair conditioning agent; surfactant—cleansing agent
Sodium Myristoyl Sarcosinate (30364-51-3)	The sodium salt of Myristoyl Sarcosine. It conforms generally to the formula: 	Hair conditioning agent; surfactant—cleansing agent
Potassium Cocoyl Sarcosinate	The potassium salt of Cocoyl Sarcosine	Hair conditioning agent; surfactant—cleansing agent
Potassium Lauroyl Sarcosinate (38932-32-0)	The potassium salt of Lauroyl Sarcosine. It conforms to the formula: 	Hair conditioning agent; surfactant—cleansing agent
Sodium Oleoyl Sarcosinate (14351-62-3)	The sodium salt of Oleoyl Sarcosine that conforms to the formula: 	Skin conditioning agent—miscellaneous
Sodium Palmitoyl Sarcosinate (4028-10-8)	The sodium salt of Palmitoyl Sarcosine that conforms to the formula: 	Hair conditioning agent; skin-conditioning agent—miscellaneous; surfactant—cleansing agent

Excerpts from the summary of the 2001 report are disseminated throughout the text of this re-review document, as appropriate. (This information is not included in the summary section.)

Several previous Cosmetic Ingredient Review (CIR) safety assessments are relevant to this safety assessment because they discuss the safety of components of the acyl sarcosines and sarcosinate salts. In 2011, the Panel concluded that Cocos Nucifera (Coconut) Oil and Elaeis Guineensis (Palm) Oil are safe in the present practices of use and concentration.[3] In 1987, the Panel published a report with the conclusion that Oleic, Lauric, Palmitic, Myristic, and Stearic Acids are safe in present practices of use and concentration in cosmetics[4]; this conclusion was reaffirmed in 2006.[5]

This safety assessment includes relevant published and unpublished data that are available for each endpoint that is evaluated. Published data are identified by conducting an exhaustive search of the world's literature. A listing of the search engines and websites that are used and the sources that are typically explored, as well as the endpoints that the Panel typically evaluates, is provided on the CIR website (https://www.cir-safety.org/supplementaldoc/preliminary-search-engines-and-websites; https://www.cir-safety.org/supplementaldoc/cir-report-format-outline). Unpublished data are provided by the cosmetics industry, as well as by other interested parties.

Much of the new toxicity data included in this safety assessment was found on the European Chemicals Agency (ECHA) website.[6] The ECHA website provides summaries of information generated by industry, and it is those summary data that are reported in this safety assessment when ECHA is cited.

Chemistry

Definition and Structure

Sarcosine, also known as *N*-methylglycine or *N*-methylaminoacetic acid, is derived from the decomposition of creatine or caffeine.[1] Sarcosine is also a naturally occurring amino acid found in marine animals. It conforms generally to the formula shown in Figure 1.

The ingredients in this report are each an amide comprising a fatty acyl residue and sarcosine, with connectivity occurring via the nitrogen atom of sarcosine and the carbonyl of the fatty acyl residue. These ingredients are either free acids (the carboxylic functional group of the sarcosine residue), or are simple salts thereof Figure 2. The salts in this report recite the term "sarcosinate" in the name and were referred to in the previous report as "sarcosinates" or "sarcosinates amides." Since these previously utilized terms could erroneously be interpreted to mean esters or amides with connectivity through the carbonyl of sarcosine, these salts are hereto referred to simply as fatty acyl sarcosine salts.

Physical and Chemical Properties

The ingredients included in this safety assessment are viscous liquids or waxy solids (Table 2). The free acids have molecular weights of approximately 280–350 Da. The salts are formed from the carboxylic acid moiety and, among the ingredients reviewed herein, are simple alkali metal (sodium and potassium) or ammonium salts.

The modification of the hydrocarbon chain imparts greater solubility and crystallinity to the molecule.[1] Acyl sarcosines are somewhat stronger acids than the parent fatty acids, and they form salts in the neutral and mildly acidic pH range. The salts are similar physically and chemically to fatty acid soaps; the fatty acyl sarcosine salts are, however, more soluble in water and less affected by water hardness than are common soaps.

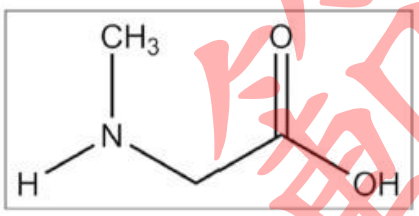


Figure 1. Sarcosine.

Method of Manufacture

The acyl sarcosines are the condensation products of sarcosine with natural fatty acids and are produced commercially by the reaction of sodium sarcosine and the parent fatty acid chlorides.[1] The acyl sarcosines can then be neutralized to form the sodium or ammonium salts.

The acyl sarcosinates are often supplied as 30% or 95% aqueous solutions.[1] According to a manufacturer, only internally prepared sodium sarcosinate is used as a starting material. The sodium sarcosinate is then reacted directly with the acyl chloride, which has been prepared from the free fatty acid by treatment with phosphorus trichloride.

Impurities/Composition

Thirty percent aqueous solutions of Lauroyl Sarcosine and Sodium Lauroyl Sarcosinate were analyzed for nitrosamines (test method unavailable).[1] The detection limits were 65 ppb for *N*-nitrososarcosine in Lauroyl Sarcosine and 15 ppb in Sodium Lauroyl Sarcosinate, respectively; no nitrosamines were detected. The synthesis reaction is kept in a closed system for up to several days prior to the succeeding reaction to prevent contamination with nitrite precursors. The reaction conditions are not conducive to the formation of nitrosamines as contaminants, and neither nitrates nor nitrites are used in the manufacturing process.

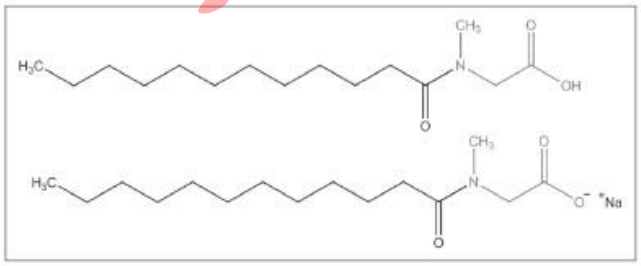


Figure 2. Myristoyl Sarcosine and Sodium Myristoyl Sarcosinate, a representative fatty acyl sarcosine and salt, respectively.

Table 2. Physical and Chemical Properties.

Property	Description	Reference
Cocoyl Sarcosine		
Physical characteristics	Yellow, viscous, oily liquid	1
Molecular weight	280–290 Da	1
Solubility	Insoluble in water; soluble in most organic solvents, including glycols, glycerin, silicones, phosphate esters, and aliphatic hydrocarbons	1
Melting point	22–28°C	1
Specific gravity	0.965–0.975 (25°/25°C)	1
Lauroyl Sarcosine		
Physical characteristics	White to off-white waxy solid to semisolid with a mild, fatty acid odor	1
Molecular weight	280–290 Da	1
Solubility	Insoluble in water; soluble in most organic solvents, including glycols, glycerin, silicone, phosphate esters, and aliphatic hydrocarbons	1
Melting point	28–36°C	1
Specific gravity	0.969	1
Density	0.996 g/cm³ (25°C)	25
Log P_{ow}	4.1 (QSAR)	25
Oleoyl Sarcosine		
Physical characteristics	Amber-colored viscous liquid	22
Molecular weight	353.55	7
Solubility	Insoluble in water; soluble in most organic solvents	1
Melting point	0°C (solidification point)	7
Density	0.95 g/cm³	7
Log P_{ow}	>6	7
Stearoyl Sarcosine		
Molecular weight	340–350 Da	1
Specific gravity	0.924	1
Solubility	Insoluble in water; soluble in most organic solvents	1
Sodium Lauroyl Sarcosinate		
Physical characteristics	Available commercially as a colorless to slightly yellow, 30% aqueous solution, as solid flakes, or as a substantially anhydrous white powder with 97% active content	1
	White powder (≥95% active content)	26,31
	Clear liquid (30% active)	8
	Clear, almost colorless liquid (29–31% active)	9
	Pale yellow clear liquid (30% active)	11
Particle size distribution	<75 µ, 15%; 75 µ, 52.2%; 125 µ, 28.4%; 250 µ, 3.6%; 500 µ, 0.6%; 1000 µ, 0.2% (95% active content)	26
Solubility	Soluble in water	1
Melting point	140°C (powder form)	1
	146.1°C (95% active content)	26
Specific gravity	0.99–1.03 (25°/25°C)	1

Precursors necessary for the "hypothetical formation" for polynuclear aromatic hydrocarbons are also absent from the synthesis reactions and none of the starting materials are prepared or provided in a hydrocarbon solvent.[1] Similarly, the presence of dioxins was considered "exceedingly improbable," as no phenolic compounds were present in any of the synthesis reactions.

Oleoyl Sarcosine. Oleoyl Sarcosine is reported to be 97% pure.[7] It may contain 2% free fatty acids.

Sodium Lauroyl Sarcosinate. According to several suppliers, sodium Lauroyl Sarcosinate (30% active) contains 1–1.5% (max.) Sodium Laurate, 2.5% (max.) free fatty acid, 0.2–0.5% (max.) inorganic salt, and 0.35% (max.) chloride.[8–11]

Nitrosation

Sarcosine can react with oxidizing materials and can be nitrosated to form *N*-nitrososarcosine,[1] a compound that is a liver carcinogen.[12] *N*-nitrososarcosine has been formed by the reaction of sarcosine with sodium nitrite in an acid solution and by passing nitrous acid fumes through a sarcosine solution.[1] *N*-nitrososarcosine can also be produced by nitrosating *N*-methylsarcosine hydrochloride or by treating creatine in an acid medium with an aqueous solution of sodium nitrite. Primary routes of potential human exposure to *N*-nitrososarcosine are inhalation, ingestion, and dermal contact. *N*-nitrososarcosine has been detected in foodstuffs, particularly meat, at concentrations of 2–56 µg/kg of sample. It can be produced by various reactions in air, water, soil, food, and animal systems.

When 50 mg of Sodium Lauroyl Sarcosinate was incubated with 100 mg of sodium nitrite in 10% hydrochloric acid, investigators detected sarcosine, Lauroyl Sarcosine, and *N*-nitrososarcosine using thin-layer chromatography.[1] The yield of *N*-nitrososarcosine was 6.0%.

Use

Cosmetic

The safety of the cosmetic ingredients included in this safety assessment is evaluated based on data received from the US Food and Drug Administration (FDA) and the cosmetics industry on the expected use of these ingredients in cosmetics. Use frequencies of individual ingredients in cosmetics are collected from manufacturers and reported by cosmetic product category in FDA's Voluntary Cosmetic Registration Program (VCRP) database. Use concentration data are submitted by Industry in response to surveys, conducted by the Personal Care Products Council (Council), of maximum reported use concentrations by product category.

Based on 2016 VCRP data[13] and the results of a 2015 Council survey,[14] 10 of the 14 ingredients included in this safety assessment are currently in use. Sodium Lauroyl Sarcosinate has the highest frequency of use, with 485 reported uses; the majority of these uses are in rinse-off formulations, primarily bath soaps and detergents (230 uses) and shampoos (113 uses; Table 3). Sodium Lauroyl Sarcosinate also has the highest concentration of use, with maximum use concentrations up to 15% in rinse-off products. The highest reported leave-on concentration is 5% Sodium Myristoyl Sarcosinate in eye shadow formulations.

All but one of the in-use ingredients has been reviewed previously by the Panel, and the frequencies of use of these ingredients have not changed significantly. Concentration of use data was not provided at the time of the original safety assessment; therefore, it is not apparent whether the concentration of use has changed. (Because those values were not available, a concentration limit of 5% was established for leave-on products, based upon the highest concentration tested in human repeat-insult patch tests.[1])

Table 4 provides a listing of the fatty acyl sarcosines and salts not currently reported to be in use.

Several of the ingredients included in this assessment are used in products that may be ingested (eg, <5% Sodium Myristoyl Sarcosinate in lipstick), are used near the eye (eg, 5% Sodium Myristoyl Sarcosinate in eye shadow), or come in contact with mucous membranes (eg, ≤9% Sodium Lauroyl Sarcosinate in bath soaps and detergents). Additionally, some of the fatty acyl sarcosines and salts are listed in the VCRP in product types that can be sprays, but it is not known whether or not the reported uses are in sprays. In practice, 95–99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters >10 µm, with propellant sprays yielding a greater fraction of droplets/particles <10 µm compared with pump sprays.[15,16] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and thoracic regions of the respiratory tract and would not be respirable (ie, they would not enter the lungs) to any appreciable amount.[17,18] Sodium Myristoyl Sarcosinate and Sodium Palmitoyl Sarcosinate were reported to be used in face powders at concentrations of 0.15% and 0.081%, respectively. Conservative estimates of inhalation exposures to respirable particles during the use of loose-powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace.[19-21]

All of the fatty acyl sarcosines and salts named in the report are listed in the European Union inventory of cosmetic ingredients, and none of the listed ingredients are restricted from use in any way under the rules governing cosmetic products in the European Union.

Non-Cosmetic

Several of the fatty acyl sarcosines and salts are approved for the following indirect food additive uses:

- *N*-Acyl sarcosines, where the acyl group is lauroyl, oleoyl, or derived from the combined fatty acids of coconut oil, are approved as antistatic and/or antifogging agents at levels not to exceed a total of 0.15% by weight of polyolefin film and ethylene-vinyl acetate copolymer film for which average thickness of the copolymer films shall not exceed 0.003 inches. [21CFR178.3130]
- In polymers (specifically, cellophane), *N*-acyl sarcosines, where the acyl group is lauroyl or stearoyl, are approved for use only as release agents in coatings at levels not to exceed a total of 0.3% by weight of the finished packaging cellophane, and Sodium Lauroyl Sarcosinate is approved for use at 0.35% only in vinylidene chloride copolymer coatings. [21CFR177.1200]

Table 3. Current and Historical Frequency and Concentration of Use According to Duration and Exposure.

	No. of uses		Max conc of use (%)		No. of uses		Max conc of use (%)	
	Cocoyl Sarcosine				Lauroyl Sarcosine			
	2016[13]	1998[1]	2015[14]	**	2016[13]	1998[1]	2015[14]	**
Totals*	22	33	0.01–1	**	NR	6	6.2–6.3	**
Duration of use								
Leave-on	16	24	0.01–1	**	NR	NR	NR	**
Rinse-off	5	9	0.7	**	NR	6	6.2–6.3	**
Diluted for (bath) use	1	NR	NR	**	NR	NR	NR	**
Exposure type								
Eye area	1	2	NR	**	NR	NR	NR	**
Incidental ingestion	NR	NR	NR	**	NR	NR	NR	**
Incidental inhalation-spray	3[a]	2[a]	NR	**	NR	NR	NR	**
Incidental inhalation-powder	1	NR	NR	**	NR	NR	NR	**
Dermal contact	17	22	0.7–1	**	NR	1	6.2	**
Deodorant (underarm)	NR	NR	NR	**	NR	NR	NR	**
Hair-non-coloring	5	9	0.01	**	NR	5	6.3	**
Hair-coloring	NR	NR	NR	**	NR	NR	NR	**
Nail	NR	NR	NR	**	NR	NR	NR	**
Mucous membrane	3	NR	0.7	**	NR	1	NR	**
Baby products	NR	NR	NR	**	NR	NR	NR	**
	Myristoyl Sarcosine				Oleoyl Sarcosine			
	2016[13]	1998[1]	2015[14]	**	2016[13]	1998[1]	2015[14]	**
Totals*	1	4	NR	**	2	5	NR	**
Duration of use								
Leave-on	NR	NR	NR	**	NR	3	NR	**
Rinse-off	1	4	NR	**	2	2	NR	**
Diluted for (bath) use	NR	NR	NR	**	NR	NR	NR	**
Exposure type								
Eye area	NR	NR	NR	**	NR	NR	NR	**
Incidental ingestion	NR	NR	NR	**	NR	1	NR	**
Incidental inhalation-spray	NR	NR	NR	**	1[b]	1; 2[b]	NR	**
Incidental inhalation-powder	NR	NR	NR	**	1[b]	2[b]	NR	**
Dermal contactc	1	4	NR	**	2	2	NR	**
Deodorant (underarm)	NR	NR	NR	**	NR	NR	NR	**
Hair-non-coloring	NR	NR	NR	**	NR	1	NR	**
Hair-coloring	NR	NR	NR	**	NR	1	NR	**
Nail	NR	NR	NR	**	NR	NR	NR	**
Mucous membrane	NR	NR	NR	**	NR	1	NR	**
Baby products	NR	NR	NR	**	NR	NR	NR	**
	Stearoyl Sarcosine				Ammonium Lauroyl Sarcosinate			
	2016[13]	1998[1]	2015[14]	**	2016[13]	1998[1]	2015[14]	**
Totals*	1	4	NR	**	2	NR	NR	**
Duration of use								
Leave-on	NR	NR	NR	**	NR	NR	NR	**
Rinse-off	1	4	NR	**	2	NR	NR	**
Diluted for (bath) use	NR	NR	NR	**	NR	NR	NR	**

(continued)

Table 3. (continued)

	Stearoyl Sarcosine				Ammonium Lauroyl Sarcosinate			
	2016[13]	1998[1]	2015[14]	**	2016[13]	1998[1]	2015[14]	**
Exposure type								
Eye area	NR	NR	NR	**	NR	NR	NR	**
Incidental ingestion	NR	NR	NR	**	NR	NR	NR	**
Incidental inhalation-spray	NR	NR	NR	**	NR	NR	NR	**
Incidental inhalation-powder	NR	NR	NR	**	NR	NR	NR	**
Dermal contact	1	4	NR	**	NR	NR	NR	**
Deodorant (underarm)	NR	NR	NR	**	NR	NR	NR	**
Hair-non-coloring	NR	NR	NR	**	2	NR	NR	**
Hair-coloring	NR	NR	NR	**	NR	NR	NR	**
Nail	NR	NR	NR	**	NR	NR	NR	**
Mucous membrane	NR	NR	NR	**	NR	NR	NR	**
Baby products	NR	NR	NR	**	NR	NR	NR	**

	Sodium Cocoyl Sarcosinate				Sodium Lauroyl Sarcosinate			
	2016[13]	1998[1]	2015[14]	**	2016[13]	1998[1]	2015[14]	**
Totals*	38	20	0.036–6	**	485	357	0.00025–15	**
Duration of use								
Leave-on	5	2	0.036–0.7	**	22	73	0.23–0.9	**
Rinse-off	33	14	0.6–6	**	450	268	0.00025–15	**
Diluted for (bath) use	NR	4	NR	**	13	16	0.15–6	**
Exposure type								
Eye area	1	NR	0.036	**	5	NR	0.45	**
Incidental ingestion	NR	NR	NR	**	8	1	0.066	**
Incidental inhalation-spray	4[b]	1[b]	NR	**	2[a]; 3[b]	22[a]; 44[b]	NR	**
Incidentalc inhalation-powder	4[b]	1[b]	0.7[c]	**	3[b]	44[b]	0.35–0.9[c]	**
Dermal contact	25	10	0.036–3.9	**	347	316	0.00025–10	**
Deodorant (underarm)	NR	NR	NR	**	NR	NR	NR	**
Hair-non-coloring	13	6	6	**	118	40	2.3–15	**
Hair-coloring	NR	NR	NR	**	12	NR	1.5	**
Nail	NR	NR	NR	**	NR	1	NR	**
Mucous membrane	2	6	2.4	**	257	46	0.00025–9	**
Baby products	2	1	NR	**	3	NR	NR	**

	Sodium Myristoyl Sarcosinate				Sodium Palmitoyl Sarcosinate	
	2016[13]	1998[1]	2015[14]	**	2016[13]	2015[14]
Totals*	36	2	0.15–6	**	21	0.00018–3
Duration of use						
Leave-on	1	NR	0.15–5	**	20	0.00018–0.88
Rinse-off	35	2	0.9–6	**	1	3
Diluted for (bath) use	NR	NR	NR	**	NR	NR
Exposure type						
Eye area	1	NR	0.67–5	**	NR	0.14
Incidental ingestion	NR	NR	<5	**	NR	0.00057
Incidental inhalation-spray	NR	NR	NR	**	9[a]; 5[b]	NR
Incidental inhalation-powder	NR	NR	0.15; 3.5[c]	**	1; 5[b]	0.081
Dermal contact	28	2	0.15–6	**	19	0.00053–3
Deodorant (underarm)	NR	NR	NR	**	NR	NR
Hair-non-coloring	8	NR	3.5	**	1	NR

(continued)

Table 3. (continued)

	Sodium Myristoyl Sarcosinate				Sodium Palmitoyl Sarcosinate	
	2016[13]	1998[1]	2015[14]	**	2016[13]	2015[14]
Hair-coloring	NR	NR	NR	**	NR	NR
Nail	NR	NR	NR	**	1	0.00018
Mucous membrane	5	NR	<5–6	**	NR	0.00057
Baby products	NR	NR	NR	**	NR	NR

NR, not reported.
*Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.
**Concentration of use data was not available at the time of the original assessment.
[a]Includes products that can be sprays, but it is not known whether the reported uses are sprays.
[b]Not specified whether this product is a spray or a powder or neither, but it is possible it may be a spray or a powder, so this information is captured for both categories of incidental inhalation.
[c]Includes products that can be powders, but it is not known whether the reported uses are powders.

Table 4. Ingredients currently not reported to be used.

Ammonium Cocoyl Sarcosinate
Potassium Cocoyl Sarcosinate#
Potassium Lauroyl Sarcosinate#
Sodium Oleoyl Sarcosinate#

#Not previously reviewed.

- Oleoyl Sarcosine is approved for use as a corrosion inhibitor in lubricants with incidental food contact at levels not to exceed 0.5% by weight of the lubricant. [21CFR178.3570]
- Sodium Lauroyl Sarcosinate is approved in adhesives without limitations. [21CFR175.105]

Oleoyl Sarcosine is used in lubricants and greases, metal working fluids, washing and cleaning products, hydraulic fluids, textile treatment products and dyes, metal surface treatment products, and leather treatment products.[22] It is used in the formulation of mixtures and/or re-packaging, building and construction work and agriculture, forestry, and fishing. Also, Oleoyl Sarcosine is used for the manufacture of plastic products, mineral products (eg plasters and cement), fabricated metal products, machinery and vehicles, furniture and textiles, and leather or fur.

Toxicokinetics

Dermal Penetration

The amount of transdermal penetration from 1% Lauroyl Sarcosine (0.5 g) in an ointment was ~1660 µg over 24 hours in Wistar rat, as determined using high-performance liquid chromatography; addition of 30% vitamin E or 10% squalene enhanced Lauroyl Sarcosine penetration.[1]

Penetration Enhancement

Lauroyl Sarcosine (30%) increased the penetration of isosorbide dinitrate through the skin of the rat; the addition of 30% vitamin E or 10% squalene maintained or enhanced the effect of Lauroyl Sarcosine.[1] In a study of the effects of surfactants on epidermal permeability, 30% Sodium Lauroyl Sarcosine did not increase permeability.

Lauroyl Sarcosine. The effect of Lauroyl Sarcosine (98% pure) on transdermal fluorescein delivery across the epidermis of human cadaver skin was determined using Franz cells.[23] The vehicles were phosphate buffered solution (PBS; in which Lauroyl Sarcosine was generally insoluble) and aq. ethanol solution. A 0.7 cm^2 skin surface was exposed to 0.3 mL of test solution. Lauroyl Sarcosine only did not significantly enhance transdermal flux. With ethanol, skin permeability increased with increasing Lauroyl Sarcosine concentrations (1–3%) in 25–50% ethanol solution, and transdermal delivery of fluorescein was increased by 47-fold using formulations containing 3% Lauroyl Sarcosine in aq. 50% ethanol solutions. The effects of higher concentrations of ethanol (ie, 75% or 100%) as the vehicle resulted in weaker enhancement effects. Lauroyl Sarcosine and ethanol synergistically increased skin permeability, and the researchers concluded that permeability was increased due to a mechanism that involved synergistic lipid-fluidization activity in the stratum corneum.

Sodium Lauroyl Sarcosinate. In the study described above, the researchers also examined the effect of Sodium Lauroyl Sarcosinate on transdermal fluorescein delivery across human cadaver skin epidermis.[23] Sodium Lauroyl Sarcosinate was completely dissolved in PBS. Only a "very small increase in transdermal flux" (0.061 ± 0.013 µg) was observed.

Absorption, Distribution, Metabolism, and Excretion

When [^{14}C]Sodium Lauroyl Sarcosinate was administered to rats (route of administration not available) during a metabolism study, 82–89% of the 50 mg/kg dose was excreted in the urine and feces within 24 hours.[1] For the next 24 hours, 1–2% was excreted. Nearly all of the excreted material was

found in the urine. In a study in which [^{14}C]Sodium Lauroyl Sarcosinate was applied to the teeth, oral mucosa, and tongue of rats, the mean distribution of the radiolabel was 1.12% in the teeth, 2.22% in the oral mucosa, and 2.95% in the tongue immediately after dosing. At 24 hours, the mean distribution was 0.79% in the teeth, 0.92% in the oral mucosa, 0.57% in the tongue, 1.6% in the liver, 0.8% in the kidneys, 1.8% in the feces, and 42.2% in the urine. The data indicated that Sodium Lauroyl Sarcosinate was not absorbed by the tissues of the mouth but was swallowed and absorbed into the blood. Approximately 34% of the radioactivity was excreted in the urine over a period of 4 hours, and 42% was excreted within 24 hours.

Sarcosine is a natural amino acid found in muscles and other body tissues; it is found naturally as an intermediate in the metabolism of choline to glycine.[24] Oleoyl Sarcosine is a normal metabolite in man.[7]

Toxicological Studies

The fatty acyl sarcosines and sarcosinate salts have low oral toxicity.[1] The oral LD_{50} values of Sodium Lauroyl Sarcosinate, Cocoyl Sarcosine, and Sodium Cocoyl Sarcosinate were 4.2 to 6.0 g/kg in rats. The oral LD_{50} of Cocoyl Sarcosine in mice was 2.1 g/kg. Ten male Yale Sherman Wistar rats per group were given a single dose (gavage) of 2.5% aqueous Sodium Lauroyl Sarcosine; no deaths occurred in groups given up to 1000 mg/kg, 1 rat each died in the 1200- and 1500-mg/kg groups, 2 died in the 1750 mg/kg group, 4 died after treatment with 2000 mg/kg, 7 died in the 2250 mg/kg group, and all 10 rats died in the group given 2500 g/kg. Weanling rats fed 0.5–2% Sodium Lauroyl Sarcosinate for up to 6 months had no signs of toxicity. During a 2-year feeding study using Wistar rats, the no-observed-effect level of Sodium Lauroyl Sarcosinate was 1000 mg/kg/day.

Acute Toxicity Studies

Dermal

Sodium Myristoyl Sarcosinate. A dose of 2000 mg/kg Sodium Myristoyl Sarcosinate in arachis oil was applied for 24 hours to the backs and flanks of 5 male and 5 female RCC Han:WIST rats using semi-occlusive patches.[25] Approximately 10% of the body was covered. Observations were made 0.5, 1, 2, and 4 hours after dosing and then once daily for 14 days. All animals survived until study termination. Very slight erythema, which was observed in 7/10 animals, was fully reversible within 5 days. The dermal LD_{50} of Sodium Myristoyl Sarcosinate was >2000 mg/kg in male and female rats.

Oral

Oleoyl Sarcosine. One study reported that the oral LD_{50} of Oleoyl Sarcosine was >5000 mg/kg, by gavage, in male and female Sprague-Dawley rats,[22] and another reported it as 9200 mg/kg in the rat.[25] (Details were not provided.)

Sodium Lauroyl Sarcosinate. Male and female Sprague-Dawley rats were given a single dose by gavage of 5000 mg/kg aq. Sodium Lauroyl Sarcosinate.[26] One female died on day 2; clinical signs were not observed in any of the remaining animals. The oral LD_{50} was >5000 mg/kg.

Sodium Oleoyl Sarcosinate. The oral LD_{50} of Sodium Oleoyl Sarcosinate in rats was 6000 mg/kg.[1]

Inhalation

Oleoyl Sarcosine. Ten male and 10 female Sprague-Dawley rats were exposed nose/head only to Oleoyl Sarcosine in 10% ethanol for 4 hours, according to Organisation for Economic Development (OECD) Guideline 403 (acute inhalation study).[22] The LC_{50} for male and female rats was >1.01–1.85 mg/L air. No additional details were provided.

Sodium Lauroyl Sarcosinate. Groups of 5 male and 5 female Wistar:Han rats were exposed nose/head only to aq. 0.5, 1, or 5 mg/L air Sodium Lauroyl Sarcosinate (34.5% pure) for 4 hours.[26] The mass median aerodynamic diameters (MMADs) of the aerosol particles at target concentrations of 0.5, 1, and 5 mg/L were 2.6–3.1 µm, 2.0–2.7 µm, and 2.5–4.5 µm, respectively; the researchers stated that at 5 mg/L, the MMAD measurements showed an abnormal distribution, which may have been caused by the high test substance concentration in relation with high relative humidity, but the results were sufficient to conclude that the droplets size was suitable to warrant a correct exposure with sufficient distribution over the lungs. Two females and 3 males of the 5 mg/L group were found dead immediately after exposure, and the remaining animals were killed within 1 hour after exposure for humane reasons; death was attributed to acute respiratory tract irritancy. No mortality occurred in the 0.5 or 1.0 mg/L groups; shallow respiration was noted in all animals of these 2 groups. Some treatment-related gross and microscopic lesions were observed in the lungs of some animals at all test concentrations. The LC_{50} of Sodium Lauroyl Sarcosinate (34.5% pure) was between 1 and 5% for male and female rats.

The acute inhalation toxicity of Sodium Lauroyl Sarcosinate (96.2% pure) was evaluated in Wistar rats following a 4-hour nose-only exposure; the test was performed according to US Environmental Protection Agency (EPA) OPPTS 870.1300 guideline for acute inhalation toxicity.[25] Groups of 5 males were exposed to 0.05 or 0.5 mg/L, and 5 males and 5 females were exposed to 1 or 5 mg/L. The MMAD of the aerosol particles at target concentrations of 0.05, 0.5, 1, and 5 mg/L were 4.1–4.6 µm, 2.5–3.2 µm, 3.5–3.8 µm, and 5.8–6.2 µm, respectively. The 10 animals exposed to 5 mg/L died within 1–2 hours of dosing, and the 10 animals exposed to 1 mg/mL and 4/5 of the animals exposed to 0.5 mg/L died within 1–2 days after dosing; none of the 5 animals exposed to

0.05 mg/L died during the study. During exposure, labored respiration was only observed in the 1 mg/L group only. After exposure, no clinical signs were noted in the low or high dose groups: lethargy, flat/hunched posture, labored respiration, piloerection, and red discoloration of the mouth and nose among the males of the 0.5 mg/L group and most females (but not males) in the 1 mg/L group. At necropsy, red foci were noted on the lungs in animals of all groups except the lowest dose group. The LC_{50} of Sodium Lauroyl Sarcosinate in rats was 0.05–0.5 mg/L air following the 4-hour exposure.

Short-Term Toxicity Studies

Oral

Sodium Lauroyl Sarcosinate. Groups of 15 male and 15 female Sprague-Dawley albino rats were dosed orally by gavage daily with 0, 30, 100, and 250 mg/kg Sodium Lauroyl Sarcosinate in distilled water for 91 or 92 days.[25] Body weight gains were decreased in males of the 100 and 250 mg/kg groups; the decrease was statistically significant compared to controls for 5 of 13 weeks in the mid-dose group and 8 of 13 weeks in the high doses group. Absolute stomach weights (in males), stomach-to-body weight ratios, and stomach-to-brain-weight ratios (in males and females) were statistically significantly increased in the 100 and 250 mg/kg dose groups. There was an increase in stomach wall thickness and yellow discoloration of non-glandular gastric mucosa, and histopathology revealed an increase in incidence and severity of squamous cell hyperplasia, hyperkeratosis/parakeratosis, inflammation, and edema of the non-glandular mucosa in both male and females of these groups. Weights of several other organs that were statistically significantly different from control values were not considered toxicologically significant. There were no toxicologically significant changes in hematology or clinical chemistry parameters. No test material-related mortality was reported. The no-observed effect level (NOEL), lowest observable adverse effect level (LOAEL; local effects), and no-observable adverse effect level (NOAEL; systemic effects) for male and female animals were 30, 100, and 250 mg/kg/day, respectively.

Inhalation

Oleoyl Sarcosine. In a 28-day inhalation study performed according to OECD Guideline 412 (Repeated Dose Inhalation Toxicity: 28/14-day), groups of 3 male and 3 female Fischer 344 rats were exposed nose-/head-only to 0, 0.006, 0.02, or 0.06 mg/L Oleoyl Sarcosine in <10% ethanol.[22] The daily exposure time was not specified; however, according to OECD Guideline 412, daily exposure is 6 hours in this type of study. The MMAD of the aerosol particles were 1.11, 1.15, and 1.22 µm for the low, mid, and high concentrations, respectively. All test concentrations caused effects at several sites of the respiratory system with indications for a local irritation, squamous metaplasia and epithelium proliferation and submucous acute inflammation at the base of the epiglottis; these changes may be explained by the amounts of inert material deposited within the respiratory system. In the lungs and bronchi, the most prominent finding was a focal early stage of fibrosis. The researchers stated that due to the high amount of test substance deposits in the lungs, especially in the 0.02 and 0.06 mg/L groups, these changes may be explained as an overloading of the tissue and do not necessarily imply an intrinsic toxicity of the test material; an intrinsic toxicity is unlikely because the test material is insoluble and the shape of the particles is not fibrous. There was an effect on testes, thymus, brain, lung, and kidneys weights, but details were not provided. The NOEL was <0.006 mg/L air in males and females; the basis for the effect level was local irritation. The no-observed adverse effect concentration (NOAEC) was >0.06 mg/L air in males, and the basis for that effect level was an effect on organ weight.

Developmental and Reproductive Toxicity

The feeding of up to 1000 mg/kg/day Sodium Lauroyl Sarcosinate did not adversely affect fertility of albino Sherman Wistar rats during a 2-year oral toxicity study.[1]

Sodium Lauroyl Sarcosinate

A prenatal developmental toxicity study (OECD Guideline 414) was conducted for Sodium Lauroyl Sarcosinate (95% pure) in Sprague-Dawley rats.[26] Groups of 24 gravid female rats were dosed once daily by gavage with 0, 30, 100, and 250 mg/kg/day of the test article in distilled water on days 5–10 of gestation, and the animals were killed on day 20 of gestation. Sodium Lauroyl Sarcosinate was not embryotoxic or teratogenic. Maternal body weight gains (adjusted) in the mid- and high-dose group were decreased during gestation as compared to the controls. Feed consumption was decreased in the high dose group; the decrease was statistically significant between days 8–11 and days 14–17 of gestation. Two high-dose dams died during the study, one on day 10 and one on day 18 of gestation. The dam that died on day 18 of gestation had sloughing on the non-glandular region of the stomach, 7 dead fetuses had sloughing in the right uterine horn, and 5 dead fetuses had sloughing in the left uterine horn, and the high-dose females killed at study termination all had sloughing on the non-glandular region of the stomach; this effect was not observed in the low- or mid-dose groups. The NOAEL (maternal toxicity), LOAEL (maternal toxicity), and NOEL (developmental toxicity) were 30, 100, and ≥250 mg/kg/day Sodium Lauroyl Sarcosinate, respectively.

Genotoxicity

In Vitro

Sodium Lauroyl Sarcosinate was not considered mutagenic in five strains of *Salmonella typhimurium* during plate

incorporation assays and spot tests.[1] In addition, Sodium Lauroyl Sarcosinate did not induce double-strand DNA breaks in the comet assay using human white blood cells and V79 Chinese Hamster cells, but the compound was cytotoxic.

Oleoyl Sarcosine. Oleoyl Sarcosine in dimethyl sulfoxide at concentrations of ≥5000 µg/plate, with or without metabolic activation, was not mutagenic in an Ames test with *S. typhimurium* TA1535, TA1537, TA100, and TA9825 or in an Ames test with *S. typhimurium* TA97a, TA98, TA100, TA102, or TA1535.[22] Positive and vehicle controls gave expected results.

Sodium Lauroyl Sarcosinate. The genotoxic potential of Sodium Lauroyl Sarcosinate (96.2% pure) was evaluated in an in vitro mammalian chromosomal aberration assay in lymphocytes.[26] Cells were treated with 22.5–360 µg/mL for 4 hours with or without metabolic activation and with 22.5–270 µg/mL for 24 hours without metabolic activation. Minimal essential media served as the vehicle. Sodium Lauroyl Sarcosinate was not genotoxic. Solvent and positive controls gave expected results.

Carcinogenicity

Carcinogenicity data of the fatty acyl sarcosines and their salts were not available; however, the ingredients were not considered likely carcinogens as they and their metabolites "do not belong to any class of compounds that contains a significant number of mutagens or oncogens."[1]

Dermal Irritation and Sensitization

Sodium Lauroyl Sarcosinate was non-irritating to rabbits when administered as a 20–30% solution, at a concentration of 2% in formulation, or as the pure powder.[1] A formulation containing 30% Sodium Myristoyl Sarcosinate was not a primary skin irritant in rabbits, and 0.01% aq. Sodium Lauroyl Sarcosinate was non-sensitizing to the skin of guinea pigs.

During a clinical study using 27 subjects, cocobetaine (it was unclear whether the cocobetaine tested was Cocoyl Sarcosine or the related, cocoyl *N*-dimethyl glycine derivative) markedly influenced skin water vapor loss and caused erythema, scaling, and fissuring of the skin of the volar forearm.[1] In another study, Cocoyl Sarcosine and Sodium Lauroyl Sarcosinate retarded moisture loss from the skin via the formation of a hydrophobic protective layer on the epidermal surface; in an epicutaneous patch test using highly dermatitic subjects, "practically no reaction" was observed. In other clinical studies, Sodium Lauroyl Sarcosinate (2–5%) was non-irritating and non-sensitizing.

Dermal Irritation

In Vitro

Sodium Lauroyl Sarcosinate. The irritation potential of Sodium Lauroyl Sarcosinate was evaluated in an In Vitro Skin Corrosion Human Skin Model Test (OECD Guideline 431) using reconstructed human epidermis.[26] Twenty mg of the test material in 0.9% sodium chloride solution was applied to the tissue for 3, 60, or 240 minutes, and tissue viability was measured using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) uptake. Sodium Lauroyl Sarcosinate was non-corrosive to reconstructed human epidermis. Appropriate negative and positive controls gave valid results.

Animal

Oleoyl Sarcosine. Oleoyl Sarcosine, 0.5 mL, was applied neat to the shaved intact and abraded skin of 3 male and 3 female New Zealand White rabbits under an occlusive patch for 24 hours.[22] The test sites were scored upon patch removal and over a 7-day period. The mean erythema score at 24 and 72 hours was 2.5–2.8 and 2.7–3, respectively. Additionally, at 72 hours, the treated areas developed slight necrosis and the skin hardened. Oleoyl Sarcosine was classified as irritating.

Sodium Lauroyl Sarcosinate. The dermal irritation potential of Sodium Lauroyl Sarcosinate was evaluated in 6 female New Zealand White rabbits.[25] The test material was diluted 1:3 in water to give 10% active material, and occlusive patches containing 0.5 mL were applied for 24 hours to shaved intact and abraded skin of each animal. Well-defined erythema was observed at both intact and abraded treatment sites of all 6 animals following the 24 hours dosing period, and slight edema was observed at 4 intact and 2 abraded treatment sites. After 72 hours, well-defined erythema remained at both the intact and abraded sites of 4 animals, and very slight erythema was observed at both sites in one animal. Slight edema was observed at the abraded site of one animal, and very slight edema was observed at 3 abraded sites and 3 intact sites. Test sites were scored at 24 and 72 hours, and the mean scores for erythema and edema were 1.83/4 and 1.06/4, respectively; erythema and edema were not fully reversible within 72 hours.

Sensitization

Animal

Oleoyl Sarcosine. In a guinea pig maximization test (GPMT) using groups of 10 male and 10 female Pirbright White guinea pigs, the intradermal induction consisted of 3 pairs of injections of a 1:1 mixture of Freund's Complete Adjuvant (FCA) and saline; 5% Oleoyl Sarcosine in saline; and a mixture of Oleoyl Sarcosine with FCA/saline.[22,25] The epicutaneous induction concentration was 30% Oleoyl Sarcosine in petrolatum. The challenge was performed on day 20 and consisted of a 24-hour patch at a concentration of 3% in petrolatum. The test site was evaluated after 48 hours; 3 animals had very slight erythema and 2 had well-defined erythema. The researchers classified the test substance as not sensitizing.

Photosensitization

Animal

Oleoyl Sarcosine. A photosensitization study of Oleoyl Sarcosine was conducted using groups of 10 male and 10 female Pirbright White guinea pigs.[27] Induction consisted of open applications of 0.1 mL of a 0.1% suspension of the test substance in 80% DAE (40% dimethylacetamide, 30% acetone, and 30% ethanol) and 20% physiological saline that were applied topically to the shaved skin on the necks of the animals 4 times/wk for 3 weeks. One hour after each application, the animals were irradiated for 10 minutes; during week 1, the animals were exposed to ultraviolet A (UVA) and visible light using a Schott WG 335, 3 mm filter, and during weeks 2 and 3, they were exposed to UVA, UVB, and visible light using a Schott WG 280, 3 mm filter. The test sites were scored 24 hours after each induction application during induction week 1. The sites were not scored during induction weeks 2 and 3; during this time, a total of four adjuvant injections of 0.1 mL FCA/saline were made to the 4 corners of the application site on Monday and Wednesday of both weeks.

The first challenge was performed 16 days after the last induction irradiation; open applications of 0.1 mL of the test substance was applied to the dorsal skin of the animals for 3 days, and the sites were irradiated 1 hour after the application with a suberythematogenic dose of UVA, UVB, and visible light. The second challenge was performed after a 14-day non-treatment period; the test material was applied in the same manner as the first challenge, but this time the application was followed with 10 minutes irradiation with a suberythematogenic dose of UVA and visible light. The test sites were evaluated 24 hours after each challenge application. Any animal in which the irritation score after challenge was 1+ point above the score from week 1 of induction was considered to be photosensitized. The test animals were compared to the control group that was treated with the vehicle alone.

Three control animals and 2 test animals died during the study; the deaths were not related to dosing. Three of 17 control animals had slight erythema during the first challenge. However, 17 and 15 of the 18 test animals had positive results after the first and second challenges, respectively. Oleoyl Sarcosine was considered to possess a photocontact-allergenic potential in guinea pigs.

Ocular Irritation

Sodium Cocoyl Sarcosinate (10%) at neutral or slightly acid pH caused slight, temporary ocular irritation but no corneal damage in rabbits according to the procedures of the Draize-Woodard test.[1] In another ocular irritation study using rabbits, a 5% aqueous solution of Sodium Lauroyl Sarcosinate caused minimal conjunctival irritation and no apparent damage to the cornea.

In Vitro

Sodium Myristoyl Sarcosinate. The ocular irritation potential of 20% Sodium Myristoyl Sarcosinate (92.1% pure) in physiological saline was evaluated in the Bovine Corneal Opacity and Permeability (BCOP) test.[25] The test article was considered to be an ocular corrosive or severe irritant in the BCOP test.

Animal

Oleoyl Sarcosine. Oleoyl Sarcosine was instilled into one eye of rabbits according to EPA guidelines; the eyes of half the rabbits were rinsed after 30 seconds.[7] Details on the dose and number of animals were not provided. Draize scores of 47 and 40 were reported for unrinsed and rinse eyes, respectively. Oleoyl Sarcosine was classified as moderately irritating to rabbit eyes.

In another study, detachment and clouding of the cornea was seen in rabbits treated with either Oleoyl Sarcosine or its sodium salt.[7] After treatment with the sodium salt, the effects on the cornea had worsened after 1 week; this change was not reversible after 15 days.

Sodium Cocoyl Sarcosinate and Sodium Lauroyl Sarcosinate. Sodium Cocoyl Sarcosinate (10%) at neutral or slightly acid pH caused slight, temporary ocular irritation but no corneal damage in rabbits according to the procedures of the Draize-Woodard test.[1] In another ocular irritation study using rabbits, a 5% aqueous solution of Sodium Lauroyl Sarcosinate caused minimal conjunctival irritation and no apparent damage to the cornea.

Sodium Myristoyl Sarcosinate. One-tenth milliliter of a mixture of Sodium Myristoyl Sarcosinate and sodium myristate was instilled neat into the conjunctival sac of the right eye of 6 rabbits, and the contralateral eye served as the control.[28] All animals had a positive response to the test article, and the maximum average eye irritation score was 55.3 at 24 hours after instillation. The mixture of Sodium Myristoyl Sarcosinate and sodium myristate was extremely irritating to rabbit eyes and considered a primary eye irritant.

Mucosal Irritation

Sodium Lauroyl Sarcosinate (20% aq. solution, 2% in formulation, powder) was non-irritating to the gums and oral mucosa of rabbits.[1]

Clinical Reports

Case Reports

Sodium Lauroyl Sarcosinate. A female patient developed an acute severe eczematous reaction on her hands, face, and neck,

and the reaction was related to use of a hand soap.[29] After open and unoccluded patch test resulted in a +3 bullous reaction to the product, patch testing with some of the individual constituents was performed. A +3 bullous reaction to a 30% aq. solution of Sodium Lauroyl Sarcosinate in sterile water was reported. In 2 subjects patch tested with the soap and Sodium Lauroyl Sarcosinate, negative results were obtained.

In another report, a female patient with recurrent hand dermatitis had a positive reaction to semi-open application of a liquid cleanser that contained Sodium Lauroyl Sarcosinate.[30] Positive reactions were observed in follow-up patch testing with 0.1, 0.5, and 1% aq. Sodium Lauroyl Sarcosinate; at 98 hours, the scores were "–," "+/–," and "+" at these concentrations, respectively.

Summary

In 2001, the Panel published a safety assessment with the conclusion that 5 fatty acyl sarcosines and 5 sarcosinate salts are safe as used in rinse-off products, safe for use in leave-on products at concentrations of ≤5%, and the data are insufficient to determine the safety for use in products where the fatty acyl sarcosines and salts are likely to be inhaled. These ingredients should not be used in cosmetic products in which *N*-nitroso compounds may be formed. This assessment is a re-review of those original ingredients, as well as 4 additional salts.

Sarcosine (which is also known as *N*-methylglycine or *N*-methylaminoacetic acid) is a natural amino acid found in muscles and other body tissues, and it is found naturally as an intermediate in the metabolism of choline to glycine. Oleoyl Sarcosine is also a normal metabolite in man.

Ten of the 14 ingredients included in this safety assessment are currently in use. Sodium Lauroyl Sarcosinate has the highest frequency of use, with 485 reported uses; the majority of these uses are in rinse-off formulations, primarily bath soaps and detergents (230 uses) and shampoos (113 uses). Sodium Lauroyl Sarcosinate also has the highest concentration of use, with maximum use concentrations up to 15% in rinse-off products. The highest reported leave-on concentration is 5% Sodium Myristoyl Sarcosinate in eye shadow formulations.

Lauroyl Sarcosine and ethanol synergistically increased skin permeability, as demonstrated by up to a 47-fold increase in transdermal delivery of fluorescein across human cadaver epidermis using 3% lauroyl sarcosine in aq. 50% ethanol. Lauroyl Sarcosine and Sodium Lauroyl Sarcosinate alone (in PBS) did not significantly affect penetration.

Sodium Myristoyl Sarcosinate had a dermal LD_{50} of >2000 mg/kg in male and female rats. In acute oral studies in rats, oleoyl sarcosine had an LD_{50} of 9200 mg/kg, Sodium Lauroyl Sarcosinate had an LD_{50} of >5000 mg/kg, and Sodium Oleoyl Sarcosinate had an LD_{50} of 6000 mg/kg. In a 3-month gavage study of Sodium Lauroyl Sarcosinate in rats, the NOEL, LOAEL (local effects), and NOAEL (systemic effects) were 30, 100, and 250 mg/kg/day, respectively.

Acute inhalation studies were performed in rats; with a 4-hour exposure, Oleoyl Sarcosine had a LC_{50} of >1.01–1.85 mg/L air, Sodium Lauroyl Sarcosinate (34.5% pure) had an LC_{50} between 1 and 5%, and Sodium Lauroyl Sarcosinate (96.2% pure) had an LC_{50} of 0.05–0.5 mg/L air. A 28-day inhalation study was performed in rats with Oleoyl Sarcosinate; the NOEL was <0.006 mg/L air, and the NOAEC was 0.06 mg/L air.

No embryotoxicity or teratogenicity was observed in a prenatal developmental toxicity study in which gravid rats were dosed by gavage with up to 250 mg/kg/day Sodium Lauroyl Sarcosinate on days 5–10 of gestation. The NOAEL and LOAEL for maternal toxicity were 30 and 100 mg/kg/day.

Oleoyl Sarcosine was not mutagenic in an Ames test (≥5000 µg/plate, with or without metabolic activation), and Sodium Lauroyl Sarcosinate (22.5–360 µg/mL for 4 hours with or without metabolic activation; 22.5–270 µg/mL for 24 hours without metabolic activation) was not genotoxic in an in vitro mammalian chromosomal aberration assay in lymphocytes.

Sodium Lauroyl Sarcosinate was non-corrosive to reconstructed human epidermis in an In Vitro Skin Corrosion Human Skin Model Test. Undiluted Oleoyl Sarcosine was irritating to rabbit skin, and Oleoyl Sarcosine was classified as not sensitizing in a GPMT in which 3 and 2/20 guinea pigs had very slight and well-defined erythema, respectively, 48 hours after challenge with 3% Oleoyl Sarcosine in petrolatum. Oleoyl Sarcosine was also considered to possess photocontact-allergenic potential in guinea pigs. A single 24-hour application of Sodium Lauroyl Sarcosinate (10% active material) produced mean erythema and edema scores of 1.83/4 and 1.06/4 in rabbits, and the effects were not fully reversible within 72 hours.

Sodium Myristoyl Sarcosinate, 20%, was considered to be an ocular corrosive or severe irritant in vitro in the BCOP test, and a mixture of Sodium Myristoyl Sarcosinate and sodium myristate was extremely irritating to rabbit eyes and considered a primary eye irritant. Oleoyl sarcosine was classified as moderately irritating to rabbit eyes.

Discussion

A safety assessment of 5 fatty acyl sarcosines and 5 fatty acyl sarcosine salts was published in 2001 with the conclusions that these ingredients are safe as used in rinse-off products, safe for use in leave-on products at concentrations of ≤5%, and the data are insufficient to determine the safety for use in products where the fatty acyl sarcosines and their salts are likely to be inhaled. Also, the conclusion stated that these ingredients should not be used in cosmetic products in which *N*-nitroso compounds may be formed. Concentration of use data was not provided at the time of the original safety assessment; because those values were not available, the concentration limit of 5% was established for leave-on products based upon the highest concentration tested in human repeat-insult

patch tests. Concentration of use data is now available, and because sensitization is not observed in studies at the highest concentration currently reported to be used, the Panel re-opened the safety assessment to remove the 5% concentration limit for leave-on products.

The Panel determined 4 previously unreviewed fatty acyl sarcosine salts used as cosmetic ingredients are structurally similar to the ingredients reviewed in the original assessment, and that the data from the original safety assessment, together with the new data presented in this report, support their safety. Therefore, these 4 ingredients are included in this review.

Some of the ingredients included in this report, particularly Lauroyl Sarcosine, can potentially enhance the penetration of other ingredients through the skin. The Panel cautioned that care should be taken in formulating cosmetic products that may contain these ingredients in combination with any ingredients whose safety was based on their lack of dermal absorption data, or when dermal absorption was a concern.

Sarcosine, a starting material in the manufacture of the acyl sarcosines and sarcosinates, can react with oxidizing materials and can be nitrosated to form *N*-nitrososarcosine, a known animal liver carcinogen. As a result, the Panel concluded that fatty acyl sarcosines and salts should not be used in cosmetic products in which *N*-nitroso compounds can be formed.

The Panel was concerned that the potential exists for dermal irritation with the use of products formulated using fatty acyl sarcosines and sarcosinate salts. The Panel specified that products containing these ingredients must be formulated to be non-irritating.

A photosensitization study indicated that Oleoyl Sarcosine may possess photocontact-allergenic potential in guinea pigs. The Panel noted that the chemical structure of Oleoyl Sarcosine does not have a chromophore, so there are no structural alerts for photosensitization. Additionally, the study did not indicate that an unirradiated control was used. The Panel stated that the allergenic response observed in the study was not to Oleoyl Sarcosine and was most probably due to a contaminant.

The Panel acknowledged that some of the fatty acyl sarcosines and sarcosinate salts may contain cocoyl fatty acyl substituents and expressed concern about pesticide residues and heavy metals that may be present in botanical ingredients. They stressed that the cosmetics industry should continue to use current good manufacturing practices to limit impurities.

Additionally, the Panel discussed the issue of incidental inhalation exposure of fatty acyl sarcosines and their salts. Some of these ingredients are listed in the VCRP in product types that can be sprays, but it is not known whether or not the reported uses are in sprays. However, Sodium Myristoyl Sarcosinate and Sodium Palmitoyl Sarcosinate are reported to be used in face powders at concentrations of 0.15% and 0.081%, respectively, and these products may become airborne. Single dose, 4-hour inhalation studies of 10% Oleoyl Sarcosine and Sodium Lauroyl Sarcosinate (96.2% pure) reported LC_{50} value of >1.01–1.85 mg/L air, and 0.05–0.5 mg/L, respectively; a 28-day inhalation study of oleoyl sarcosine in rats found that an intrinsic toxicity is unlikely because the test material is insoluble and the shape of the particles is not fibrous. The Panel also noted that droplets/particles from spray and loose-powder cosmetic products would not be respirable to any appreciable amount. Furthermore, droplets/particles deposited in the nasopharyngeal or bronchial regions of the respiratory tract present no toxicological concerns based on the chemical and biological properties of these ingredients. Coupled with the small actual exposure in the breathing zone and the concentrations at which the ingredients are used, the available information indicates that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic effects. A detailed discussion and summary of the Panel's approach to evaluating incidental inhalation exposures to ingredients in cosmetic products is available at http://www.cir-safety.org/cir-findings.

Conclusion

The Panel concluded that the following ingredients are safe as used in cosmetics when formulated to be non-irritating. The Panel cautions that these ingredients should not be used in cosmetic products in which *N*-nitroso compounds can be formed.

Cocoyl Sarcosine	Potassium Cocoyl Sarcosinate*
Lauroyl Sarcosine	Potassium Lauroyl Sarcosinate*
Myristoyl Sarcosine	Sodium Cocoyl Sarcosinate
Oleoyl Sarcosine	Sodium Lauroyl Sarcosinate
Stearoyl Sarcosine	Sodium Myristoyl Sarcosinate
Ammonium Cocoyl Sarcosinate*	Sodium Oleoyl Sarcosinate*
Ammonium Lauroyl Sarcosinate	Sodium Palmitoyl Sarcosinate

*Not reported to be in current use. Were ingredients in this group not in current use to be used in the future, the expectation is that they would be used in product categories and at concentrations comparable to others in this group.

Author's Note

Unpublished sources cited in this report are available from the Director, Cosmetic Ingredient Review, 1620 L Street, NW, Suite 1200, Washington, DC 20036, USA.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: The articles

in this supplement were sponsored by the Cosmetic Ingredient Review. The Cosmetic Ingredient Review is financially supported by the Personal Care Products Council.

References

1. Andersen FA, ed. Final report on the safety assessment of cocoyl sarcosine, lauroyl sarcosine, myristoyl sarcosine, oleoyl sarcosine, stearoyl sarcosine, sodium cocoyl sarcosinate, sodium lauroyl sarcosinate, sodium myristoyl sarcosinate, ammonium cocoyl sarcosinate, and ammonium lauroyl sarcosinate. *Int J Toxicol*. 2001;20(suppl 3):1-14.
2. Nikitakis J, Breslawec HP. *International Cosmetic Ingredient Dictionary and Handbook*. 15 ed. Washington, DC: Personal Care Products Council; 2014.
3. Burnett CL, Fiume MM, Bergfeld WF, et al. Final report on the safety assessement of plant-derived fatty acid oils as used in cosmetics. Available on the CIR website. 2011.
4. Elder RL, ed. Final report on the safety assessment of oleic acid, lauric acid, palmitic acid. myristic acid, and stearic acid. *J Am Coll Toxicol*. 1987;6(3):321-401. http://www.cir-safety.org/ingredients.
5. Andersen FA, ed. Annual review of cosmetic ingredient safety assessments - 2004/2005. *Int J Toxicol*. 2006;25(suppl 2):40-47.
6. European Chemical Agency (ECHA). Information on Chemicals. http://echa.europa.eu/information-on-chemicals;jsessionid=A978100B4E4CC39C78C93A851EB3E3C7.live1. Last Updated 2016. Accessed February 12, 2016.
7. Oleoyl Sarcosine [MAK Value Documentation, 2001]. The MAK Collection for Occupational Health and Safety. http://onlinelibrary.wiley.com/doi/10.1002/3527600418.mb1025kske0016/pdf. Last Updated 2012. Accessed February 23, 2016.
8. Guangzhou Tinci High-Tech Materials Co, Ltd. Product Bulletin: AMIN LS 30 (Sodium Lauroyl Sarcosinate; 30% Active). http://www.tinci.com/Editor/eWebeditor/uploadfile/20101222102049316.pdf. Last Updated 2008. Accessed February 12, 2016.
9. Innospec. Pureact LSR (Sodium Lauroyl Sarcosinate; 29-31% Active). http://tempo.ca/wp-content/uploads/2013/03/PUREACT-LSR-TDS-11-01-01.pdf. Last Updated 2011. Accessed February 12, 2016.
10. Miwon Commercial Co, Ltd. MIAMI L30 (Sodium Lauroyl Sarcosinate, 30% Active). http://www.mwc.co.kr/sub2/pdf/TDS%20MIAMI%20L30(2012.02).pdf. Last Updated 2012. Accessed February 12, 2016.
11. Shanghai OLI Enterprises Co., Ltd. Technical data sheet: OLI-4202 aqua sodium lauroyl sarcosinate; 30% active. http://www.kalekimya.com/admin/tds/1417086948_TDS_for_OLI-4202_Aqua_Sodium_Lauroyl_Sarcosinate.pdf. Last Updated 2016. Accessed February 12, 2016.
12. Wogan GN, Paglialunga S, Archer MC, Tannenbaum SR. Carcinogenicity of nitrosation products of ephedrine, sarcosine, folic acid, and creatinine. *Cancer Res*. 1975;35(8):1981-1984.
13. Food and Drug Administration (FDA). *Frequency of Use of Cosmetic Ingredients*. College Park, MD: FDA Database; 2016.
14. Personal Care Products Council. Concentration of Use by FDA Product Category: Sarcosines and Sarcosinate Amides. Unpublished data submitted by Personal Care Products Council. October 15, 2015.
15. Johnsen MA. The influence of particle size. *Spray Technol Mark*. 2004;14(11):24-27.
16. Rothe H. *Special Aspects of Cosmetic Spray Evalulation*. Washington, DC: Unpublished data presented at the 26 September CIR Expert Panel Meeting. September 26, 2011.
17. Bremmer HJ, Prud'homme de Lodder LCH, Engelen JGM. Cosmetics Fact Sheet: To Assess the Risks for the Consumer; Updated version for ConsExpo 4. 2006. Report No. RIVM 320104001/2006. pp. 1-77.
18. Rothe H, Fautz R, Gerber E, et al. Special aspects of cosmetic spray safety evaluations: Principles on inhalation risk assessment. *Toxicol Lett*. 2011;205(2):97-104.
19. CIR Science and Support Committee of the Personal Care Products Council (CIR SSC). 11-3-2015. Cosmetic Powder Exposure. Unpublished data submitted by the Personal Care Products Council.
20. Aylott RI, Byrne GA, Middleton JD, Roberts ME. Normal use levels of respirable cosmetic talc: preliminary study. *Int J Cosmet Sci*. 1979;1(3):177-186. PM:19467066.
21. Russell RS, Merz RD, Sherman WT, Sivertson JN. The determination of respirable particles in talcum powder. *Food Cosmet Toxicol*. 1979;17(2):117-122. PM:478394.
22. European Chemicals Agency (ECHA). (Z)-N-methyl-N-(1-oxo-9-octadecenyl)glycine (CAS No. 110-25-8; Oleoyl Sarcosine). http://echa.europa.eu/registration-dossier/-/registered-dossier/2155. Last Updated 2015. Accessed February 22, 2016.
23. Kim YC, Park JH, Ludovice PJ, Prausnitz MR. Synergistic enhancement of skin permeability by N-lauroylsarcosine and ethanol. *Int J Pharmaceutics*. 2008;352(1-2):129-138. PM:18079075.
24. McKinley Resources, Inc. Technical data sheet: Sarcosine. http://raw-materials.mckinleyresources.com/Asset/TDS-Sarcosine.pdf. Last Updated 2016. Accessed February12, 2016.
25. European Chemicals Agency (ECHA). N-lauroylsarcosine (CAS No. 97-78-9). http://echa.europa.eu/registration-dossier/-/registered-dossier/5710. Last Updated 2015. Accessed February 12, 2016.
26. European Chemicals Agency (ECHA). Sodium N-Lauroylsarcosinate (CAS No. 137-16-6). http://echa.europa.eu/registration-dossier/-/registered-dossier/14123. Last Updated 2015. Date Accessed February 23, 2016.
27. Ciba-Geigy Corporation. Initial submission: Effect of skin photosensitization with FAT 61'004 A in guinea pigs with cover letter dated 052092; 1981. https://ntrl.ntis.gov/NTRL/dashboard/searchResults.xhtml?searchQuery=OTS0539883. Accessed January 28, 2016. Available from the National Technical Information Service (NTIS). OTS0539883.
28. Food and Drug Research Laboratories. Initial Submission: Primary Eye Irritation Study of Hamposyl M-30 in New Zealand

White Rabbits (Fianlreport) with Attachments and Cover Letter; 1989. https://ntrl.ntis.gov/NTRL/dashboard/searchResults.xhtml?searchQuery=OTS0535993. Accessed January 28, 2016. Report No. Study No. 89.3873.007. Available from the National Technical Information Service (NTIS); OTS0535993.
29. Zemtsov A, Fett D. Occupational allergic contact dermatitis to sodium lauroyl sarcosinate in the liquid soap. *Contact Dermatitis*. 2005;52(3):166-167. PM:15811039.
30. Hanson JL, Warshaw EM. Contact allergy to surfactants in a hypoallergenic liquid cleanser. *Dermatitis*. 2015;26(6):284-286. PM:26551608.
31. Guangzhou Tinci High-Tech Materials Co, Ltd. Product Specifications: AMIN LS Na (Sodium Lauroyl Sarcosinate, >≥95% Active). http://gztinci.en.alibaba.com/product/1728545904-221002310/AMIN_LS_Na.html. Last Updated 2015. Accessed February 12, 2016.

2. Cosmetics Info 網站：

https://www.cosmeticsinfo.org/ingredients/sodium-lauroyl-sarcosinate/