化粧品產品資訊檔案(範例)

<清爽型防曬乳>

＜PIF **無特定之格式**，本範例**僅提供參考用**＞

中華民國 112 年 10 月

目　　錄

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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	清爽型防曬乳
產品類別	化粧水/油/面霜/乳液類
產品劑型	乳劑
用途	防曬
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：○○市○○區○○路○○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：○○市○○區○○路○○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：○○市○○路○○段 XX 號 公司負責人：李o基 聯絡電話：02-2xxx-xxxx 統一編號：0123XXXX

範例

(2) 完成產品登錄之證明文件

登錄號碼：0123XXXXTEST3000000000

10.	0123XXXXTEST3000000000	清爽型防曬乳	防曬乳、防曬霜、防曬凝膠、防曬油	乳劑	結案	1091008	成功	01

案件資訊

* 登錄編號：	0123XXXXTEST 3000000000 注意：新增後不得再修改【登錄編號】。	* 聯絡人：	OOO
提交日期：	1091008	登錄期限：	1130701
案件狀態：	結案	版次：	01

廠商資訊

公司名稱：	AJP化粧品股份有限公司	電話：	02-2xxx-xxxx
地址：	oo市oo路oo段XX號		

產品資訊

* 國產/輸入：	國產 輸入		
* 是否為組合式產品：	否	產品品牌：	
* 產品類型：	單一產品		
* 產品種類：	防曬乳、防曬霜、防曬凝膠、防曬油 查詢	* 產品劑型：	乳劑 查詢
* 產品用途：	防曬 查詢		
* 製造作業場所：	XX化粧品股份有限公司 查詢	* 包裝作業場所：	YY股份有限公司 查詢

產品名稱：	*中文品名	英文品名
	清爽型防曬乳	

製造、包裝作業場所：製造、包裝作業場所維護

若查無製造場所或包裝場所時，請先至「製造場所維護作業」確認對應之製造場所或包裝場所已維護場所類別或已建立資料

* 使用注意事項：外用產品,使用時避免接觸眼睛,若不慎接觸請以大量清水沖洗，使用後若有不適請立即停止使用,並向醫師諮詢。

產品類型：單一產品

產品型號：清爽型防曬乳

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	提醒事項
1	Cetearyl Alcohol 查詢	適量		
2	PEG-40 HYDROGENATED CASTOR OIL 查詢	適量		
3	Sodium Cetearyl Sulfate 查詢	適量		
4	Decyl Oleate 查詢	適量		
5	Ethylhexyl Methoxycinnamate 查詢	標註量 3.0000000000000	防曬劑	用途：防曬劑,限量 0.0000%~10.0000%
6	BUTYL METHOXYDIBENZOYLMETHANE 查詢	標註量 0.5000000000000	防曬劑	用途：防曬劑,限量 0.0000%~5.0000%
7	Propylparaben 查詢	標註量 0.1000000000000	防腐劑	用途：防腐劑,限量 0.0000%~0.1400%
8	WATER 查詢	適量		
9	Phenylbenzimidazole Sulfonic Acid 查詢	標註量 2.7800000000000	防曬劑	用途：防曬劑,限量 0.0000%~8.0000%
10	Sodium Hydroxide 查詢	適量	化粧品成分使用限制(使用於pH調整液)	用途：潤髮劑,限量 0.0000%~2.0000%
11	Methylparaben 查詢	標註量 0.3000000000000	防腐劑(以acid計,混合使用)	用途：防腐劑(以acid計,混合使用),限量0.0000%~0.8000%
12	DISODIUM EDTA 查詢	適量		
13	Carbomer 查詢	適量		

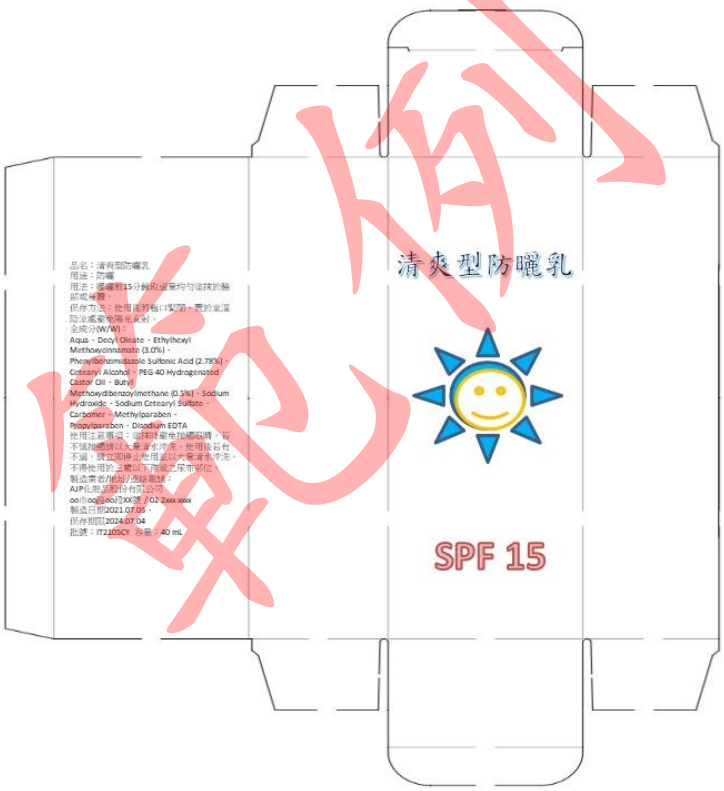
範例

(3) 全成分名稱及其各別含量

INCI Name	Cas No.	w/w%	功能
Aqua	7732-18-5	73.57	溶劑
Decyl Oleate	3687-46-5	15.0	潤膚劑
Ethylhexyl Methoxycinnamate	5466-77-3	3.0	防曬劑
Phenylbenzimidazole Sulfonic Acid	27503-81-7	2.78	防曬劑
Cetearyl Alcohol	67762-27-0 / 8005-44-5	2.205	乳化劑
Sodium Hydroxide (45 % solution)	1310-73-2	1.2	pH 調節劑
PEG-40 Hydrogenated Castor Oil	61788-85-0	0.63	乳化劑
Butyl Methoxydibenzoylmethane	70356-09-1	0.5	防曬劑
Sodium Cetearyl Sulfate	59186-41-3	0.315	乳化劑
Carbomer	9007-20-9 / 9003-01-4 / 76050-42-5 / 9062-04-8 / 9007-16-3 / 9007-17-4	0.3	增稠劑
Disodium EDTA	139-33-3/ 6381-92-6	0.1	螯合劑
Methylparaben	99-76-3	0.3	防腐劑
Propylparaben	94-13-3	0.1	防腐劑
Total		100.00	

樣例

(4) 產品標籤、仿單、外包裝或容器

項目	資 料
內包裝/ 容器 (正反面)	
外盒	

範例

標籤/仿單	品名：清爽型防曬乳 用途：防曬 用法：曝曬前 15 分鐘取適量均勻塗抹於臉部或身體。 保存方法：使用後將瓶口緊閉、置於室溫陰涼處避免陽光直射。 全成分(W/W)： Aqua、Decyl Oleate、Ethylhexyl Methoxycinnamate (3.0%)、Phenylbenzimidazole Sulfonic Acid (2.78%)、Cetearyl Alcohol、PEG-40 Hydrogenated Castor Oil、Butyl Methoxydibenzoylmethane (0.5%)、Sodium Hydroxide、Sodium Cetearyl Sulfate、Carbomer、Methylparaben、Propylparaben、Disodium EDTA 使用注意事項：塗抹時避免接觸眼睛，若不慎接觸請以大量清水沖洗。使用後若有不適，請立即停止使用並以大量清水沖洗。不得使用於三歲以下孩童之尿布部位。 製造業者/地址/連絡電話： 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 2021.07.05、 保存期限 2024.07.04 批號：IT2105CY 容量：40 mL

範例

(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

範例

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、產品劑型：

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.

範例

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

Phase	INCI Name	w/w%
A	Cetearyl Alcohol	2.205
	PEG-40 Hydrogenated Castor Oil	0.63
	Sodium Cetearyl Sulfate	0.315
	Decyl Oleate	15.0
	Ethylhexyl Methoxycinnamate	3.0
	Butyl Methoxydibenzoylmethane	0.5
	Propylparaben	0.1
B	Aqua	53.57
	Phenylbenzimidazole Sulfonic Acid	2.78
	Sodium Hydroxide (45 % solution)	0.9
	Methylparaben	0.3
	Disodium EDTA	0.1
C	Aqua	20.0
	Carbomer	0.3
	Sodium Hydroxide (45 % solution)	0.3

樣品

製程簡述：

1.將 A 相加熱 75~80°C。將 B 相加熱至 80°C (必要時可煮沸至溶液呈透明後，再降溫至 75~80°C)。

2.再將 A 相混合物加入攪拌中的 B 相混合物。

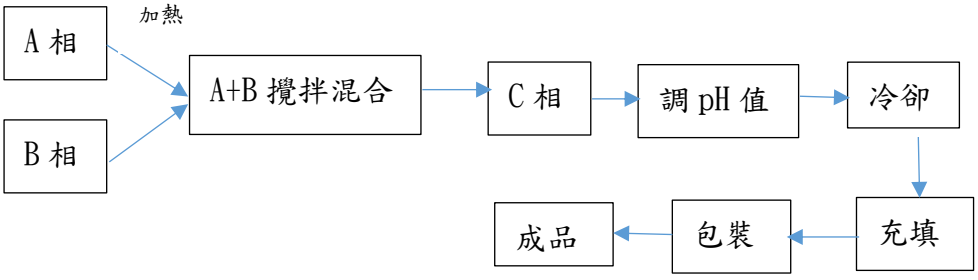
3.將 C 相的 Carbomer 加入水中，以攪拌器攪拌使其分散，再以氫氧化鈉中和。

4.將 C 相加入攪拌中的 A 相與 B 相後，均質 3 分鐘。

5.以氫氧化鈉調整其 pH 值，持續攪拌至完全冷卻。

6.補足散失的水量，並均質之。

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：曝曬前 15 分鐘取適量均勻塗抹於臉部或身體。

使用族群：青少年、成年人。

使用頻率：每日最多兩次。

(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。如有不良影響和嚴重不良影響的資料時會立即更新於本產品資訊檔案，並及時提供給安全資料簽署人員。

範例

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

清爽型防曬乳成品 CoA			
檢測項目	**規格**	**實際檢驗結果**	**檢驗方法**
外觀	乳狀	乳狀	目視
顏色	白色至淡黃色	白色至淡黃色	目視
氣味	無	無添加香精	嗅覺
pH (at 25 °C)	7.5 ± 0.5	7.30	使用已校正之 pH meter 依 pH meter 檢測方法測定
黏度(at 25 °C)	2000 ~ 4000 mPas	3050 mPas	使用已校正之黏度計依黏度計檢測方法測定
密度(at 25 °C)	0.970 ± 0.05 g/cm^3	1.01 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：

Aqua CoA			
檢測項目	**規格**	**實際檢驗結果**	**檢驗方法**
pH (at 25 °C)	6.0~8.5	7.35	使用已校正之線上(on line) pH meter 測定
導電度(at 25 °C)	<20 µS/cm	15.0 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)	

INCI name：Decyl Oleate

decyl oleate

Modify Date: 2021-02-13 22:11:03

	Common Name	decyl oleate		
	CAS Number	3687-46-5	**Molecular Weight**	422.72700
	Density	0.866g/cm3	**Boiling Point**	494.8℃ at 760 mmHg
	Molecular Formula	$C_{28}H_{54}O_2$	**Melting Point**	N/A
	MSDS	N/A	**Flash Point**	77.1℃

Chemical & Physical Properties

Density	0.866g/cm3
Boiling Point	494.8℃ at 760mmHg
Molecular Formula	$C_{28}H_{54}O_2$
Molecular Weight	422.72700
Flash Point	77.1℃
Exact Mass	422.41200

PSA	26.30000
LogP	9.70780
Index of Refraction	1.459
Water Solubility	Practically insoluble in water, miscible with ethanol (96 per cent), with methylene chloride and with light petroleum (bp: 40-60 °C).

範例

INCI name：Ethylhexyl Methoxycinnamate

Appearance	:	liquid
Physical state	:	liquid
Colour	:	light yellow
Odour	:	mild
Odour Threshold	:	No data available
pH	:	No data available
Melting point/freezing point	:	-13 °F / -25 °C
Boiling point/boiling range	:	387.9 - 392 °F / 197.7 - 200 °C (4 hPa)
Flash point	:	192.7 °C
Evaporation rate	:	not determined
Upper explosion limit	:	Upper explosion limit not determined
Lower explosion limit	:	Lower explosion limit not determined
Vapour pressure	:	not determined
Relative vapour density	:	not determined
Relative density	:	No data available
Density	:	1.005 - 1.013 g/cm3 (20 °C)
Solubility(ies)		
Water solubility	:	insoluble

样品

INCI name：Phenylbenzimidazole Sulfonic Acid

PHYSICAL AND CHEMICAL PROPERTIES

Physical state: Solid	**Appearance:** Crystalline powder.	**Color:** White.
Odor: None.	**Taste** No information available.	**Formula** C13H10N2O3S
Molecular/Formula weight (g/mole): 274.28	**Flammability (solid, gas)** no data available	**Flashpoint (°C/°F):** No information available
Flash Point Tested according to: Not available	**Autoignition Temperature (°C/°F):** No information available	**Lower Explosion Limit (%):** No information available
Upper Explosion Limit (%): No information available	**Melting point/range(°C/°F):** >300 °C/572 °F	**Decomposition temperature(°C/°F):** No information available
Boiling point/range(°C/°F): No information available	**Bulk density:** No information available	**Density (g/cm3):** No information available
Specific gravity: No information available	**pH** No information available	**Vapor pressure @ 20°C (kPa):** No information available
Evaporation rate: No information available	**Vapor density:** 9.46	**VOC content (g/L):** No information available
Odor threshold (ppm): No information available	**Partition coefficient (n-octanol/water):** No information available	**Viscosity:** No information available
Miscibility: No information available	**Solubility:** Soluble in Water	

INCI name：Cetearyl Alcohol

Certificate of Analysis

(Representative Sample Certificate)

Product Name:	Cetearyl Alcohol
INCI Name:	Cetearyl Alcohol
CAS Number:	67762-27-0
Lot Number:	Not available (data may vary slightly with different lots or batches)
Expiration Date:	24 months from production date

Analytical Tests	Specification	Actual Analysis
Appearance @ 25°C	White Flake/Pastille	White Pastilles
Hydroxyl Value, mg KOH/g	208.0 – 228.0	214.7
Saponification Value, mg KOH/g	3.0 Max	0.25
Iodine Value, cg 12/g	4.0 Max	0.15
Moisture, % w/w	0.10 Max	0.09
Color (APHA)	40 Max	5
C14 & Lower	2.0 Max	0.22
C16	22-32	29.30
C18	66-76	69.24
C20 & Higher	5.8 Max	0.61
Total Alcohol, %	96.8 Min	99.80

樣張

INCI name：Sodium Hydroxide

Physical and Chemical Properties

Appearance	Clear to slightly turbid, viscous liquid
Physical state	Liquid
Form	Viscous liquid
Colour	Clear water-white
Odor	Odorless
Odor threshold	Not Available
pH	> 14 (at high alkali concentration in water, pH scale is not applicable)
Melting point/freezing point	57.2 °F (14 °C) / 57.2 °F (14 °C) (approximately)
Initial boiling point and boiling range	284 °F (140 °C) @ 760 mmHg
Flash point	Not Applicable
Evaporation rate	Not Applicable (the only evaporation that occurs is water)
Flammability (solid, gas)	Not Available
Upper/lower flammability or explosive limits	
Flammability limit – lower (%)	Not Applicable
Flammability limit – upper (%)	Not Applicable
Explosive limit – lower (%)	Not Applicable
Explosive limit – upper (%)	Not Applicable
Vapor pressure	0.2 kPa 1.5 mm Hg
Vapor pressure temp.	77 °F (25 °C)
Vapor density	Not Available
Relative density	1.52 g/cm³
Solubility (ies)	
Solubility (water)	Soluble in all proportions
Solubility (other)	Soluble in absolute alcohol, methanol and glycerol. Moderately soluble in ethanol. Insoluble in acetone and diethyl ether.
Partition coefficient (n-octanol/water)	Not available
Auto-ignition temperature	Not Applicable
Decomposition temperature	Not Available
Viscosity	25.39 cSt (40% solution)
Viscosity temperature	68 °F (20 °C)
Other information	
Specific gravity	1.52 at 20 °C

INCI name：PEG-40 Hydrogenated Castor Oil

Appearance	
Physical state:	solid
Form:	Paste
Color:	White
Odor:	Slight characteristic odor
Odor Threshold:	No data available.
pH:	No data available.
Melting Point:	< 104 °F/40 °C
Boiling Point:	No data available.
Flash Point:	509 °F/265 °C (Cleveland open cup)
Evaporation Rate:	No data available.
Flammability:	No data available.
Explosive limit - upper:	No data available.
Explosive limit - lower:	No data available.
Vapor pressure:	No data available.
Vapor density (air=1):	No data available.
Density:	1.0333 g/ml (122 °F/50 °C) 1.0258 g/ml (140 °F/60 °C) 1.0183 g/ml (158 °F/70 °C)
Relative density:	No data available.
Solubility in Water:	Emulsion(1%,25C)
Solubility (other):	Soluble in lower alcohols
Partition coefficient (n-octanol/water):	No data available.
Self Ignition Temperature:	No data available.
Decomposition Temperature:	No data available.
Kinematic viscosity:	No data available.
Dynamic viscosity:	360 mPa.s (122 °F/50 °C) 255 mPa.s (140 °F/60 °C) 215 mPa.s (158 °F/70 °C)
Particle properties:	No data available.

INCI name：Butyl Methoxydibenzoylmethane

PHYSICAL AND CHEMICAL PROPERTIES

Appearance	Refer to Spec Sheet
Physical state	Powder\Crystal.
Form	Powder. Crystalline powder.
Color	Refer to Spec Sheet
Odor	Characteristic.
Odor threshold	Not available.
pH	Not available.
Melting point/freezing point	182.3 °F (83.5 °C)
Initial boiling point and boiling range	865.4 °F (463 °C)
Flash point	> 200.0 °F (> 93.3 °C) Closed Cup
Evaporation rate	Not available.
Flammability (solid, gas)	Not available.
Upper/lower flammability or explosive limits	
Flammability limit - lower (%)	Not available.
Flammability limit - upper (%)	Not available.
Explosive limit - lower (%)	Not available.
Explosive limit - upper (%)	Not available.
Vapor pressure	0.0000002 kPa (77 °F (25 °C))
Vapor density	10.8
Relative density	1.22 g/cm³ at 20 °C relation to density of water at 4°C
Solubility(ies)	
Solubility (water)	Insoluble
Partition coefficient (n-octanol/water)	Not available.
Auto-ignition temperature	Not available.
Decomposition temperature	Not available.
Viscosity	Not available.
Other information	
Explosive properties	Not explosive.
Flammability class	Combustible IIIB estimated
Molecular formula	C20H22O3
Molecular weight	310.39 g/mol 430.39 g/mol
Oxidizing properties	Not oxidizing.

范例

INCI name：Sodium Cetearyl Sulfate

sodium,hexadecyl sulfate,octadecyl sulfate

Modify Date: 2021-01-23 13:42:39

Common Name	sodium,hexadecyl sulfate,octadecyl sulfate		
CAS Number	59186-41-3	Molecular Weight	694.03500
Density	N/A	Boiling Point	N/A
Molecular Formula	$C_{34}H_{70}NaO_8S_2$	Melting Point	N/A
MSDS	N/A	Flash Point	N/A

Properties

Names

Name	sodium,hexadecyl sulfate,octadecyl sulfate
Synonym	More Synonyms

Chemical & Physical Properties

Molecular Formula	$C_{34}H_{70}NaO_8S_2$
Molecular Weight	694.03500
Exact Mass	693.44100
PSA	149.62000
LogP	12.83080

样例

INCI name：Carbomer

Product Name: Carbomer Batch : 2021xxxx

ITEM	SPECIFICATION	RESULT
Appearance	White powder	Complies
Aqueous solution viscosity (0.5%)	45000-65000 cp	57000 cp
Clarity, % transmittance（420 nm）	≥88%	90%
Moisture	≤2.0%	0.73%
Residual ethyl acetate and cyclohexane	≤0.45%	Complies
Heavy metals	≤10 ppm	Complies

Storage: Low temperature store，Keep away from strong light and heat.

Shelf life: 2 years when properly stored.

Conclusion: Meet the requirements

范例

INCI name： Disodium EDTA

Information on basic physical and chemical properties:

- **Appearance:** White
- **Physical State:** Solid
- **Odor:** Odorless
- **pH:** 4-6 in5% aq. solution
- **Melting Point:** 252°C
- **Ignition Temperature:** No data available
- **Decomposition Temperature:** > 252°C
- **Vapor Pressure:** No data available
- **Relative Vapor Density:** No data available
- **Density:** No data available
- **Volatility:** No data available
- **Bulk Density:** ca.700 kg/m^3
- **Odor Threshold:** No data available
- **Viscosity, dynamic:** No data available
- **Water/Oil Dist. Co eff.:** No data available
- **Ionicity (in Water):** No data available
- **Partition Co-efficient: n-octanol/water:** No data available
- **Boiling Point/Range:** No data available
- **Flash Point:** No data available
- **Sublimation Point:** No data available
- **Specific Gravity:** No data available
- **Water Solubility:** 100 g/l at 20°C

9.2. Other information:

Molecular Formula: $C_{10}H_{14}N_2Na_2O_8 \cdot 2H_2O$

Molecular Weight: 372.23 g/mol

INCI name： Methylparaben

methylparaben

Modify Date: 2021-01-23 10:42:42

Common Name	methylparaben		
CAS Number	99-76-3	**Molecular Weight**	152.147
Density	1.2±0.1 g/cm3	**Boiling Point**	265.5±13.0 °C at 760 mmHg
Molecular Formula	$C_8H_8O_3$	**Melting Point**	125-128 °C(lit.)
MSDS	Chinese USA	**Flash Point**	116.4±12.6 °C

Chemical & Physical Properties

Density	1.2±0.1 g/cm3
Boiling Point	265.5±13.0 °C at 760 mmHg
Melting Point	125-128 °C(lit.)
Molecular Formula	$C_8H_8O_3$
Molecular Weight	152.147
Flash Point	116.4±12.6 °C
Exact Mass	152.047348
PSA	46.53000
LogP	1.87
Vapour Pressure	0.0±0.6 mmHg at 25°C
Index of Refraction	1.547
Stability	Stable. Incompatible with strong oxidizing agents, strong bases.
Freezing Point	131℃

样品

INCI name： Propylparaben

Propyl 4-hydroxybenzoate

Modify Date: 2021-01-23 17:44:55

Common Name	Propyl 4-hydroxybenzoate		
CAS Number	94-13-3	**Molecular Weight**	180.201
Density	1.1±0.1 g/cm3	**Boiling Point**	294.3±13.0 °C at 760 mmHg
Molecular Formula	$C_{10}H_{12}O_3$	**Melting Point**	95-98 °C(lit.)
MSDS	Chinese USA	**Flash Point**	124.6±12.6 °C

Chemical & Physical Properties

Density	1.1±0.1 g/cm3
Boiling Point	294.3±13.0 °C at 760 mmHg
Melting Point	95-98 °C(lit.)
Molecular Formula	$C_{10}H_{12}O_3$
Molecular Weight	180.201
Flash Point	124.6±12.6 °C
Exact Mass	180.078644
PSA	46.53000
LogP	2.93
Vapour Pressure	0.0±0.6 mmHg at 25°C
Index of Refraction	1.532
Stability	Stable. Incompatible with strong oxidizing agents, strong bases.
Water Solubility	<0.1 g/100 mL at 12 ºC

样品

(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之各個成分毒理資料，另存放於清爽型防曬乳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：Decyl Oleate

- 急性毒性：大鼠急性口服毒性 LD_{50}> 5000 mg/kg bw。[1] 大鼠急性皮膚毒性 LD_{50}> 2000 mg/kg bw。[4]
- 腐蝕性和刺激性：在兔子初級皮膚刺激研究中，測試 10%玉米油溶液、20%礦物油溶液和未稀釋 Decyl Oleate 的主要刺激指數(Primary Irritation Index, PII)依序為 0.08、0.05 和 0.28，而在改良 Draize 試驗中，未稀釋的 Decyl Oleate 無刺激性。[1]。以改進 Draize 方法評估 100% Decyl Oleate 的兔眼刺激性。觀察 1 小時和 1、2、3、4 和 7 天結果顯示 Decyl Oleate 非常輕微的眼刺激性。[2]
- 皮膚致敏性：8 週的兔子研究中，每天使用 15%溶液會產生一些丘疹或水泡，但通常耐受性良好，未稀釋則導致 3 隻兔子(但未說明總數)和 1 隻兔子的皮膚增厚，並且耐受性差；在天竺鼠試驗結果顯示 15%溶液在玉米油無致敏性。[1]
- 重複給藥毒性：在 28 天大鼠灌食研究，每週 5 天給予 100、500 或 1000 mg/kg bw 之劑量，NOAEL 為 1000 mg/kg bw/day。[3,4]
- 致突變性/遺傳毒性：在鼠傷寒沙門氏菌 TA98、TA100、TA1535、TA1537 和 TA1538 菌株的沙門氏菌致突變性試驗中，濃度 4 至 2500 µg/plate 之間的 Decyl Oleate 不具致突變性。[3]
- 致癌性：無數據。[3]
- 生殖毒性：無數據。[3]
- 毒理代謝動力學：無數據。[3]
- 經皮吸收：無數據。不可進行模型計算，因為在水中的溶解度極差，尤其是由於極高的 log K_{OW}。在大鼠急性皮膚毒性研究中直至測試的最高劑量 2000 mg/kg 仍未觀察到全身毒性跡象，因此 Decyl Oleate 未被指定標示"H"(即可通過皮膚吸收毒理相關劑量的物質)，因此，在人體的皮膚吸收被認為非常有限，皮膚暴露對於危害評估來說可以忽略不計。[4,5]
- 光毒性：無數據。[3]
- 人體數據：在人類反覆刺激斑貼試驗(Human Repeat-Insult Patch Test,

範例

HRIPT) 測試中，103 名受試者施用含 1%~5% Decyl Oleate 配方後及 402 名受試者中施用 4 種含 5.5% Decyl Oleate 的四個配方後無產生過敏現象。[1]

- 其他安全性資料：根據 CIR 評估報告使用 Decyl Oleate 在化粧品的濃度範圍為≤ 0.1%至 50% (CIR 1982)，而 2003 年報告則為 0.5%–88% (CIR 2003)。[3]
- 參考資料：

1. Safety Assessment of Alkyl Esters as Used in Cosmetics. IJT 34(Suppl.2):5-69, 2015.
2. Final Report on the Safety Assessment of Decyl and Isodecyl Oleates. JACT 1(2):85-95, 1982.
3. The MAK-Collection for Occupational Health and Safety: Annual Thresholds and Classifications for the Workplace, 2002.
4. ECHA 網站: https://echa.europa.eu/registration-dossier/-/registered-dossier/13270/7/1 .
5. Hartwig A, MAK Commission.n-Decyl oleate. MAK Value Documentation, supplement-Translation of the German version from 2019. MAK Collect Occup Health Saf. Sep;6(3), Doc056, 2021.

2. INCI name：Ethylhexyl Methoxycinnamate

- 急性毒性：小鼠急性口服毒性 LD_{50} >8 g/kg bw，大鼠急性口服毒性 LD_{50}>20 mL/kg bw。[1]
- 腐蝕性和刺激性：20 隻天竺鼠給予未稀釋之測試物質每天兩次共 16 天，間隔 3 天未施用後再以每天給予測試物質共 3 天，結果無致敏反應。另一項試驗分兩組每組 4 隻，一組每天注射未稀釋之測試物質 0.05 ml 共 5 天，在另一組中將 0.025 ml 含測試物質的 50% 丙酮溶液施用於 2 cm^2 的兩側剃毛皮膚區域，無證據顯示具有致敏性。[1]
- 皮膚致敏性：20 隻天竺鼠給予未稀釋之測試物質每天兩次，共 16 天，無致敏反應。[1]
- 重複給藥毒性：在大鼠 13 週的皮膚暴露毒性研究中，每週 5 天在剃毛皮膚上施用 0、55.5、277 和 555 mg/kg bw 的劑量。NOAEL 為 555 mg/kg bw/day。[1]

範例

- 致突變性/遺傳毒性：常用沙門氏菌 TA1538 菌株突變試驗，無代謝活化下呈陽性被認為是批次效應，而另一實驗室結果則有非常微弱的陽性反應，但兩重複及再次的 Ames 測試則未發現。以酵母菌、人類淋巴球細胞的突變試驗及 BALB/c 3T3 細胞的細胞轉化試驗均為陰性，中國倉鼠 V79 細胞的突變菌落有輕微增加。果蠅試驗結果顯示性聯隱性的頻率增加，餵養測試則沒有證據顯示誘變情形，而異體細胞突變與重組試驗呈陰性。綜合上述多項致突變性研究結果未顯示致突變性。[1]
- 致癌性：無數據。[1]
- 生殖毒性：在兔子及大鼠的測試結果顯示，非生殖毒性物質。[1]
- 毒理代謝動力學：8 名健康志願者的測試結果除尿液中約 0.2%以外均為陰性，沒有說明所使用濃度。[1]
- 經皮吸收：在 7.5%濃度應用於不同載體中，在迷你豬皮膚的完整表面暴露 6 小時，結果發現低於 4%的 Ethylhexyl Methoxycinnamate 被豬皮吸收，而不同載體的滲透率值沒有顯著差異。[2] 另一份評估資料採用的經皮吸收率為 2%。[3]
- 光毒性：S.cerevisiae 的光致突變試驗為陰性，CHO 細胞體外光致致裂試驗呈陰性。[1]
- 人體數據：在 10 位受試者中，以貼片施用 24 小時，然後將區域暴露於紫外線照射下觀察紅斑產生情形，結果顯示不具光毒性。[1]
- 參考資料：

1. European Commission, Reports of the Scientific Committee on Cosmetology (Ninth Series): 2-Ethylhexyl-4-methoxycinnamate (5466-77-3), 1999.
2. ECHA 網站: https://echa.europa.eu/registration-dossier/-/registered-dossier/15876/7/2/3 .
3. UV-Filters in Sun Protection Products, Opinion of the Federal Institute for Risk Assessment, 6th August, 2003.

3. INCI name：Phenylbenzimidazole Sulfonic Acid

- 急性毒性：小鼠急性口服毒性 LD_{50} >5000 mg/kg bw，大鼠急性口服毒性 LD_{50} >1600 mg/kg bw，大鼠急性皮膚毒性 LD_{50} >3000 mg/kg bw，大鼠急性腹腔注射毒性 LD_{50} 介於 1000 ~ 1500 mg/kg bw。[1]

- 腐蝕性和刺激性：根據在兔子的研究被評估為對皮膚無刺激性，對於結膜亦不具刺激性。[1]
- 皮膚致敏性：現有研究顯示無證據顯示為皮膚致敏物質。[1] 兩項在白化天竺鼠的皮膚致敏研究，在遵循 OECD 指引 406 和 GLP 原則下進行，研究結果均為陰性，在測試動物中未顯示任何皮膚過敏反應。[2]
- 重覆給藥毒性：在大鼠中進行 13 週口服研究結果，NOAEL 為 1000 mg/kg bw /day。[1]
- 致突變性/遺傳毒性：兩項細菌基因突變測試中，測試物質均未顯示具有突變活性，而陽性對照樣品則出現預期的誘導突變效應。另一體外染色體畸變測試的結果顯示，與對照相比測試物質並不會導致結構染色體畸變數量的增加。[1]
- 致癌性：無數據。[1]
- 生殖毒性：Wistar 大鼠在交配後第 6 天到第 15 天，每天以灌食給予 1000 mg/kg bw /day 的劑量，除了用水量增加外，此劑量未顯示對母體的毒性作用，亦無胚胎毒性及致畸性。[2]
- 毒理代謝動力學：對懷孕大鼠的吸收、分佈和排泄研究顯示，任何器官（口服與靜脈注射兩種途徑）中均未發現累積的跡象。靜脈注射後在大腦和胎兒中發現微量放射性，口服暴露途徑中這些器官未發現放射性，顯示未通過血/腦和胎盤屏障。至 48 小時，可從體內完全排除。[1]
- 經皮吸收：在人體研究中，將 1 g 含有 80 mg 放射性標記測試物質 (1.86 MBq)的凝膠塗抹於 6 名健康男性志願者上臂，非封閉覆蓋物保護，6 小時後去除凝膠並在施用 120 小時候採集血樣。結果顯示皮膚吸收率約 0.2%。[2]
- 光毒性：天竺鼠試驗中，於照射組陽性對照的測試部位有表現出輕微的紅斑(24 小時-3/10；48 小時-7/10)；其他測試組別均不受影響。以 3T3-NRU 光毒性測試，計算出的光刺激係數(photo-irritation factor, PIF)為 1.4，根據標準判定無光毒性。[1]
- 人體數據：分別將濃度 5%和 10% Neo Heliopan (Phenylbenzimidazole Sulfonic Acid)施用於 50 名志願者的背部，並保持原位 48 小時，暴露終止後 48 小時和 72 小時評估均未觀察到皮膚反應。以 5%和 10%進行重複開放型應用測試，每天兩次將 0.1mL 擦拭 20 名志願者的肘前窩連續 14 天，均未觀察到皮膚反應。[1]

◆ 參考資料：

1. SCCP/1056/06- Opinion on phenylbenzimidazole sulfonic acid and its salts COLIPA S45, 2006.
2. ECHA 網站: https://echa.europa.eu/registration-dossier/-/registered-dossier/5464/7/5/1 .

4. INCI name：Cetearyl Alcohol

◆ 不純物：Cetearyl Alcohol 鯨蠟硬脂醇為脂肪醇混合物，主要由 20%~35%的 Cetyl Alcohol 鯨蠟醇和 65%~80%的 Stearyl Alcohol 硬脂醇組成。可能含有不純物有碳氫化合物(主要由正十六烷和正十八烷組成)約 0.1%~1.4%，奇數直鏈醇約 1%~3.5%，支鏈初級醇約 0.2%~2%。[1]

◆ 急性毒性：Cetyl Alcohol 鯨蠟醇之大鼠急性口服毒性 LD_{50} 大於 8.2 g/kg bw。[1]

◆ 腐蝕性和刺激性：將含有 3.0% Cetearyl Alcohol 的乳膏塗抹在紐西蘭白化兔的皮膚上時，觀察到輕度刺激。而 Cetyl Alcohol (含 50.0%凡士林)塗在白化兔磨損和完整的皮膚上，對皮膚的刺激很小至輕微。當注入白化兔眼睛時，Cetyl Alcohol 被視為無刺激性。[1]

◆ 皮膚致敏性：無數據。參考 Isostearyl Alcohol 異硬脂醇(5.0%在丙二醇中)和含 5.0%異硬脂醇的止汗劑在天竺鼠的試驗結果非致敏物。在人體皮膚塗抹 25%異硬脂醇後，沒有觀察到皮膚刺激或致敏的跡象。[1]

◆ 重複給藥毒性：無數據。參考 Behenyl alcohol 山嵛醇在 CD 大鼠中進行 26 週口服研究結果，NOAEL 為 1000 mg/kg bw /day。[2]

◆ 致突變性/遺傳毒性：無數據。參考 Isostearyl Alcohol 異硬脂醇以鼠傷寒沙門氏菌 LT2 突變測試結果無致突變性。[1]

◆ 致癌性：無數據。[1]

◆ 生殖毒性：無數據。[1]

◆ 毒理代謝動力學：無數據。大部分長鏈脂肪醇的吸收、代謝和排泄數據來自鯨蠟醇和硬脂醇。[1]

◆ 光毒性：無數據。參考 Cetyl Alcohol 在 52 名受試者中評估含有 4.0%鯨蠟醇的唇膏產品之光致敏潛力，所有受試者均未發現光敏感反應；在另一項研究含有 1.0%鯨蠟醇的護膚製劑在測試 407 名受試者中

未引起光敏反應。[1]

- 人體數據：在含有 3.0% Cetearyl Alcohol 面霜進行的人體皮膚致敏性研究中，未有受試者出現陽性反應。[1]
- 其他安全性資料：CIR 專家小組認為脂肪醇，包括鯨蠟硬脂醇在化粧品中使用是安全的[1]，經重新審查新的可用研究以及關於使用類型和濃度資訊更新，專家小組確認鯨蠟硬脂醇、鯨蠟醇、異硬脂醇的安全性，鯨蠟硬脂醇的使用濃度範圍為 0.0002%~15%。[3] 鯨蠟硬脂醇包括在美國 FDA 的安全和允許食品添加劑清單中。[4]
- 參考資料：

1. Final Report on the Safety Assessment of Cetearyl Alcohol, Cetyl Alcohol, Isostearyl Alcohol,Myristyl Alcohol, and Behenyl Alcohol. JACT 7(3):359-413, 1988.
2. Iglesias G, Hlywka J, Berg JE, Khalil MH, Pope LE and Tamarkin D. The toxicity of behenyl alcohol. I. Genotoxicity and subchronic toxicity in rats and dogs. Regul Toxicol Pharmacol. 36(1):69-79, 2002.
3. Annual Review of Cosmetic Ingredient Safety Assessments: 2005/2006, IJT 27(Suppl. 1):77-142, 2008.
4. CFR-code of federal regulations title 21: Part 172 - food additives permitted for direct addition to food for human consumption, 2020.

5. INCI name：Sodium Hydroxide

- 不純物：雜質為氯化鈉±2%、碳酸鈉≤1.0%、硫酸鹽≤0.2%，而其他雜質小於 0.1%。[1]
- 急性毒性：在口服毒性研究中，氫氧化鈉的口服會導致受測動物胃部廣泛受損；而在皮膚暴露毒性研究中，經 50%氫氧化鈉處理的小鼠在一小時內將試驗物沖洗掉，其存活率更高。大鼠的急性吸入毒性 LC_{50}> 0.75 mg/L(暴露 2 小時)。[2]
- 腐蝕性及刺激性：氫氧化鈉對所有組織都有腐蝕性，濃蒸氣會嚴重損害眼睛和呼吸系統。根據法規(EC)1272/2008，該物質被歸類為危險物質：皮膚腐蝕 1A，濃度≥5%引起嚴重的皮膚灼傷和眼損傷。毒性與 pH 相關，隨著 pH 值的增加，毒性更大。0.05% w/w 溶液的 pH 值約為 12，0.5%溶液約 13，5%溶液約 14。[3]
- 皮膚致敏性：人類反覆刺激斑貼試驗顯示，氫氧化鈉以高達 1.0%的

濃度誘導並以 0.125%的濃度激發時不致敏，但有觀察到皮膚刺激反應。[2]

- 重複給藥毒性：無氫氧化鈉局部作用的重複皮膚劑量數據。[2]
- 致突變性/遺傳毒性：在幾種不同的體外測定中，氫氧化鈉沒有遺傳毒性。[2]
- 致癌性：未發現有關無機氫氧化物的相關已公開致癌性數據。[2]
- 生殖毒性：無數據。[2]
- 毒理代謝動力學：無數據。[2]當人體皮膚接觸低(無刺激性)濃度時，由於離子吸收率低，NaOH 的攝取相對較低，通過暴露 NaOH 而攝入的 OH^- 估計不會改變血液 pH 值，而通過暴露 NaOH 而攝入的鈉遠低於通過食物攝取鈉。預計 NaOH 一般狀況下身體無法利用。[2]
- 光毒性：無數據。[2]
- 人體數據：利用四種不同的貼片系統在進行之人類皮膚斑貼測試，分別是 Finn 貼片、Hill Top 貼片、Van der Bend 貼片和 Webril 貼片，確定 1% NaOH 對皮膚的刺激反應。[1]
- 參考資料：

1. European Union Risk Assessment Report - Sodium Hydroxide, 2007.
2. CIR Final report. Safety assessment of inorganic hydroxides as used in cosmetics. 2016. IJT 40(Suppl. 2):16-35, 2021.
3. PubChem. https://pubchem.ncbi.nlm.nih.gov/compound/14798

6. INCI name：PEG-40 Hydrogenated Castor Oil

- 不純物：PEG 是環氧乙烷和水的縮合產物，其鏈長由聚合的環氧乙烷的摩爾數控制。PEG 可能微量的乙氧基化的副產物 1,4-二噁烷，而 1,4-二噁烷已知是致癌物，應使用額外的純化步驟將其從成分中去除。[1]
- 急性毒性：含 0.25% PEG-40 Hydrogenated Castor Oil 之配方在大鼠急性口服毒性 LD_{50} 大於 15.0 g/kg bw。[2]
- 皮膚刺激性：未稀釋的 PEG-40 Hydrogenated Castor Oil 塗在白化兔子的背部 20 小時後會引起皮膚發紅和結痂，當在兔子的外耳上施用 20 小時，只有輕微的短暫變紅。[2]
- 眼睛刺激性：未稀釋及 50%的 PEG-40 Hydrogenated Castor Oil 水溶液為在兔結膜囊中滴入 0.05 mL，並在 24 和 48h 觀察。兩種濃度下

範例

結膜均出現短暫變紅。[2]

- 皮膚致敏性：大多臨床數據顯示不具致敏性。[2]
- 重複給藥毒性：在 90 天的大鼠餵食研究中，每組 15 隻 Sherman-Wistar 大鼠飲食中分別添加含有 0.01%、0.04%、0.16%、0.64%、2.5%或 5.0% PEG-40 Hydrogenated Castor Oil。結果未發現明顯的肉眼或微觀病變，無毒理作用的劑量 5%相當於 2500 mg/kg bw。[2]
- 致突變性/遺傳毒性：無數據。參考 PEG- 35 Castor Oil 在小鼠試驗的結果顯示不具致突變性。[2]
- 致癌性：無數據。參考 PEG-30 Castor Oil 在大鼠試驗及其他 PEG Castor Oil 在小鼠試驗的結果顯示不具致癌性。[2]
- 生殖毒性：在小鼠和大鼠的灌食研究中，100,000 ppm 劑量下未發現發育毒性。[2]
- 毒理代謝動力學：無數據。參考 PEG-35 Castor Oil (87.8 mg PEG-35 castor oil/mg drug)用於癌症患者治療的結果，PEG-35 Castor Oil 的半衰期和清除率分別為 35.7+18.9 小時和 0.216+0.075 L/h，PEG-35Castor Oil 作為製劑載體可能會導致藥物相互作用和賦形劑相關毒副作用。[1]
- 光毒性：無數據。
- 人體數據：24 小時單次封閉型皮膚斑貼試驗測試含有 0.25% PEG-40 Hydrogenated Castor Oil 的配方，20 個受測者中只有 1 個有輕微的致敏。[2]
- 其他安全性資料：CIR 專家小組認為 PEG-30、-33、-35、-36 和-40 Castor Oil 可安全用於化粧品濃度高達 50%，PEG-30 及-40 Hydrogenated Castor Oil 是在濃度高達 100%可安全使用。[1]
- 參考資料：

1. Safety Assessment of PEGylated oils as used in cosmetics. IJT 33(Suppl 4):13-39, 2014.
2. Final report on the safety assessment of PEG-30, -35, -36, and -40 castor oil and PEG-30 and -40 hydrogenated castor oil. IJT 16(Suppl.3):269-306, 1997.

範例

7. INCI name：Butyl Methoxydibenzoylmethane

- 急性毒性：大鼠急性口服毒性 LD_{50} 大於 16 g/kg bw，給藥組的附睪沒有精子或精子量少。小鼠(口服和腹腔投藥)在 8 mg/kg bw 劑量下觀察異常體徵，但並未引起死亡。大鼠覆蓋 24 小時之急性皮膚暴露試驗結果最高至 1000 mg/kg bw 未造成任何死亡，未發現與化合物相關之皮膚損傷，LD_{50} 估計大於 1 g/kg bw。[1]
- 皮膚刺激性：兔子研究分為 5 組(3 個實驗組、溶劑對照組及程序對照組)，每組包括 10 隻雄性和 10 隻雌性動物，每組有 5 隻動物的皮膚受傷，而另 5 隻則無。每天將 30、60 和 360 mg/kg bw/day 的實驗組覆蓋 6 個小時，連續 21 天，而使用的成分在卡必醇(Carbitol)中濃度分別為 1.5%、5%及 18%。在溶劑對照組中發現了輕微刺激，在實驗組中出現紅斑嚴重度具劑量依存性，30 mg/kg bw/day 時輕微，擦傷並無影響。除施用部位外，體重、食物或水的消耗量或血液學檢查均未發現因成分引起的變化。另一兔子試驗分兩組，每組 6 隻兔子，一組進行測試物質測試，一組進行溶劑對照組。將成分以 10%濃度溶於乙醇/2-苯乙醇(50/50)中；在 4 cm^2 的面積上，將 0.5 mL 塗抹在每隻動物的擦傷處和非擦傷處，覆蓋 4 小時。載體的原始刺激指數為 1.17，而成分溶液的刺激指數為 1.39。[1]
- 眼睛刺激性：將 Butyl Methoxydibenzoylmethane 溶於鄰苯二甲酸二乙酯，以兔子進行 Draize 眼睛刺激性測試。直至溶解度極限 20%時對眼睛無不良反應。[1]
- 皮膚致敏性：使用 Magnusson 及 Kligman 最大化方法以天竺鼠研究，以皮下注射 0.1ml 5%於完全弗氏佐劑(Freund's Complete Adjuvant, FCA)、5%於 FCA 生理食鹽水中及單獨 FCA 進行誘導。7 天後，表皮給予 20%懸浮液覆蓋 2 天，在第 21 天進行激發；分別給予 20%和 6% 24 小時，結果無致敏證據。[1]
- 重複給藥毒性：在 13 週大鼠研究中，以 4 組 12 隻雄性及 12 隻雌性大鼠分別在食物中給予 200、450 和 1000 mg/kg bw，結果無與投藥相關的死亡情形。中劑量組和最高劑量組的食物消耗減少且雌性的紅血球細胞下降。所有劑量組的動物血漿蛋白平均較高，但似乎與劑量無關。而中劑量和最高劑量的雌性動物的相對肝臟重量均增加。以最高劑量增加給予 6 隻大鼠之後 4 週恢復，犧牲後觀察大鼠的肝臟重量與對照大鼠相似。根據對肝臟重量增加的看法，無影響劑量 NOAEL 可能為 200 或 450 mg/kg bw/day。[1]

衛部

- 致突變性/遺傳毒性：非致癌物質。最高 500 µg 溶於 DMSO 進行 Ames 試驗，無論是否存在代謝酵素激活，測試均為陰性。[1]
- 生殖毒性：非生殖毒性物質。大鼠研究中劑量 1000 mg/kg bw/day 下既不具有胚胎毒性也不致畸，也不損害大鼠後代出生後發育。[2]
- 毒理代謝動力學：大鼠體內試驗標記化合物 1%溶液，將溶解在卡必醇(Carbitol)中的溶解劑以 120 mg/cm^2 的劑量施用 6 小時，在角質層和更深層中發現的量分別為 1.4%和 2.3%。[1]
- 經皮吸收：BfR 風險評資料採用的經皮吸收率為 0.56%。[3]
- 光毒性：在 25 名志願者研究中，將 2%成分摻入凡士林，其中添加 2% DMSO 作為最大化試劑，通過 UVA + UVB 285~400 nm 產生紅斑所需要時間來確定每個受試者的最小紅斑劑量(Minimal Erythemal Dose, MED)。誘導完成後約 10 天進行激發，施用於 2 個新部位並封閉 24 小時，這些部位暴露於 10 J/cm^2 的 UVA，320~400 nm，結果無光致敏證據。[1]
- 人體數據：一項含 11 名男性和 40 名女性受試者的人類反覆刺激斑貼試驗，其中 8 人未完成研究。在閉塞情況下，約 10 次將約 0.2 mL 的 10%溶液施用 24 小時，休息間隔為 24 或 48 小時。完成後休息 10 天然後在原始測試點和新測試點激發，結果沒有觀察到不良反應。[1]
- 參考資料：

1. European Commission, Reports of the Scientific Committee on Cosmetology (Ninth Series): Butyl Methoxydibenzoylmethane (70356-09-1), 1999.
2. ECHA 網站: https://echa.europa.eu/registration-dossier/-/registered-dossier/14835/7/9/3 .
3. BfR, UV-Filters in Sun Protection Products. Opinion of the Federal Institute for Risk Assessment, 6th August, 2003.

8. INCI name：Sodium Cetearyl Sulfate

- 不純物：Sodium Cetearyl Sulfate 鯨蠟硬脂基硫酸鈉是 cetyl sulfate 鯨蠟硫酸鈉和 stearyl sulfate 硬脂基硫酸鈉的混合物鈉鹽，硬脂基硫酸鈉中存在以下雜質：無機氯化物(最大值為 2.2%)鯨蠟硬脂基硫酸鈉中存在雜質：無機氯化物(最大值為 2.2%)，非硫化物(最大值為

範例

4%)和無機硫酸鹽(最大值為 5.5%)。[1]

- 急性毒性：10 隻雄性 Wistar 大鼠(平均體重 150 g)通過胃管以 10 g/kg bw 劑量施用測試物質，觀察動物 8 天，結果給藥劑量未達到 LD_{50}。[1]
- 皮膚刺激性：20.0%的鯨蠟硬脂酸鈉水溶液對兔子的皮膚沒有刺激性，但是 10%未稀釋溶液為輕度刺激性物質。與 sodium lauryl sulfate 月桂基硫酸鈉相比，鯨蠟硬脂基硫酸鈉對皮膚的刺激性小。[1]
- 眼睛刺激性：以 Draize 眼睛刺激性試驗，20.0%的鯨蠟硬脂酸鈉水溶液不會刺激兔子眼睛。[1]
- 皮膚致敏性：在 Pirbright 雌性天竺鼠(平均體重 463 g)的皮膚致敏研究中，分別在誘導階段和激發階段分別以 25.0%和 1.0%濃度進行，在研究過程中實驗組或對照組都沒有觀察到反應。[1]
- 重複給藥毒性：無數據。[1] 由於鯨蠟硬脂基硫酸鈉與 Sodium Lauryl Sulfate 十二烷基硫酸鈉這兩種成分的化學相似性，因此十二烷基硫酸鈉的安全性測試數據被認為可用於該成分的安全性評估。大鼠 90 天口服毒性 NOAEL 為 100 mg/kg/day，LOAEL 為 500 mg/kg/day。[2]
- 致突變性/遺傳毒性：無數據。[1] 參考 90 天飼餵 1.13%和 0.56%十二烷基硫酸鈉的大鼠試驗，大鼠骨髓中染色體畸變的發生率與對照組無顯著差異。[3]
- 致癌性：無數據。[1] 參考十二烷基硫酸鈉的一年長期研究，給米格魯餵食飼料中十二烷基硫酸鈉濃度最高 2.0%下亦未發現致癌作用。[3]
- 生殖毒性：無數據。[1] 使用懷孕的 JCL/ACR 小鼠評估十二烷基硫酸鈉的致畸潛力。在妊娠第 6 天至第 13 天，每天(劑量 1.5 ml/kg) 0.4、4.0 和 6.0%的水溶液分別用於三組小鼠的背部。在 0.4%受測組後代中觀察到腦疝、腭裂、眼瞼張開、多指畸形和馬蹄內翻足，在 4.0%和 6.0%受測組中也觀察到腭裂和眼瞼張開，在 4.0%和 6.0%受測組中分別觀察到數目異常和彎曲的尾巴。此外，隨著十二烷基硫酸鈉濃度的增加，骨化顯著延遲，未經治療的小鼠後代的異常包括睜開眼瞼、多指、彎曲的尾巴和畸形足。在水處理對照的後代中僅觀察到腹疝和眼瞼張開。睜眼和腭裂被認為是 JCL/ACR 小鼠中日益嚴重的現象。因此，這些異常在實驗和對照小鼠中的發生可能顯著也可能不顯著。[3]

範例

- 毒理代謝動力學：無數據。[1] 參考十二烷基硫酸鈉以天竺鼠進行的經皮吸收評估，將測試物質在蒸餾水中在側面擦拭 10 分鐘，用水沖洗部位，並用非阻塞性貼劑覆蓋 24 小時。在糞便、腎臟或屍體中未檢測到放射性，而在呼出的 CO_2 和尿液中檢測到 0.1%的實驗劑量。大多數放射性在測試部位、測試部位沖洗處或貼布上被檢測到。而在大鼠腹腔內或皮下注射十二烷基硫酸鈉後，排泄的主要途徑是通過尿液。[3]
- 光毒性：無數據。[1] 而含有 2.5%十二烷基硫酸鈉的粉底產品不會造成 599 名受試者中的任何一位誘發光敏反應。[3]
- 人體數據：無數據。[1] 參考十二烷基硫酸鈉人類反覆刺激斑貼試驗，當受測者使用含 1.26%十二烷基硫酸鈉時，於誘導和激發階段會觀察到反應；而鯨蠟硬脂基硫酸鈉的動物測試，在 25.0%誘導和 1.0%激發階段後並不會對動物產生任何反應。基於數據，CIR 專家認為鯨蠟硬脂基硫酸鈉對人的皮膚刺激性和致敏潛力低於十二烷基硫酸鈉，因此認為無需要求鯨蠟硬脂基硫酸鈉的人體致敏試驗數據。[3]
- 參考資料：

1. Final report on the safety assessment of sodium cetearyl sulfate and related alkyl sulfates as used in cosmetics. IJT 29 (Suppl. 2):115-132, 2010.
2. SIDS Initial Assessment Report For SIAM 5. Sodium dodecyl sulphate (CAS No: 151-21-3):17, 2005.
3. Final Report on the Safety Assessment of Sodium Cetearyl Sulfate. JACT 11(1):145-155, 1992.

9. INCI name：Carbomer

- 不純物：Carbomer 的雜質可能包括水、苯、丙酸、乙酸、丙烯酸、重金屬、鐵、砷和鉛，CIR 專家小組提醒應注意可能作為雜質存在的苯，並建議應盡可能降低雜質含量。[1]
- 急性毒性：對大鼠、天竺鼠、小鼠和狗進行的急性口服研究表示，Carbomer 經攝入後毒性低，大鼠的口服急性 LD_{50}= 2500 mg/kg bw，大鼠的皮膚暴露 LD_{50} >3000 mg/kg bw。[1]
- 皮膚刺激性：0.5% Carbomer 水溶液對皮膚有輕微刺激性。[1]
- 眼睛刺激性：100% Carbomer 對眼睛有刺激性。以 Draize 眼睛刺激

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性測試，兩個 Carbomer-934 100%溶液樣品結果主要刺激指數為 0.2，表示有很低的刺激性。由於 Carbomer 是吸濕性的凝膠形成聚合物，因此預期它們會因從眼組織中吸出水分而引起某種刺激性。[1]

- 皮膚致敏性：無動物數據。人類反覆刺激斑貼試驗數據顯示低致敏化能力。[1]
- 重複給藥毒性：雄性和雌性大鼠分為四組(每組每性別 30 隻)，飲食接受 0 (對照組)、300、1000 或 3000 mg PA (high-molecular-weight crosslinked polyacrylate)/kg bw/day，在 32 天或 93 天犧牲。結果顯示，最高 3000 mg/kg/day 組的大鼠並無組織病理學、血液學、體重或臨床化學變化。但是，PA 會導致尿中鈉和磷的排泄量增加，而鎂、鈣和鉀的排泄量降低。[2] 在大鼠飲食中以 0.1%、0.5%或 5.0%攝入 Carbomer 持續 6.5 個月，其器官重量發生了各種變化；而狗在餵食 0.5 或 1.0 g/kg/day Carbomer 6.5 個月，觀察到胃腸道刺激和肝臟 Kupffer 細胞內明顯的色素沉積，另一項狗餵食 1.0 g/kg /day Carbomer 連續 32 個月的研究結果則沒有明顯影響。[3] 在一項 13 週的飲食毒性研究中，Sprague-Dawley 大鼠給予 Carbopol 974(假定純度 100%)，四組(每組每性別 10 隻)分別接受 0、12,500、25,000 和 50,000 mg/kg 飲食 (相當於雄性每天 0、744、1,513 和 3,147 mg/kg bw 而雌性為 0、835、1,681 和 3,416 mg/kg bw)，另一項研究則在狗的飲食中給予 Carbopol 974(假定純度 100%)至少 13 週，三組(每組每性別 4 隻)分別接受 0、12,500、25,000 和 50,000 mg/kg bw(相當於雄性每天 0、420、802 和 1,657 mg/kg bw 而雌性為 0，394，784 和 1642 mg/kg bw)。在大鼠結果在高劑量觀察到對體重和體重增加的影響以及對臨床化學參數的一些輕微影響。專家組認為體重和體重增加的減少可能反映了營養素和 Carbomer 之間的相互作用，導致營養素吸收不良，這被認為是一種不良影響，因此專家群確定 NOAEL 為 1,513 mg/kg bw/day；狗的研究結果顯示劑量高達 50,000 mg/kg bw 飲食無任何毒性作用，NOAEL 為 1,642 mg/kg bw per day 即測試的最高劑量。[4]
- 致突變性/遺傳毒性：在 Ames 測試顯示，非致突變物質。[1]
- 生殖毒性：非生殖毒性物質。[1]
- 毒理代謝動力學：大鼠口服吸收率低 3.5%。[1]
- 光毒性：無光毒性。[1]
- 人體數據：人類反覆刺激斑貼試驗和其他研究顯示出較低的刺激性

和致敏能力。[1]

- 其他安全性資料：Carbomer 的安全性已經過化粧品成分審查(Cosmetic Ingredient Review, CIR)專家小組的評估。CIR 專家小組評估了科學數據並得出結論，Carbomer 聚合物作為化粧品和個人護理產品的成分是安全的。2001 年，作為計劃重新評估成分的一部分，CIR 專家小組考慮了有關 Carbomer 聚合物的現有新數據，並重申了上述結論。CIR 專家小組審查了急性口服研究，顯示 Carbomer 聚合物在攝入時具有低毒性。觀察到最小的皮膚刺激和無到中度的眼睛刺激。使用 Carbomer 聚合物進行的亞慢性餵食研究導致體重低於正常體重，但在器官中未觀察到異常變化。在 Carbomer 的研究中發現了一些胃腸道刺激和肝臟特定細胞(Kupffer cells)內的顯著色素沉積。Carbomer 的臨床研究顯示，這些聚合物在高達 100%的濃度下對皮膚的刺激和致敏的可能性很小。Carbomer 聚合物表現出低光毒性和光接觸致敏性的可能性。[5]
- 參考資料：

1. Final Amended Report. Amended Safety Assessment of Acrylates Copolymers as Used in Cosmetics, CIR, 2018.
2. Effects of oral administration of a high-molecular-weight crosslinked polyacrylate in rats. Fundam Appl Toxicol 17 (1): 128-35, 1991.
3. Final report on Carbomers -934, -910, -934P, -940, -941, and -962. JACT 1(2):109-141, CIR, 1982.
4. Safety evaluation of crosslinked polyacrylic acid polymers (carbomer) as a new food additive. EFSA Journal;19(8):6693, 2021.
5. Cosmetics Info 網站：https://cosmeticsinfo.org/ingredient/carbomer-0

10. INCI name：Disodium EDTA

- 不純物：預計無重大雜質，但應監測重金屬。CIR 指出化粧品使用的 Disodium EDTA，重金屬含量一般應低於 10 ppm，甲醛含量低於 100 ppm。[1]
- 急性毒性：大鼠急性口服毒性 LD_{50} 為 2800 mg/kg bw，急性吸入毒 LOAEL 為 30 mg/m³ air。[2]

- 刺激性：對皮膚沒有刺激性，對眼睛沒有刺激性。[1]
- 皮膚致敏性：無數據。參考 Na_3EDTA 類似化合物不具致敏性。[1]
- 重複給藥毒性：在一項為期兩年的研究中，33 隻大鼠分 5 組給予了 0、0.5、1 和 5% Disodium EDTA。5%實驗組比其他組的大鼠表現出腹瀉和少食，沒有觀察到對體重增加的顯著影響，凝血時間、紅細胞計數或骨頭也沒有受到不利影響。動物的死亡率與 Disodium EDTA 量無關。死亡率最高的是對照組。各種器官的肉眼和顯微鏡檢查顯示兩組之間無顯著差異 [3]。在一項為期 13 週的重複給藥毒性研究中，餵食 Disodium EDTA（0%、1%、5%、10%）的大鼠在最高劑量下顯示出死亡率，此外，在 5%（約 4206 mg/kg bw/day）及以上的劑量下，食物消耗減少（消瘦 10%）和腹瀉。Disodium EDTA NOAEL 為 1%（約 692 mg/kg bw/day）。[5]
- 致突變性/遺傳毒性：高劑量的體外和體內研究具弱致突變性，不致引起人類致突變性。[4]
- 致癌性：無數據。參考 Na_3EDTA 類似化合物以 7500 ppm 劑量餵食大鼠及小鼠達 103 週，結果無致癌性。[1]
- 生殖毒性：口服 EDTA 劑量高於 1000 mg/kg bw/day 可能導致鋅消耗不足，使試驗動物產生生殖/發育毒性 [1]。EDTA 使用濃度低和皮膚吸收差，皮膚給藥後不太可能產生生殖毒性。[4]
- 毒理代謝動力學：不太可能通過皮膚吸收，但可以用作滲透促進劑。[1] 口服的吸收率差<3%，低於 20%劑量被胃腸吸收，吸收的物質隨著尿液迅速排出體外。[4]
- 光毒性：無數據。[1]
- 人體數據：四個正常血鈣患者在 4 小時內靜脈滴注 4 g Sodium EDTA 或 Calcium EDTA，導致更多的鈣排泄率分別為 75%~88%和 57%~70%。服用 Disodium EDTA 4 小時內，約有 60%~80%的過量鈣排泄出。當給三個人服用放射性劑量(未指定劑量)的 Calcium EDTA 時，24 小時之內就會排泄 100%。而口服的 Sodium EDTA 及 Calcium EDTA(6 g/day，共 6 天)在人體的胃腸道中吸收差。然而，在接受 Calcium EDTA 的受試者糞便中鈣的含量有增加情況。[1]
- 其他安全資料：CIR 專家小組評估科學數據並得出結論，Sodium EDTA 和相關成分用於化粧品和個人護理產品是安全的。化粧品和個人護理產品中使用濃度下的 EDTA 和相關成分不是皮膚刺激物或致敏劑。研究顯示，這些成分不是致癌物質。由於這些成分結合正

範例

常細胞分裂所需的金屬，一些研究顯示這些化合物具有弱致突變性。另研究資料顯示，口服暴露於大劑量金屬螯合劑後會對生殖和發育產生影響，這可能是正常生殖和發育所需的金屬結合的影響。CIR 專家小組審查了 EDTA 和相關成分，發現其不易透過皮膚吸收。因此，通過使用含有這些成分的化粧品和個人護理產品，皮膚接觸 EDTA 或 HEDTA 會導致非常少的皮膚滲透和全身暴露量，遠低於口服研究中顯示的產生不良影響的劑量。[6]

◆ 參考資料：

1. Final Report on the safety assessment of EDTA, Calcium Disodium EDTA, Diammonium EDTA, Dipotassium EDTA, Disodium EDTA, TEA-EDTA, Tetrasodium EDTA, Tripotassium EDTA, Trisodium EDTA, HEDTA, and Trisodium HEDTA. IJT 21(Suppl.2):95-142, 2002.
2. ECHA 網站: https://echa.europa.eu/registration-dossier/-/registered-dossier/14817/7/3/1 .
3. Seventeenth Report of the Joint FAO/WHO Expert Committee on Food Additives, Wld Hlth Org. techn. Rep. Ser., No. 539, 1974. FAO Nutrition Meetings Report Series, No. 53, 1974. ETHYLENEDIAMINETETRAACETATE, DISODIUM AND CALCIUM DISODIUMSALTS.(https://inchem.org/documents/jecfa/jecmono/v05je25.htm)
4. CSTEE, Opinion on the results of the Risk Assessment of: TETRASODIUM ETHYLENEDIAMINE TETRAACETATE (NA_4EDTA) and EDETIC ACID (EDTA) HUMAN HEALTH PART, 2003.
5. SIDS Initial Assessment Profile, COCAM 3, SIDS, 16-18 October 2012.
6. Cosmetics Info 網站：https://cosmeticsinfo.org/ingredient/disodium-edta

範例

11. INCI name：Methylparaben

- 經皮吸收：測試濃度介於 0.1%-2%，Methylparaben 對羥基苯甲酸甲酯、對羥基苯甲酸丙酯和對羥基苯甲酸丁酯在人類屍體皮膚(0.37-0.91 cm/h×10^{-4})和小鼠皮膚(1.17-1.76 cm/h×10^{-4})中的滲透係數估計值相似。[1]
- 急性毒性：大鼠急性口服毒性 LD_{50} 大於 5600 mg/kg，在已發表文獻中沒有新的口服或皮膚急性毒性研究。[1,2] 小鼠皮下注射對羥基苯甲酸甲酯，劑量大於 165 mg/kg 會暫時引起疲勞、失調、和呼吸窘迫，急性致死皮下劑量大於 333 mg/kg，而大鼠皮下注射毒性大於 500 mg/kg bw。[1,2]
- 皮膚刺激性：未稀釋的 Methylparaben 對羥基苯甲酸甲酯以 Draize 測試，九隻兔子將 0.1 mL 的對羥基苯甲酸酯塗在剃毛之皮膚上並覆蓋 24 小時，最終的主要刺激指數為 0.67，顯示對皮膚有輕微刺激性。[1]
- 眼睛刺激性：將 0.1mL 0.20%的對羥基苯甲酸甲酯滴入兔眼，在此測試濃度下，對羥基苯甲酸甲酯誘導輕度短暫性結膜充血。在關於刺激性的調查各種眼科藥物成分，0.1%至 0.2%對羥基苯甲酸甲酯在等滲溶液中滴注到眼睛中不會引起兔子和天竺鼠的眼睛刺激性。[2]
- 皮膚致敏性：對羥基苯甲酸甲酯、對羥基苯甲酸乙酯、對羥基苯甲酸丙酯和對羥基苯甲酸丁酯(0.1％在生理鹽水中)皮下注射至未指定數量的天竺鼠，每週 3 次，共 3 週(10 次注射)。結果顯示對羥基苯甲酸酯未誘導任何過敏反應。含有 0.1%至 0.8%的一種或兩種對羥基苯甲酸酯的產品配方(包括對羥基苯甲酸甲酯，對羥基苯甲酸乙酯，對羥基苯甲酸丙酯和對羥基苯甲酸丁酯)的皮膚配方進行皮膚刺激和致敏測試，沒有證據顯示這些成分的刺激性或致敏性。[2,3]
- 重複給藥毒性：口服慢性毒性每劑量各 24 隻雄性和雌性大鼠餵食含有 0、2 或 8%的對羥基苯甲酸甲酯 96 週，試驗組動物攝入量分別為 1050 mg/kg bw 及 5500 mg/kg bw， NOAEL 為 5500 mg/kg bw/day。[1,2,3]
- 致突變性/遺傳毒性：對羥基苯甲酸甲酯確實在中國倉鼠卵巢細胞試驗中增加了染色體畸變。[1,2,3]
- 致癌性：當在小鼠或大鼠皮下注射或在大鼠陰道內給藥時，對羥基苯甲酸甲酯無致癌性。[1,2]

參考版

- 生殖毒性：非生殖毒性物質。小鼠的飲食添加 0.1%或 1.0%的對羥基苯甲酸甲酯的體內研究報告顯示沒有精子毒性作用。在暴露於 1,000 ppm 或 10,000 ppm 飲食 8 週的大鼠中，對羥基苯甲酸甲酯與異常精子發生率顯著升高有關，4% ~ 5%的精子中大部分為無頭精子，對照組則為 2.3%，荷爾蒙濃度大致並無變化；研究結果顯示未觀察到不良反應的濃度是測試最高濃度 10,000 ppm，對應於對羥基苯甲酸甲酯的 NOAEL 約為 1,140 mg/kg bw/day。[1]
- 毒理代謝動力學：大鼠的肝微粒體對於對羥基苯甲酸酯類的活性最高，其次是小腸和肺微粒體。其中對羥基苯甲酸丁酯被肝微粒體最有效地水解，而對具有較短和較長烷基側鏈的對羥基苯甲酸酯則顯示出較低的水解活性。相反於大鼠小腸微粒體對較長側鏈的對羥基苯甲酸酯表現出相對較高的活性，人肝微粒體對於對羥基苯甲酸酯的水解活性最高，其活性隨側鍊長度的增加而降低。人小腸微粒體的特異性模式與大鼠小腸微粒體相似。[1,2]
- 光毒性：對含有 0.1%至 0.8%的對羥基苯甲酸甲酯、對羥基苯甲酸丙酯和/或對羥基苯甲酸丁酯的產品配方進行光致敏化和光毒性測試，沒有發現明顯的光反應性證據。[1,2]
- 人體數據：對羥基苯甲酸酯施於 50 名受試者背部，其中 5、7、10、12 和 15%對羥基苯甲酸甲酯在丙二醇中。每天施用 5 天後被移除，並對施測部位評分。濃度為 5%的對羥基苯甲酸甲酯不會產生刺激，而較高的濃度會產生一些皮膚刺激。另一 50 位受試者的人類反覆刺激斑貼試驗，結果並無皮膚致敏反應。[3,4]
- 參考資料：

1. Amended Safety Assessment of Parabens as Used in Cosmetics. International Journal of Toxicology, Vol. 39 (Supplement 1) 5S-97S, CIR, 2020.
2. Safety Assessment of parabens as Used in Cosmetics. CIR, 2018.
3. Final Amended Report on the Safety Assessment of Methylparaben, Ethylparaben, Propylparaben, Isopropylparaben, Butylparaben, Isobutylparaben, and Benzylparaben as used in Cosmetic Products. International Journalof Toxicology, 27 (Suppl. 4): 1-82, 2008.
4. Final Report on the Safety Assessment of Methylparaben, Ethylparaben, Propylparaben, and Butylparaben.JACT 3(5):147-209, 1984.

範例

12. INCI name：Propylparaben

- 經皮吸收：測試濃度介於 0.1%-2%，對羥基苯甲酸甲酯、Propylparaben 對羥基苯甲酸丙酯和對羥基苯甲酸丁酯在人類屍體皮膚(0.37-0.91 cm/h×10^{-4})和小鼠皮膚(1.17-1.76 cm/h×10^{-4})中的滲透係數估計值相似。[1]
- 急性毒性：小鼠急性口服毒性 LD_{50} 為 5600 mg/kg，在已發表文獻中沒有新的口服或皮膚急性毒性研究。[1,2] 小鼠皮下注射對羥基苯甲酸丙酯 LD_{50} 為 1.65 g/kg。[1,2]
- 皮膚刺激性：產品含有 0.2%的對羥基苯甲酸丙酯產生的刺激性最小，主要刺激指數為 0.5。[2]
- 眼睛刺激性：含有濃度為 0.1%至 0.8%的對羥基苯甲酸甲酯、對羥基苯甲酸乙酯、對羥基苯甲酸丙酯或對羥基苯甲酸丁酯的產品進行了許多兔眼睛刺激性研究，大多數產品都沒有眼睛刺激的症狀。[1]
- 皮膚致敏性：對羥基苯甲酸甲酯、對羥基苯甲酸乙酯、對羥基苯甲酸丙酯和對羥基苯甲酸丁酯(0.1%在生理鹽水中)皮下注射至未指定數量的天竺鼠，每週 3 次，共 3 週(10 次注射)。結果顯示對羥基苯甲酸酯未誘導任何過敏反應。含有 0.1%至 0.8%的一種或兩種對羥基苯甲酸酯的產品配方(包括對羥基苯甲酸甲酯，對羥基苯甲酸乙酯，對羥基苯甲酸丙酯和對羥基苯甲酸丁酯)的皮膚配方進行皮膚刺激和致敏測試，沒有證據顯示這些成分的皮膚刺激性或致敏性。[3]
- 重複給藥毒性：幼齡 Wistar 大鼠(每組 n = 20)口服對羥基苯甲酸丙酯，劑量為 3、10、100 或 1000 mg/kg bw /day。在 8 週試驗結束時測量青春期的成熟度、生殖器官重量、精子數量、運動能力和血漿激素含量並進行毒物代謝動力學分析。研究顯示沒有證據顯示對羥基苯甲酸丙酯對男性生殖有影響。此研究確定對羥基苯甲酸丙酯的 NOAEL 為 1000 mg/kg bw/day。[1,4]
- 致突變性/遺傳毒性：許多致突變性研究顯示對羥基苯甲酸丙酯是非致突變性。以 Ames 試驗研究對羥基苯甲酸丙酯的致突變潛力，以 10 到 2000 µg/plate 的劑量進行測試時，對羥基苯甲酸丙酯在有無代謝活化的情況下都是不具致突變性的。[1,3]
- 致癌性：對羥基苯甲酸丙酯胎盤測定和新生兒測定。給懷孕的嚙齒動物口服最大劑量，研究結果對羥基苯甲酸丙酯均無致癌性。[1,3]
- 生殖毒性：在一項體外研究中，精子在低至 3 mg/mL 對羥基苯甲酸

丙酯的濃度下無法存活。對羥基苯甲酸丙酯在 0.01%至 1.0%的濃度下會影響體內的精子數量。[2]

- 毒理代謝動力學：大鼠的肝微粒體對於對羥基苯甲酸酯類的活性最高，其次是小腸和肺微粒體。其中對羥基苯甲酸丁酯被肝微粒體最有效地水解，而對具有較短和較長烷基側鏈的對羥基苯甲酸酯則顯示出較低的水解活性。相反，大鼠小腸微粒體對較長的側鏈對羥基苯甲酸酯表現出相對較高的活性。人肝微粒體對於對羥基苯甲酸酯的水解活性最高，其活性隨側鍊長度的增加而降低。人小腸微粒體的特異性模式與大鼠小腸微粒體相似。[1]
- 光毒性：對含有 0.1%至 0.8%的對羥基苯甲酸甲酯、對羥基苯甲酸丙酯和/或對羥基苯甲酸丁酯的產品配方進行光致敏化和光毒性測試，沒有發現明顯的光反應性證據。[1]
- 人體數據：對羥基苯甲酸酯施於 50 名受試者背部，其中 5%、7%、10%、12%和 15%對羥基苯甲酸丙酯在丙二醇中。每天施用 5 天後被移除，並對施測部位評分。濃度為 12%的對羥基苯甲酸丙酯不會產生刺激，而較高的濃度會產生一些皮膚刺激。另一 50 位受試者的人類反覆刺激斑貼試驗，結果並無皮膚致敏反應。[2,3]
- 參考資料：

1. Amended Safety Assessment of Parabens as Used in Cosmetics. IJT 39(Suppl. 1):5-97, 2020.
2. Final Amended Report on the Safety Assessment of Methylparaben, Ethylparaben, Propylparaben, Isopropylparaben, Butylparaben, Isobutylparaben, and Benzylparaben as used in Cosmetic Products. International Journalof Toxicology, 27 (Suppl. 4): 1-82, 2008.
3. Final Report on the Safety Assessment of Methylparaben, Ethylparaben, Propylparaben, and Butylparaben.JACT 3(5):147-209, 1984.
4. RIVM Report 2017-0028.Exposure to and toxicity of methyl-, ethyl- and propylparaben, 2018.

範例

(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、密度項目進行 6 個月產品加速安定性試驗，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	清爽型防曬乳			
包裝材質	LDPE			
試驗時間 / 試驗項目	第 0 個月 40 ℃ 75 %RH	第 1 個月 40 ℃ 75 %RH	第 3 個月 40 ℃ 75 %RH	第 6 個月 40 ℃ 75 %RH
外觀	乳狀	乳狀	乳狀	乳狀
顏色	白色至淡黃色	白色至淡黃色	白色至淡黃色	白色至淡黃色
氣味	無添加香精	無添加香精	無添加香精	無添加香精
pH (at 25 °C)	7.30	7.41	7.25	7.33
黏度(at 25 °C)	3050 mPas	2950 mPas	3100 mPas	3180 mPas
密度(at 25 °C)	1.01 g/cm^3	1.00 g/cm^3	0.98 g/cm^3	0.99 g/cm^3
微生物檢測結果	未檢出	未檢出	未檢出	未檢出
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)

樣板

(12) 微生物檢測報告

產品名稱	清爽型防曬乳		
產品批號	IT2207CY		
產品製造日期	111.07.05		
包裝材質	LDPE	試驗日期	111.07.06
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。
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)		

範例

(13) 防腐效能試驗報告

樣品名稱 (Sample Name)	清爽型防曬乳				
測試日期(Date Tested): 110.05.24~110.06.21					
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	1.0×10^6	4.2×10^5	5.5×10^5	3.3×10^4	4.6×10^4
第 7 天	<10	<10	<10	1.3×10^3	2.2×10^3
第 14 天	<10	<10	<10	<10	1.2×10^2
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)				

範例

(14) 功能評估佐證資料

清爽型防曬乳之防曬係數測試係以ISO 24444:2010 Cosmetics — Sun protection test methods - In vivo determination of the sun protection factor (SPF)方法進行。

SPF TEST Result Table									**Laboratory： ABC Lab.**						
Product：清爽型防曬乳			**SPF 期望值：15**			**測試日期：110.05.01**			**UV source：Xe MP**						
N°	**TEST**		**SUBJECTS**						**RESULTS**					**CONCLUSION** $Cl_{n'}$**[%]≤17 %**	**COMMENTS**
	Exposure date	Technician name	Subject code	Skin ITA°	Photo type	MEDu ($mJ \cdot cm^{-2}$)	MEDp ($mJ \cdot cm^{-2}$)	SPFi	$SPF_{n'}$	$S_{n'}$	$C_{n'}$	$Cl_{n'}$[%] ($100c_{n'}/SPF_{n'}$)	n		
1				56,4	I	19	290	15,3	-	-	-	-		-	
2				48,6	II	29	350	12,1	-	-	-	-		-	
3				58,1	I	19	290	15,3	-	-	-	-		-	
4				43.5	II	24	420	17,5	-	-	-	-		-	
5				44,0	II	20	440	22,0	-	-	-	-		-	
6				42,7	II	17	330	19,4	-	-	-	-		-	
7				34,9	III	29	460	15,9	-	-	-	-		-	
8				57,0	I	19	260	13,2	-	-	-	-		-	
9				54,8	II	27	370	13,7	-	-	-	-		-	
10				45,3	II	19	230	12,1	**15,6**	**3,2**	**2,31**	14,8%	8	Complies	
FINAL RESULT			**Mean SPF = 15,6**				**s = 3,2**		**c= 2,31**		**Cl[%] = 14,8 %**			**95 % CI： 13,3 – 17,9 (n = 10)**	

(15) 與產品接觸之包裝材質資料

包裝材料	材質
清爽型防曬乳-瓶身	LDPE
清爽型防曬乳-瓶蓋	LDPE

III. 安全評估資料

(16) 產品安全資料

清爽型防曬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)，並依其用途、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	全身皮膚
接觸種類	駐留產品
每日使用頻率	2/day
駐留因子	1
防曬乳/霜使用表面積(cm^2)	17500
每日皮膚暴露量($E_{product}$) 對於防曬產品，在 MoS 計算中使用的皮膚暴露量為 18.0 g/day，以成人平均體重估算即為 300 mg/kg bw/day。 備註: 此為 SCCS 進行安全評估時作為防曬產品之標準暴露值，但並不表示建議消費者依此用量使用(SCCNFP/0321/02)。	

閱後即丟

清爽型防曬乳各成分 MoS 值計算

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

SED= Eproduct (每日皮膚暴露量)×C/100(配方百分比)×DAp/100(皮膚吸收率)

*M*oS= PODsys/*S*ED

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	73.57	-	-	-	>100
Decyl Oleate	15.0	1	111.1	0.450	246.9
Ethylhexyl Methoxycinnamate	3.0	4	396.4	0.360	1101.1
Phenylbenzimidazole Sulfonic Acid	2.78	0.2	500	0.017	29976.0
Cetearyl Alcohol	2.205	10	1000	0.662	1511.7
Sodium Hydroxide (45 % solution)	1.2	not relevant	not relevant	not relevant	not relevant
PEG-40 Hydrogenated Castor Oil	0.63	10	1250	0.189	6613.8
Butyl Methoxydibenzoylmethane	0.5	0.56	100	0.008	11904.8
Sodium Cetearyl Sulfate	0.315	10	50	0.095	529.1
Carbomer	0.3	10	756.5	0.090	8405.6
Disodium EDTA	0.1	10	346	0.030	11533
Methylparaben	0.3	100	350.8	0.900	389.8
Propylparaben	0.1	100	307.7	0.300	1025.7

備份

INCI name	NOAEL 校正說明
Decyl Oleate	28天每週5天的大鼠灌食毒性得知NOAEL為1000 mg/kg bw/day，考慮口服生物可用率50%及試驗天數等不確定因子，1000*50%*5/7*28/90 =111.1 mg/kg bw/day。
Ethylhexyl Methoxycinnamate	13週每週5天的大鼠皮膚毒性得知NOAEL為555 mg/kg bw/day，考慮試驗天數之不確定因子，555*5/7 =396.4 mg/kg bw/day。
Phenylbenzimidazole Sulfonic Acid	13週大鼠口服毒性得知NOAEL為1,000 mg/kg bw/day，考慮口服生物可用率50%之不確定因子，1000*50% =500 mg/kg bw/day。
Cetearyl Alcohol	交互參照Behenyl alcohol在26週大鼠口服毒性得知NOAEL為1000 mg/kg bw /day，此為更保守值故未以不確定因子進行校正。
Sodium Hydroxide	不相關，作為pH調節劑。
PEG-40 Hydrogenated Castor Oil	90天大鼠餵食毒性得知NOAEL為2,500 mg/kg bw/day，考慮口服生物可用率50%之不確定因子，將2,500*50% =1,250 mg/kg bw/day。
Butyl Methoxydibenzoylmethane	13週大鼠口服毒性得知最低NOAEL為200 mg/kg bw/day，考慮口服生物可用率50%之不確定因子，將200*50% =100 mg/kg bw/day。
Sodium Cetearyl Sulfate	90天大鼠口服毒性得知NOAEL為100 mg/kg bw/day，考慮口服生物可用率50%之不確定因子，將100*50% =50 mg/kg bw/day。
Carbomer	90天大鼠口服毒性得知NOAEL為1,513 mg/kg bw/day，考慮口服生物可用率50%之不確定因子，1513*50% =756.5 mg/kg bw/day。
Disodium EDTA	為期13週餵食大暑試驗中得知NOAEL為692 mg/kg bw/day，考慮口服生物可用率50%之不確定因子，692*50% =346 mg/kg bw/day。
Methylparaben	8週小鼠口服生殖毒性得知NOAEL為1140 mg/kg bw/day，考慮口服生物可用率50%及試驗天數等不確定因子，將1140*50% *8/13 =350.8 mg/kg bw/day。
Propylparaben	8週大鼠口服毒性得知NOAEL為1000 mg/kg bw/day，考慮口服生物可用率50%及試驗天數等不確定因子，1000*50% *8/13 =307.7 mg/kg bw/day。

範例

清爽型防曬乳安全評估結論

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據以結論，推定清爽型防曬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，對人體健康造成傷害風險低。

標籤警語和使用說明

清爽型防曬乳的包裝材料/標籤上提到了以下警告和使用說明：

使用方式：曝曬前 15 分鐘取適量均勻塗抹於臉部或身體。

使用注意事項：塗抹時避免接觸眼睛，若不慎接觸請以大量清水沖洗。使用後若有不適，請立即停止使用並以大量清水沖洗。不得使用於三歲以下孩童之尿布部位。

內含 Propylparaben 及 Methylparaben，已依我國化粧品防腐劑成分名稱及使用限制表應刊載之注意事項進行標示。

安全評估理由

清爽型防曬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. 本產品所含之三種防曬成分 Ethylhexyl Methoxycinnamate(限量 10%)、Phenylbenzimidazole sulfonic acid(限 量 8%) 及 Butyl methoxydibenzoylmethane(限量 5%)符合我國之規定，使用兩種防腐劑 Methylparaben (限量 0.4%以 acid 計)及 Propylparaben(限量 0.14%以 acid 計)之總量未超過化粧品防腐劑成分名稱及使用限制表之規定。
3. 根據本產品「清爽型防曬乳」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，證實了「清爽型防曬乳」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。
4. 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符合衛福部食藥署 110.05.13 公告之化粧品防腐效能試驗指引標準 A，表示產品微生物汙染風險受到管控，可保護產品避免受到潛在微生物汙染之風險。

範例

5. 本產品使用之包裝材質為 LDPE，根據過去類似配方及此包材之使用經驗，評估此包裝材料合適且安全。
6. 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 用於防曬產品之標準暴露值以計算安全邊際值(MoS)。此產品雖為駐留型產品，但部分成分之物理化學特性為不易皮膚吸收者，因此將皮膚吸收率納入考量估算因皮膚吸收而引起全身毒性之暴露劑量低；此外，氫氧化鈉雖然具有強腐蝕性及刺激性，但氫氧化鈉溶液係作為 pH 調節劑且最終成品 pH 為中性，故未進行該成分之安全邊際值(MoS)計算。
7. 此清爽型防曬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，這支持此產品的安全性。
8. 目前此產品尚未出現不良影響和嚴重的不良影響，如有不良影響和嚴重不良影響的相關資訊會立即更新，並及時提供給安全資料簽署人員，以重新評估此產品之安全性。

（請簽名並加上日期）

_____

安全資料簽署人員簽名及日期

附錄 1：產品及各成分之物理化學特性相關資料

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：Ethylhexyl Methoxycinnamate

		Page: 1
SAFETY DATA SHEET		Revision Date: 08/04/2020
		Print Date: 11/24/2020
		SDS Number:
		Version: 1.4

29 CFR 1910.1200 (OSHA HazCom 2012)

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product identifier

Trade name : UV filters
™ Trademark, Ashland or its subsidiaries, registered in various countries

Substance name: 2-Ethylhexyl 4-methoxycinnamate

Substance No.
EC-No.: 226-775-7

CAS-No.: 5466-77-3

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

Recommended use : Cosmetic additive

Details of the supplier of the safety data sheet	**Emergency telephone number** **Regulatory information** **Product Information**

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification
Not a hazardous substance or mixture.

GHS label elements
Not a hazardous substance or mixture.

Other hazards
None known.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Substance

Hazardous components
No hazardous ingredients

SECTION 4. FIRST AID MEASURES

General advice : No hazards which require special first aid measures.

If inhaled : If breathed in, move person into fresh air.
If unconscious, place in recovery position and seek medical advice.
If symptoms persist, call a physician.

In case of skin contact : First aid is not normally required. However, it is recommended that exposed areas be cleaned by washing with soap and water.

In case of eye contact : Remove contact lenses.
Protect unharmed eye.

If swallowed : Do not give milk or alcoholic beverages.
Never give anything by mouth to an unconscious person.
If symptoms persist, call a physician.

Most important symptoms and effects, both acute and delayed : The most important known symptoms and effects are described in the labelling (see Section 2.2) and/or Section 11.

Notes to physician : No hazards which require special first aid measures.

SECTION 5. FIREFIGHTING MEASURES

Suitable extinguishing media : Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.
Water spray
Foam
Carbon dioxide (CO2)
Dry chemical

Hazardous combustion products : Carbon dioxide (CO2)
Carbon monoxide

Hydrocarbons

Specific extinguishing methods : Product is compatible with standard fire-fighting agents.

Further information : Standard procedure for chemical fires.

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

SECTION 6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures : Persons not wearing protective equipment should be excluded from area of spill until clean-up has been completed.

Environmental precautions : Prevent further leakage or spillage if safe to do so.

Methods and materials for containment and cleaning up : Soak up with inert absorbent material (e.g. sand, silica gel, acid binder, universal binder, sawdust).
Keep in suitable, closed containers for disposal.

Other information : Comply with all applicable federal, state, and local regulations.

SECTION 7. HANDLING AND STORAGE

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

Advice on safe handling : Smoking, eating and drinking should be prohibited in the application area.
For personal protection see section 8.

Materials to avoid : No materials to be especially mentioned.

Further information on storage stability : No decomposition if stored and applied as directed.

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Components with workplace control parameters
Contains no substances with occupational exposure limit values.

Engineering measures : General room ventilation should be adequate for normal conditions of use. However, if unusual operating conditions exist, provide sufficient mechanical (general and/or local exhaust) ventilation to maintain exposure below exposure guidelines (if applicable) or below levels that cause known, suspected or apparent adverse effects.

Personal protective equipment

Respiratory protection : In the case of vapour formation use a respirator with an approved filter within the capabilities of the respirator/filter combination.
Where concentrations are above recommended limits or are unknown, or a cartridge type respirator is not adequate, wear a positive-pressure supplied-air respirator.

Hand protection
- Material : butyl-rubber
- Break through time : 480 min
- Glove thickness : > 0.5 mm

Remarks : The exact break through time can be obtained from the protective glove producer and this has to be observed. Gloves should be discarded and replaced if there is any indication of degradation or chemical breakthrough.

Eye protection : Not required under normal conditions of use. Wear splash-proof safety goggles if material could be misted or splashed into eyes.

Skin and body protection : Wear as appropriate:
Safety shoes
Wear resistant gloves (consult your safety equipment supplier).

Hygiene measures : General industrial hygiene practice.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance : liquid

Physical state	:	liquid
Colour	:	light yellow
Odour	:	mild
Odour Threshold	:	No data available
pH	:	No data available
Melting point/freezing point	:	-13 °F / -25 °C
Boiling point/boiling range	:	387.9 - 392 °F / 197.7 - 200 °C (4 hPa)
Flash point	:	192.7 °C
Evaporation rate	:	not determined
Upper explosion limit	:	Upper explosion limit not determined
Lower explosion limit	:	Lower explosion limit not determined
Vapour pressure	:	not determined
Relative vapour density	:	not determined
Relative density	:	No data available
Density	:	1.005 - 1.013 g/cm3 (20 °C)
Solubility(ies)		
Water solubility	:	insoluble
Solubility in other solvents	:	No data available
Partition coefficient: n-octanol/water	:	not determined
Thermal decomposition	:	No data available
Viscosity		
Viscosity, dynamic	:	not determined
Viscosity, kinematic	:	not determined

Oxidizing properties : Not applicable

SECTION 10. STABILITY AND REACTIVITY

Reactivity : No decomposition if stored and applied as directed.

Chemical stability : Stable under recommended storage conditions.

Possibility of hazardous reactions : Product will not undergo hazardous polymerization.

Incompatible materials : strong bases
Strong oxidizing agents

Hazardous decomposition products : Carbon monoxide
Carbon dioxide (CO_2)

SECTION 11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure : Inhalation
Skin contact
Eye Contact
Ingestion

Acute toxicity
Not classified based on available information.
Skin corrosion/irritation
Not classified based on available information.
Serious eye damage/eye irritation
Not classified based on available information.
Product:
Remarks: Unlikely to cause eye irritation or injury.

Respiratory or skin sensitisation
Skin sensitisation: Not classified based on available information.
Respiratory sensitisation: Not classified based on available information.
Germ cell mutagenicity
Not classified based on available information.
Carcinogenicity
Not classified based on available information.
Reproductive toxicity
Not classified based on available information.

STOT - single exposure
Not classified based on available information.
STOT - repeated exposure
Not classified based on available information.
Aspiration toxicity
Not classified based on available information.
Product:
No aspiration toxicity classification

Further information
Product:
Remarks: No data available

Carcinogenicity:

IARC	No component of this product present at levels greater than or equal to 0.1% is identified as probable, possible or confirmed human carcinogen by IARC.
OSHA	No component of this product present at levels greater than or equal to 0.1% is on OSHA's list of regulated carcinogens.
NTP	No component of this product present at levels greater than or equal to 0.1% is identified as a known or anticipated carcinogen by NTP.

SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity
Product:
Ecotoxicology Assessment

Short-term (acute) aquatic hazard	:	Not classified based on available information.
Long-term (chronic) aquatic hazard	:	Not classified based on available information.

Persistence and degradability
Product:

Biodegradability	:	Result: Readily biodegradable. Biodegradation: 78 % Exposure time: 28 d Method: OECD Test Guideline 301F

No data available

Bioaccumulative potential
No data available
Mobility in soil
No data available
Other adverse effects
No data available
Product:
Additional ecological information : No data available

SECTION 13. DISPOSAL CONSIDERATIONS

Disposal methods

General advice : Dispose of in accordance with all applicable local, state and federal regulations.

Contaminated packaging : Empty remaining contents.

SECTION 14. TRANSPORT INFORMATION

International transport regulations

REGULATION

ID NUMBER	PROPER SHIPPING NAME	*HAZARD CLASS	SUBSIDIARY HAZARDS	PACKING GROUP	MARINE POLLUTANT / LTD. QTY.

U.S. DOT - ROAD

Not dangerous goods

CFR_RAIL_C

Not dangerous goods

U.S. DOT - INLAND WATERWAYS

Not dangerous goods

TDG_ROAD_C

Not dangerous goods

TDG_RAIL_C

Not dangerous goods

TDG_INWT_C

Not dangerous goods

INTERNATIONAL MARITIME DANGEROUS GOODS

Not dangerous goods

INTERNATIONAL AIR TRANSPORT ASSOCIATION - CARGO

Not dangerous goods

INTERNATIONAL AIR TRANSPORT ASSOCIATION - PASSENGER

Not dangerous goods

MX_DG

Not dangerous goods

***ORM = ORM-D, CBL = COMBUSTIBLE LIQUID**

Marine pollutant		no

Dangerous goods descriptions (if indicated above) may not reflect quantity, end-use or region-specific exceptions that can be applied. Consult shipping documents for descriptions that are specific to the shipment.

SECTION 15. REGULATORY INFORMATION

TSCA list
No substances are subject to TSCA 12(b) export notification requirements.

EPCRA - Emergency Planning and Community Right-to-Know Act

CERCLA Reportable Quantity
This material does not contain any components with a CERCLA RQ.

SARA 304 Extremely Hazardous Substances Reportable Quantity

This material does not contain any components with a section 304 EHS RQ.

SARA 311/312 Hazards : No SARA Hazards

SARA 302 : This material does not contain any components with a section 302 EHS TPQ.

SARA 313 This material does not contain any chemical components with known CAS numbers that exceed the threshold (De Minimis) reporting levels established by SARA Title III, Section 313.

US State Regulations

Pennsylvania Right To Know

2-Ethylhexyl 4-methoxycinnamate	5466-77-3

New Jersey Right To Know

2-Ethylhexyl 4-methoxycinnamate	5466-77-3

California Prop. 65

This product does not contain any chemicals known to State of California to cause cancer, birth defects, or any other reproductive harm.

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

DSL : All components of this product are on the Canadian DSL

AICS : On the inventory, or in compliance with the inventory

ENCS : 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

TCSI : On the inventory, or in compliance with the inventory

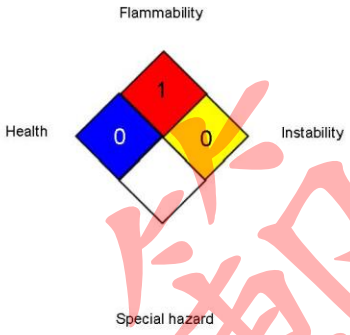
TSCA : On or in compliance with the active portion of the TSCA inventory

Inventories
AICS (Australia), DSL (Canada), IECSC (China), REACH (European Union), ENCS (Japan), ISHL (Japan), KECI (Korea), NZIoC (New Zealand), PICCS (Philippines), TCSI (Taiwan), TSCA (USA) - On or in compliance with the active portion of the TSCA inventory

SECTION 16. OTHER INFORMATION

Further information

NFPA 704:



HMIS® IV:

HMIS® ratings are based on a 0-4 rating scale, with 0 representing minimal hazards or risks, and 4 representing significant hazards or risks. The "*" represents a chronic hazard, while the "/" represents the absence of a chronic hazard.

Full text of H-Statements

Full text of other abbreviations

AICS - Australian Inventory of Chemical Substances; ASTM - American Society for the Testing of Materials; bw - Body weight; CERCLA - Comprehensive Environmental Response, Compensation, and Liability Act; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DOT - Department of Transportation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; EHS - Extremely Hazardous Substance; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide;

範例

Sources of key data used to compile the Safety Data Sheet :

Revision Date : 08/04/2020

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：Ethylhexyl Methoxycinnamate

1. European Commission, Reports of the Scientific Committee on Cosmetology (Ninth Series): 2-Ethylhexyl-4-methoxycinnamate (5466-77-3), 1999.

S 28: *2-ETHYLHEXYL-4-METHOXYCINNAMATE*

1. General

1.1 Primary name

2-ethylhexyl-4-methoxycinnamate

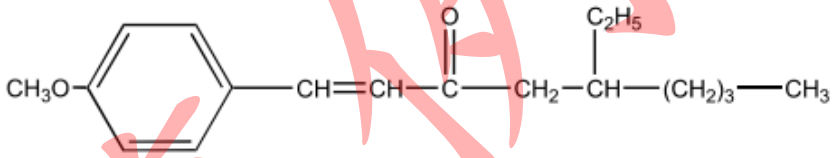
1.2 Chemical names

2-ethylhexyl-4-methoxycinnamate

1.3 Trade names and abbreviations

Parsol MCX

1.5 Structural formula



1.6 Empirical formula

Emp. formula: $C_{15}H_{26}O_2$
Mol weight: 290

1.8 Physical properties

Appearance: Colourless pale yellow slightly oily liquid.

1.9 Solubility

Miscible with alcohols, propylene glycol, etc.
Immiscible with water.

2. Function and uses

Use level up to 10 %.

TOXICOLOGICAL CHARACTERISATION

3. Toxicity

3.1 Acute oral toxicity

Oral LD_{50}: Mouse, greater than 8 g/kg b.w. Rat, greater than 20 ml/kg b.w.

3.4 Repeated dose oral toxicity

Rat. Three week oral study. Groups of 5 male and 5 female animals were given 0, 0.3, 0.9 and 2.7 mg/kg b.w./day by gavage for 3 weeks. All animals of the top dose groups exhibited loss of body weight and a reduced relative and absolute weight of the thymus. Male rats showed a decrease in absolute weight of the left kidney and female rats showed a decrease in the absolute weight of the heart. At the two lower doses, the only significant alteration observed was an increased absolute weight of the pituitary gland in male rats receiving the lowest dose. As the number of animals was small, the investigators considered this not to be biologically significant. The NOAEL was put at 0.9 ml/kg b.w./day.

3.7 Subchronic oral toxicity

Rat. Thirteen week oral study. Four groups of 12 male and 12 female SPF rats received the compound in the diet at levels of 0, 200, 450 and 1000 mg/kg b.w./day. During the experiment the usual clinical observations were carried out, as well as extensive haematological and biochemical studies. Full gross necropsy was carried out on all survivors. Histological investigations were carried out in half the animals of the control and top dose groups. The organs studied included the heart, lungs, liver, stomach, kidneys, spleen, thyroid and retina. In the remaining animals histological examination of the liver only was carried out. Six control animals and 6 top dose animals were allowed to recover over 5 weeks, and then examined.

The results of the experiment showed no dose related mortality. The kidney weights of top dose animals were increased, but were normal in the recovery animals; the increase was attributed to a physiological response to an increased excretion load. There was a diminution of glycogen in the liver, and a slight increase in iron in the Kupfer cells in the high dose animals. Two of these also showed minimal centrilobular necrosis of the liver with some infiltration; similar less marked findings were made in 2 of the control animals as well. These findings were attributed to infection. High dose females had increased GLDH which reversed during the recovery period. The NOAEL was put at 450 mg/kg b.w./day.

3.8 Subchronic dermal toxicity

Rat. Thirteen week dermal study. Four groups of 10 male and 10 female SD rats were treated by an application of various concentrations of a.i. in light mineral oil. The doses were 0, 55.5, 277 and 555 mg/kg b.w./day applied to shaved skin 5 days a week for 13 weeks. (The top dose is believed to be about 135 times the amount which would be used daily by the average consumer). Various laboratory and clinical tests were carried out during the experiment.

All animals survived. All animals showed a slight scaliness at the site of application, which was attributed to the vehicle. Body weight gain was greatest at the low dose. Haematological investigations showed no significant change. SAP was elevated in high dose animals, but not significantly. The relative liver weight in high dose animals was elevated, but appeared normal on microscopical examination. The authors put the NOAEL at 555 mg/kg b.w./day, but in view of the liver findings this may be 227 mg/kg b.w./day.

6. Teratogenicity

Rabbit. Groups of 20 female animals were mated and given a.i. in doses of 0, 80, 200 and 500 mg/kg b.w./day by gavage during the period of organogenesis. Except for a slight reduction of maternal and foetal weight in the top dose animals, no abnormality was found.

Rat. Following a pilot study, groups of 36 rats were mated and treated with 0, 250, 500 and 1000 mg/kg b.w./day of a.i. (probably by gavage) during days 6-14 of pregnancy. Owing to an error, the preparation of the control foetuses led to their destruction, so this part of the test was repeated under identical conditions. Subgroups of each dose group were allowed to litter normally and rear the offspring. The percentage of resorptions in the high dose group was elevated by comparison with the other groups. The investigator records, however, that this relatively high rate is the usual one with this strain of rat in this laboratory, and he attributes the difference to an unusually low level of resorption in the other groups. No other abnormality was found.

7. Toxicokinetics (incl. Percutaneous Absorption)

Tests for percutaneous absorption.

(a) *In vitro* tests. Rat. Naked rat skin. This was studied in a chamber experiment. Most of the material was found in the stripped skin; there was less in the stratum corneum, and least in the chamber. The approximate amounts found in the chamber were: after 6 hrs, 1.13 %; after 16 hrs, 11.4 %; and at 24 hrs 17,9 %. The figures for the horny layer and the strippings combined were, respectively, 31.4 %, 44.4 % and 45.7 % (percentages of applied doses). Solutions of 3 % and 20 % of a.i. gave similar results. In another set of experiments, various amounts of "Parsol 1789" (4-tert-butyl-4'-methoxydibenzoylmethane) were added to the a.i. in the formulation. There seemed to be no effect on the absorption of the a.i.

Pig. A similar experiment using mini-pig skin was carried out in which "Parsol 1789" was used as well as the a.i. Using 3 sorts of formulation, about 3 % of a.i. was found in the chamber in 6 hrs. Using the concentrations proposed for a particular commercial use (i.e., 7.5 % of "Parsol 1789" and 2 % of a.i.) about 2.2 % was found in the chamber. It is calculated by the authors that the total absorption for a 75 kg consumer would be about 70 mg, or 0.9 mg/kg b.w. (Note however that the maximum proposed use level of a.i. is 10 %).

Man. A test on human abdominal skin in a chamber was carried out. With 7.5 % a.i., about 0.03 % is found in the camber in 2 hours, 0.26 % in 6 hours, and 2.0 % in 18 hours. Various combinations of a.i. and "Parsol 1789" were investigated.

(b) *In vivo* tests. Man. Eight healthy volunteers had small amounts of radioactive a.i. applied to the interscapular region. One group of 4 had the material applied under a watch glass; the other 4 had it applied on gauze, whith occlusion in one case. Tests for absorption of a.i. were negative except for about 0.2 % in urine. The concentrations used were not stated.

In a preliminary experiment, a capsule containing 100 mg of a.i. was taken orally. As a lipophilic substance, the a.i. is very likely to be metabolised; it is known in any case to be hydrolysed by plasma esterases, although slowly. The cumulative excretion of 4methoxycinnamate in the urine over 24 hours was studied by GC/MS of the methyl ester

derivative. (This method would also detect 4-hydroxycinnamic acid). Over 24 hours, 13.2 % of the amount ingested was recovered, equivalent to 21.5 % of the amount that would be expected if the a.i. were completely absorbed. In the main part of the experiment, an o/w cream containing 10 % a.i. was used. Applications of 2 grams of this material (= 200 mg a.i.) were made to the interscapular area of each of 5 male subjects, aged 29 to 46. The area of skin covered was 25x30 cm. After application, the area was covered with 3 layers of gauze, left in place for 12 hours. Blood was taken at times 0, 0.5, 1, 2, 3, 5, 7, and 24 hours. Urine was collected at 0, 1, 2, 3, 4, 5, 6, 7, 12, 24, 48, 72 and 96 hours.

The control plasma samples showed a level equivalent to about 10 ng/ml before any application had been made. There was no evidence of any rise in plasma levels during the experiment. The urine showed a "physiological" level of 100 to 300 ng/ml. No significant increase in this amount was found in any sample. The authors conclude that very little, if any, of the compound was absorbed under the conditions of the experiment.

8. Mutagenicity

Salmonella mutagenesis assays were performed on the usual strains. There was a positive result with TA 1538 without metabolic activation. This was thought to have been a batch effect. From another laboratory, a very weak positive was found with TA 1538 without activation, at 10 µl/plate; it was not found in 2 replicates, nor in a second Ames test. A test for mutagenesis and crossing over in *S. cerevisiae* was negative. A test using Chinese hamster V 79 cells showed a very slight increase in mutant colonies with dose. A test in human lymphocytes *in vitro* was negative.

A test for cell transformation in Balb/c 3T3 cells was negative. A test for unscheduled DNA synthesis was negative.

Tests in *Drosophila:* There was an increase in the frequency of sex-linked recessive lethals. There was no evidence of mutagenicity in feeding tests (adults and larvae). Somatic mutation and combination tests using wing structure were negative. Mouse. Micronucleus test. No effect was found up to 5000 mg.

Test for photomutagenic activity. These were carried out in cells of *S. cerevisiae,* which had previously been shown not to be affected by a.i. *(supra)*. Doses of a.i., dissolved in DMSO, ranged from 0.06 to 625 µg/ml, and radiation up to 500000 J m^{-2} UVA and up to 12000 UVB (50 and 1.2 J cm^{-2}). Chlorpromazine was used as the positive control. Suitable negative controls were also employed. The experiment appears to have been well carried out. The results show that UVA and (more markedly) UVB are mutagenic; and that the a.i. protects against this effect in a dose dependent manner.

10. Special investigations

Test for capacity to produce phototoxicity. Man. In 10 subjects, patches were applied for 24 hours and the areas then exposed to a suberythematous dose of UV irradiation. There was no evidence of phototoxicity.

Test for capacity to produce photosensitization. Tests which "showed that the product did not provoke photosensitization." No details supplied.

Test for inhibition of UV-induced tumors. Hairless mouse. The animals were exposed to repeated doses of UV simulating the solar energy spectrum. After a rest period, 3 applications a week were made to an area of skin of 12-o-tetradecanoyl phorbol-13-acetate (at first at 10 g/ml, but later at 2 g/ml, as the higher concentration was found to be irritant). Suitable controls were used. The test group was completely protected by 50 % a.i., and 7.5 % gave an effect equivalent to reducing the insolation four-fold. It had been suggested that the a.i. could itself have been a promoter, but there was no evidence of this.

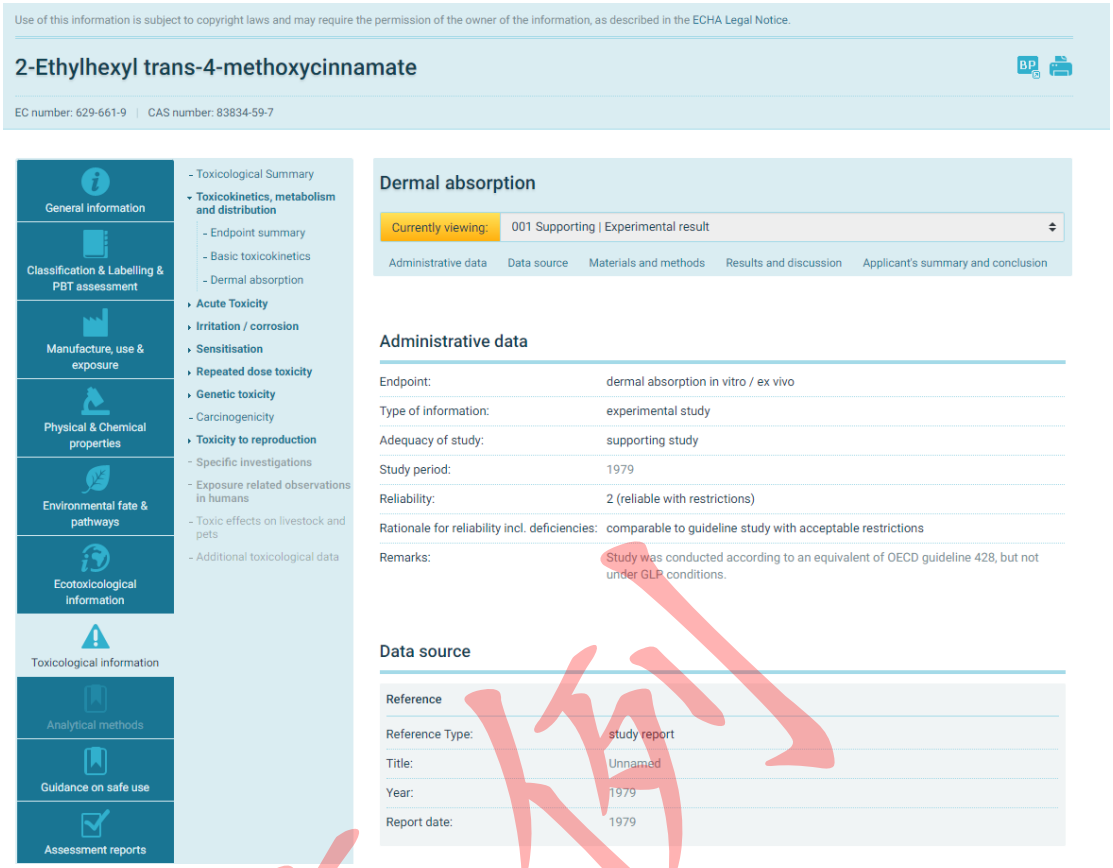
11. Conclusions

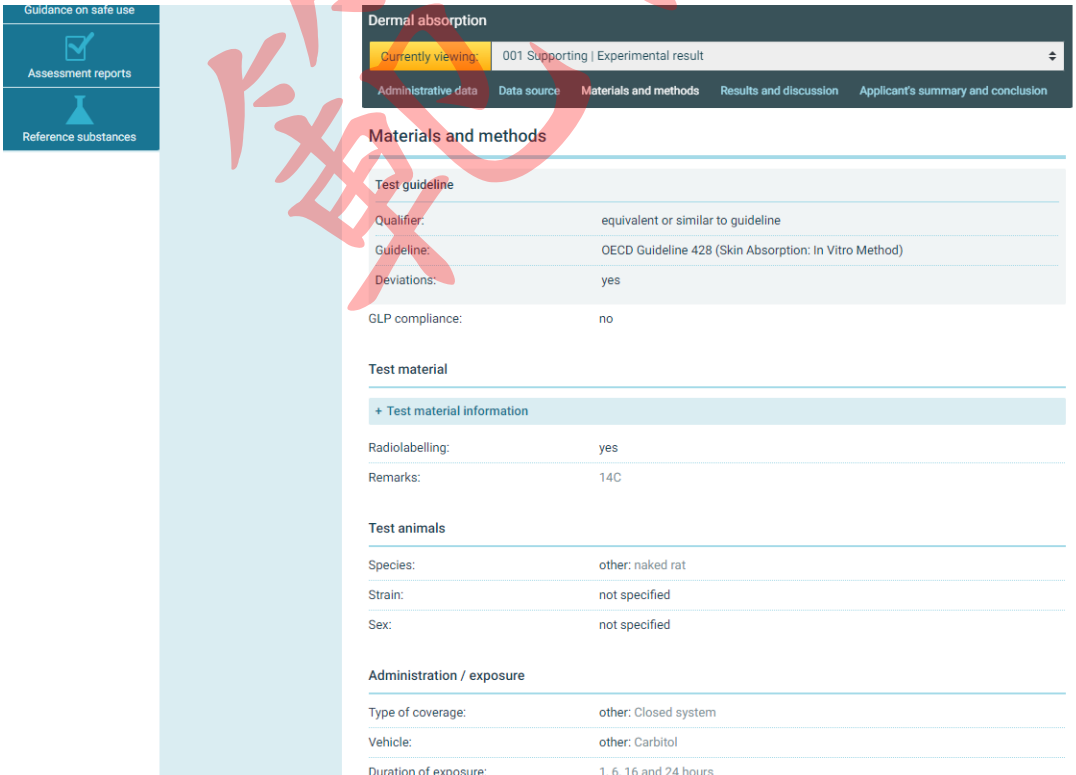
The compound appears to have low acute and subchronic toxicity, orally and dermally; it does not irritate the mucous membranes in conventional animal tests. The data presented suggest that the compound is not an irritant or sensitizer in animals and man; however, tests for sensitization were carried out at levels below the proposed maximum use level. Clinical investigation shows that this compound is very rarely responsible for allergic contact dermatitis in man. There is no carcinogenicity study, but an extensive range of mutagenicity studies were nearly all negative. A test for photomutagenicity was negative, although the dose of UVB used was rather low. Animal studies for teratogenic activity were negative. Percutaneous absorption in man appears to be very low.

Classification: A

廃棄

2.ECHA 網站: https://echa.europa.eu/registration-dossier/-/registered-dossier/15876/7/2/3 .





Dermal absorption

Currently viewing: 001 Supporting | Experimental result

Administrative data | Data source | Materials and methods | **Results and discussion** | Applicant's summary and conclusion

Remarks on result:	other: 16 hrs
Remarks:	Based on amount of test material in stripped skin and chamber liquid

Any other information on results incl. tables

Percentage of substance absorbed after 24 hrs:

1 % in carbitol: 44.3 %

3 % in carbitol: 35.6 %

10 % in carbitol: 22.7 %

About 70 - 90 % of the applied dose of Ethylhexyl Methoxycinnamate was found on the skin surface during the first 6 hours after application

The amount recovered from the stratum corneum was low and reached its maximum 24 hours after application. The steady state was attained within 6 hours.

The portion of Ethylhexyl Methoxycinnamate found in the stripped skin increased to its maximum within 16 hours. Lower levels of the test material were found 24 hours after application.

A significant part of the applied dose was found in the chamber liquid (7 - 17 %) after longer times of exposure.

Applicant's summary and conclusion

Conclusions:	In an in vitro system using naked rat skin, the skin penetration potential and resorption capacity of Ethylhexyl Methoxycinnamate were significant after longer times of exposure, based on the high amount of Ethylhexyl Methoxycinnamate found in the stripped skin, the low levels in the stratum corneum and the amount of activity recovered from the chamber liquid.
Executive summary:	Skin penetrating potential of Ethylhexyl Methoxycinnamate in naked rat skin was determined in a study using an in vitro system. The study was performed according to an equivalent of OECD guideline 428. Three concentrations of Ethylhexyl Methoxycinnamate in carbitol (1, 3 and 10 %) were applied and skin absorption rates were determined by the activity of the 14C-labelled test article. It was found that the higher amount of Ethylhexyl Methoxycinnamate is absorbed into the upper layer of the skin (stripped skin). The low levels in the stratum corneum and the amount of activity recovered from the chamber liquid indicate significant penetration and resorption capacities of Ethylhexyl Methoxycinnamate through the intact skin of the naked rat after longer times of exposure.

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3. UV-Filters in Sun Protection Products, Opinion of the Federal Institute for Risk Assessment, 6th August, 2003.

Federal Institute for Risk Assessment (BfR)

UV-Filters in Sun Protection Products

Opinion of the Federal Institute for Risk Assessment, 6th August 2003

Background

The Federal States Baden-Württemberg and Bayern have reported several problems related to UV filters in sun protection products. Questions have been raised in particular concerning

1. combined effects of UV filters and a summation limit value for UV filters,
2. a limitation for the sun protection factor,
3. the photostability of UV filters and
4. the oral toxicity of UV filters in lipsticks and lip care products.

UV filters and their combinations have frequently been a subject matter of deliberations within the Committee for Cosmetic Products (Cosmetics Committee) at the Federal Institute for Risk Assessment (BfR). The questions and proposals of the Federal States were discussed at the 64th meeting of the Cosmetics Committee.

Result

1. BfR recommends using combinations of UV filters and ingredients in the formulations of cosmetic products in a manner that enables to keep the amount of individual filters and also the sum of the filters used for the protection aimed as low as possible. The permitted maximum concentrations for the individual UV filters must not be exceeded. Furthermore, UV filters added should contribute considerably to the sun protection factor of the finished product. The health safety and the skin tolerance of the finished products must be guaranteed. At present there are no hints with respect to a concrete risk for cumulative toxic effects or increased skin penetration in products with a UV filter combination.

2. BfR further recommends a limitation for the sun protection factor, SPF, in sun protection products for healthy skin. Along the lines of precautionary consumer protection BfR is of the opinion that even a lower maximum SPF than the maximum SPF of 50+ discussed in the Cosmetics Committee could be favourable. In Australia and in the USA protection factors are restricted to 30+. A restriction to a SPF of 30+ would also be beneficial with respect to the difficulties in reproducibility of high SPFs and the correspondingly long exposure time for volunteers when determining high SPFs. The declared SPF should also be achieved under application conditions.

   Products with high UVB protection should also provide high UVA protection. In order to determine UVA protection, a uniform international harmonised method should be elaborated for the wavelength range of 320 to 400 nm. The declaration of UVA protection should be comprehensible for the consumer. A declaration as a percentage of the filtered UVA rays, for example, could help to avoid confusion with the SPF, which is a time-based protection factor. Until the establishment of an internationally accepted determination method, the declaration of UVA protection should include a reference to the determination method.

3. Since the combination of various UV filters and the formulation play a decisive role for photostability, BfR generally recommends testing the stability of the UV filters in finished products under conditions which are as close as possible to application ones. This is within the responsibility of manufacturers.

4. According to current knowledge it can be assumed that the use of decorative lipsticks and lip care sticks with UV protection only leads to a minor increase in systemic exposure of consumers to UV filters. The margin of safety (MOS) for all evaluated UV filters is at least 100 in sun protection products. In the case of additional exposure to UV filters in lipsticks and lip care sticks, the MOS according to current knowledge, falls only below 100 in the case of one filter (4-methyl benzylidene camphor).

   The margin of safety is based on the assumption of daily, lifelong exposure. For sun protection products application throughout the year must be assumed. It is not currently felt that there is a risk to the consumer through additional exposure to UV filters in lipsticks and lip care sticks. For reasons of precautionary consumer protection, however, 4-methyl benzylidene camphor should not be used in lipsticks, lip care sticks or skin care products.

Further recommendations

Sun protection products do not offer complete protection against UV rays. Their use should not lead to extended exposure to the sun nor replace sun protection through clothes. This applies in particular to children. Infants and babies should not be exposed to direct sunlight at all.

Explanation

UVB rays (wavelengths of approx. 290 to 320 nm) encourage the formation of melanin in the melanocytes of the deepest epidermal layers and therefore also the darkening of the skin through delayed pigmentation. UVB is largely involved in the development of inflammatory reactions (sunburn). Even low doses of UVB rays lead to an immunosuppressant effect. UVA rays (wavelengths of approx. 320 to 400 nm) penetrate the horny layer and reach the epidermis and dermis. They have a comparatively low effect on the triggering of sunburn but may trigger pathological light reactions. UVA rays mainly lead to an immediate pigmentation by means of reversible oxidation of melanin precursors.

The light-related ageing of the skin and the formation of tumours can be attributed both to UVB and UVA rays. The rate of UV-ray-related tumours decreases with increasing wavelength up to 350 nm. There are, however, indications that rays in the range of 380 nm may also induce a higher rate of tumours (Rünger 1999).

Because of an expanding exposure of the majority of the population to the sun, UV protection takes on an increasingly important role. UV filters are, therefore, not only used in sun protection products but to an increasing degree in hair and facial care products and in decorative cosmetics.

UV filters in cosmetics require marketing authorisation. Their use is regulated in accordance with Directive 76/768/EEC (Cosmetics Directive) and in the German Cosmetics Regulation (KVO). Permitted UV filters are listed in Annex VII of the Cosmetics Directive and in Annex 7 of the KVO. The maximum concentrations and application restraints are also listed there. Moreover, manufacturers must guarantee the health safety of their products.

UV protection can be afforded by both organic and physical filters (titanium dioxide, zinc oxide). At present, 25 organic sun protection filters are listed (KVO, Annex 7, or Cosmetics Directive, Annex VII). The use of coated microfine titanium dioxide and coated, microfine zinc oxide as UV filters is admissible in accordance with § 3b KVO up to 31 December 2003.

Furthermore, titanium dioxide is also authorised pursuant to the Cosmetics Directive in relative maximum amounts up to 25 %.

1. Combined effects of UV filters and sum limitation value for UV light filter agents

Organic UV filters absorb light quants in a specific wavelength range and convert energy into infrared rays; physical filters (titanium dioxide and zinc oxide) scatter, reflect and absorb UV rays. In order to offer protection over the entire spectrum of relevant wavelengths of 290 to 400 nm, several UV filters with different absorption maxima must be combined. By choosing a suitable combination of organic and physical filters, the content of organic filters can be reduced whilst offering the same UV protection. This is desirable since in particular photounstable organic UV filters, depending on their concentration in the finished product, can trigger phototoxic and photoallergenic reactions.

The combination of UV filters can, moreover, influence photostability. The organic UVB filters octocrylene and methylbenzylidene camphor are known to stabilise the photounstable organic UVA filter butyl methoxydibenzoylmethane. Furthermore, a possible recrystallisation of dissolved UV filters can largely be prevented by a suitable combination with liquid filters.

The galenic auxiliary substances used in the formulation also play a major role in sun protection products. They should guarantee the stability of the UV filters and may, under certain circumstances, also influence their penetration to deeper skin layers. For UV protection it is, however, necessary for the filter substances to remain and act in the horny layer. The efficiency of a sun protection product does not, therefore, depend solely on the filters used but to a large degree on the composition of the overall formulation.

Fears have repeatedly been voiced that the combination of organic UV filters could lead to interactions in the formulations and to an addition or potentiation of toxic effects. However, the BfR has received no information or data, supporting this hypothesis. The authorised filters have mostly been assessed by the Scientific Committee on Cosmetic Products and Non-Food Products intended for Consumers (SCCNFP) and must have a margin of safety (MOS) of at least 100 between the exposure in man achieved under application conditions and a dose which does not lead to any adverse effects in animal experiments (SCCNFP/0321/00/Final: *Notes of guidance for testing cosmetic ingredients for their safety evaluation*). The assessment of UV filters also takes into account the special situation of children. Compared with adults, children have a three-fold higher ratio of body surface to body weight. This problem has been extensively discussed by SCCNFP. SCCNFP came to the conclusion that a MOS of more than 100 is sufficient to guarantee the safety of children when exposed to UV filters (SCCNFP/0557/02/Final: *Position Statement on the Calculation of the Margin of Safety of ingredients incorporated in cosmetics which may be applied to the skin of children*).

From data provided by the surveying authorities, BfR knows that sun protection products with combinations of between two and six UV filters are on sale on the market. The sum of the UV filters may amount to 10 to 20 mass percent. Sun protection products for children may also contain several organic filters. Adverse reactions caused by products with UV filter combinations have not been reported to BfR up to now. The BfR Cosmetics Committee has discussed the combination of UV filters in sun protection products on several occasions. The experts do not currently see a concrete risk based on the cumulative toxic effects or a higher skin penetration in conjunction with UV filter combinations.

Recommendation

BfR recommends that UV filters and ingredients should be combined in the formulations in such a way that the number of filters as well as the relative amount of filters used for the

protection claimed is kept as low as possible. The permitted maximum concentrations for the individual UV filters must not be exceeded. Furthermore, the added UV filters should contribute to the sun protection factor of the finished product. The health safety and skin tolerance of the finished products must be guaranteed.

2. Limitation of the sun protection factor and UVA protection

The declaration of the sun protection factor serves as an indicator for the consumer related to the efficiency of the individual product to protect against sunburn. The SPF stated on the products describes UVB protection and indicates the time period were a stay in the sun should not lead to skin reddening when using the corresponding product (sunburn or erythema protection factor or erythema threshold value). With the principle of the SPF the individual skin type of the consumer is taken into account.

A limitation of the sun protection factor was deemed necessary by the experts of the Cosmetics Committee since use of sun protection products with a high SPF may encourage consumers to an extended stay in the sun. A limitation to a maximum SPF of 50+ with a minimum SPF of 60 was discussed by the Committee. An SPF of 60 implies arithmetically that individuals with sensitive skin (skin types I to II) could spend up to 10 hours in the sun without becoming sunburnt, individuals with insensitive skin (skin types III to IV) up to 30 hours. However when calculating the time periods protection is claimed for the following factors additionally have to be considered:

1. Even protection products with a high SPF do not completely filter UVB rays (sun protection products with an SPF of 20 approximately filter 95 %, products with an SPF of 50 approximately 98 % of the UVB rays).

2. The SPF is determined under standardised conditions in the laboratory by applying 2 mg of the product per cm^2 skin (Colipa Sun Protection Factor Test Method. Brussels; The European Cosmetic, Toiletry and Perfumery Association-COLIPA, 1994). If a smaller amount of the product is applied under application conditions, the declared SPF will not be achieved. Also the sun protection product may become rubbed off by clothing or towels with the consecution of a reduced protection.

3. Since the biological endpoint for the determination of the SPF is the UV erythema, the SPF is no indicator for a protection against UV-caused skin aging, tumour development or immunosuppression. High protection factors in the UVB range may give a false feeling of safety, as skin reddening as an alarm signal is delayed. Consumers therefore may become encouraged to a prolonged stay in the sun. In the consequence the exposure to UVA is increased, if the product does not offer UVA protection.

The determination methods for the SPF have widely been harmonised world-wide since 1999 and SPF declarations on products therefore are mainly comparable. At present, there is no harmonised method for the determination of UVA protection. The Australian Standard (AS/NSZ 2604, 1997) is the only standardised method so far and frequently used all over the world. Here the transmission spectrum of the product is determined at wavelengths of 320 to 360 nm. In order to comply with the standard, more than 90 % of the rays must be filtered. Further specification on UVA protection are derived from tanning determination *in vivo*, e.g. applying the Immediate Pigment Darkening Method (IPD) or the Persistent Pigment Darkening Method (PPD, the industrial standard in Japan since 1996). For these purposes test persons were exposed to rays with specific UVA doses and skin tanning is determined after several minutes (IPD) or several hours (PPD), respectively. Depending on the method used the numerical value given for the same protection may vary considerably. A comparison of UVA protection by different products is possible only to a limited degree.

Declarations, which also include UVB protection are the critical wavelength (at which 90 % of the area under the absorption curve is reached in the range of 290 to 400 nm) and the ratio of UVA to UVB protection.

For an additional qualitative description of sun protection products, the burden quotient was introduced. It is an index for the galenic quality of the product and describes the ratio of the overall amount of UV filters and the sun protection factor. However, it can only serve as additional information and not replace the declaration of efficiency on sun protection products.

Recommendation

BfR recommends a limitation for the SPF in sun protection products for healthy skin. Along the lines of precautionary consumer protection BfR is of the opinion that even a lower maximum SPF than the maximum SPF of 50+ discussed in the Cosmetics Committee could be favourable. In Australia and in the USA protection factors are restricted to 30 +[1]. A restriction to an SPF of 30+ would also be beneficial with respect to the difficulties in reproducibility of high SPFs and the correspondingly long exposure time for volunteers when determining high SPFs. The declared SPF should also be achieved under application conditions.

Products with high UVB protection should also provide high UVA protection. In order to determine UVA protection, an international harmonised method should be elaborated for the wavelength range of 320 to 400 nm. The declaration of UVA protection should be comprehensible for the consumer. A declaration as a percentage of the filtered UVA rays, for example, could help to avoid confusion with the SPF, which is a time-based protection factor. Until the establishment of an internationally accepted determination method, the declaration of UVA protection should include a reference to the determination method.

3. Photostability of UV filters

High sun protection factors imply long-lasting protection. However, this is only guaranteed when the UV filters remain stable over the protection period claimed or if their metabolites have a comparable protective effect. Various studies confirm differing photostability of permitted UV filters (e.g. Herzog and Sommer, 2000, Schwack and Rudolph, 1996, Johncoock, 1999). In order to standardise photostability tests for UV filters, corresponding methods for UVA and UVB filters were published by the umbrella association of the European cosmetics industry *Comité de Liaison des Associations Européennes de l'Industrie de la Parfumerie, des Produits Cosmétiques et de Toilette* (COLIPA), (Gonzenbach et al 1996). According to this method dissolved filters are applied under defined conditions to a glass surface, dried and exposed to UV rays. Subsequently the recovery of the amount of UV filter applied is analytically determined and absorption is measured and compared to a non-irradiated sample.

Recommendation

Since the combination of various UV filters and the formulation play a decisive role for photostability, BfR generally recommends testing the stability of the UV filters in finished products under conditions which are as close as possible to application ones. An appropriate method is currently being developed by COLIPA.

4. Oral toxicity of UV filters in lipsticks and lip care products

[1] In the USA sun protection products are considered to be over-the-counter drugs whose efficiency and safety must be proven. Products may be declared with a higher SPF than 30+ if the effect was previously proven.

Lips react more sensitively to UV rays than the rest of the facial skin. Therefore UV filters are increasingly being added to decorative lipsticks and lip care sticks. Even if no clinical studies are available to confirm the prevention of pre-cancerosis on the lip through UV filters in lip care products, it can be assumed that the sun protection for the skin also protects the lips. In this context various filter combinations are possible and the protective properties of the individual products differ. It is assumed that the relative amount of UV filters in these products is 10 % on average. From surveillance, however, also higher amounts of UV filters in lipsticks and lip care products were reported (in individual cases up to 27 %).

Exposure and Assessment

Usually the amount of lip care products applied is 10 mg per application according to estimates of SCCNFP (SCCNFP/0321/00/Final: *Notes of guidance for testing cosmetic ingredients for their safety evaluation*). For products with a high pigment content as much as 15 mg per application may be applied. In the case of daily four-fold application up to 60 mg of the products were applied to the lips. For lip care products 100 % systemic intake through swallowing is assumed. Under these preconditions for lip care products with a high pigment content and a relative amount of UV filters of 10 % a daily intake of 0.1 mg UV filter per kg body weight for adults (60 kg body weight) and 0.6 mg UV filter per kg body weight for children (10 kg body weight) can be expected.

It is difficult to estimate the systemic intake of UV filters via the skin from skin care and sun protection products. The intake depends on e.g.

- the frequency of application of products containing UV filters,
- the amount used,
- the relative amount of the filter(s),
- the filter combination and the galenics of the formulation as well as
- the ability of the UV filters to penetrate the skin.

The daily amount of skin care products applied (leave-on products: facial cream, body lotion, deodorant and hair products) amounts to 13.5 g according to estimates of SCCNFP (SCCNFP/0321/00 final: *Notes of guidance for testing cosmetic ingredients for their safety evaluation*). Skin care products may contain UV-absorbing agents both for product protection as well as for skin protection. Therefore consumers may additionally be exposed to UV filters through the daily use of these products.

The highest exposure to UV filters is certainly linked to the application of sun protection products. However, BfR has no data about the amounts of sun protection products used. It is generally assumed that 0.5 to 1.5 mg sun protection agent is used per application per cm^2 skin. Taking into account the skin penetration rates obtained in experiments and the filter-specific maximum concentration in conjunction with single application to the entire body surface (18,000 cm^2, application 1 mg/cm^2), systemic exposure was estimated for the individual filters by the Scientific Committee on Cosmetology (SCC) or by SCCNFP in conjunction with marketing authorisation (cf. selection in Table 1).

The estimated exposure to UV filters from decorative lipsticks and lip care sticks is estimated to be 0.1 mg per kg body weight for adults. Table 1 lists the estimated exposure from sun protection products for a selection of UV filters, which are also frequently used in lipsticks and lip care sticks and for which opinions are available from SCC and/or SCCNFP. For these UV filters the MOS was calculated in conjunction with parallel application of sun protection products and lip care products containing UV filters based on the assumption that the same filter is used in both products.

UV filter	amount in product [%]	dermal absorption [%]	filter $_S$ [mg/kg KG/d]	filter $_L$ [mg/kg KG/d]	NOAEL [mg/kg KG/d]	MOS $_S$	MOS $_{SL}$
S27	10	4,4	1,32	0,1	200	152	141
S28	10	2	0,6	0,1	450	750	643
S32	10	0,08	0,021	0,1	175	8333	1446
S60	4	1,9	0,228	0,1	25	110	**76**
S66	5	0,56	0,084	0,1	200	2381	1087
S69	5	1,5	0,23	0,1	1150	5000	3485

Table 1: Additional exposure of adults to UV filters in lipsticks and lip care sticks and changes in the margin of safety

S27: Isoamyl p-methoxycinnamate; S28:Octyl methoxycinnamate; S32:Octocrylene; S60: 4-Methyl benzylidene camphor; S66: Butyl methoxydibenzoyl methane; S69:Octyltriazone
Filter $_S$: estimated amount of UV filters taken up from sun products per kg body weight and day;
Filter $_L$: estimated amount of UV filters taken up from lipsticks and lip care sticks per kg body weight and day;
MOS_S: Margin of Safety for UV filters in sun protection products;
MOS_{SL}: Margin of Safety for UV filters, when used in parallel in sun protection products and lipsticks or lip care sticks

The margin of safety for all authorised UV filters is at least 100 when used in sun protection products. In the case of additional exposure of adults to the corresponding UV filters in lipsticks and lip care sticks, the MOS falls below 100 only in the case of one filter (4-methyl benzylidene camphor[2]). For children who have a three-fold higher ratio of body surface to body weight than adults, the MOS could be even lower under unfavourable conditions. Further exposure is possible from body care products, which may also contain UV filters.

The margin of safety for UV filters is based on the assumption of daily, life-long exposure. This should not, in principle, apply to sun care products although a year-round use must be assumed, as sun protection products may be used not only in summer but probably also during holidays and when using solariums.

Recommendation

It is not felt that there is a fundamental risk to the consumer through additional exposure to UV filters in lipsticks and lip care sticks. However, for reasons of precautionary consumer protection 4-methyl benzylidene camphor should not be used in lipsticks, lip care sticks or skin care products.

5. Further recommendations of BfR

Sun protection products do not offer complete protection against UV rays. Their use should therefore not lead to extended exposure to the sun nor replace sun protection through clothes.This applies in particular to children since data of the American Academy of Dermatology confirm that 80 % of sun damage takes place before the age of 18. Infants and babies up to the age of 2 should not be exposed, if at all possible, to direct sunlight.

[2] Consultations at SCCNFP are currently underway about UV filters with regard to possible bioaccumulation and the interpretation of thyroid effects in animal experiments.

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範例