Data Supplement

Alkyl Amide MIPA

Brown Algae

Capryloyl Salicylic Acid

Silica

Xylitol, Mannitol, Sorbitol

CIR EXPERT PANEL MEETING
SEPTEMBER 16-17, 2019

Commitment & Credibility since 1976

Memorandum

To: CIR Expert Panel Members and Liaisons
From: Monice M. Fiume MMF
Senior Director, CIR
Date: September 6, 2019
Subject: Wave 2 - Draft Tentative Safety Assessment of Alkyl Amide MIPA Ingredients

Updated use information was received (*aaMIPA092019w2_data*). Previously, the highest leave-on dermal use concentration was reported to be 1% Cocamide MIPA, with use reported in body and hand products. The recent submission states that the body and hand formulation, originally thought to be a leave-on product, is a rinse-off product. Consequently, the highest reported leave-on dermal use concentration is now 0.4% Oleamide MIPA in a face and neck formulation.

Additionally, a clarification of some of the ECHA data is being provided. As stated in the transmittal memo with the original mailing of this report, there was much confusion over what was actually being tested in the ECHA submissions. After further detailed review of the dossiers, I believe I have determined what was actually tested. Rather than send you a new report document, please refer to the tables in the attached document for clarification (*aaMIPA092019wave 2_ECHA clarification*). Please note, for some of the studies, it was originally thought that the test material was an alkyl amide MIPA ingredient (e.g., Cocamide MIPA); but, it is now believed that a different test substance was used, and the information was provided as read-across for certain MIPA ingredients. In many cases, the read-across source is an alkyl amide MIPA mixture (e.g., C8-18 alkyl amide MIPA). However, in one particular case, the test substance appears to be an alkyl amide ***DEA***, instead of an alkyl amide MIPA (i.e., a diethanolamide instead of a mono-isopropanolamide, respectively). Page 2 of the clarification document includes a summary of the read-across substances.

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Clarification of ECHA Dossier Test Substances

Study Type	Previously Identified Test Substance	Actual Test Substance	Read-Across, per ECHA	Results	Reference
acute dermal toxicity (rats)	Cocamide MIPA	amides, C8-18 and C18-unsatd., N-(hydroxyethyl)	Cocamide MIPA	LD_{50} > 2000 mg/kg	1
acute dermal toxicity (rats)	Isostearamide MIPA	correct as provided		LD_{50} > 2000 mg/kg	2
acute oral toxicity (rats)	Isostearamide MIPA	correct as provided		LD_{50} > 2000 mg/kg	2
short-term oral toxicity (28-day, in rats)	Cocamide MIPA	amides, C12-18 and C18-unsatd. N-(hydroxyethyl)	Cocamide MIPA	NOAEL > 750 mg/kg bw	1
short-term oral toxicity (28-day, in rats)	Isostearamide MIPA	correct as provided		NOAEL = 200 mg/kg bw/day	2
subchronic dermal toxicity (14-wk, in mice)	Isostearamide MIPA	amides, C8-18 and C18-unsatd., N,N-bis(hydroxyethyl)	Cocamide MIPA Isostearamide MIPA	NOAEL = 200 mg/kg bw/day for systemic effects and 100 mg/kg bw/day for local effects	1,2
subchronic dermal toxicity (14-wk, in rats)	Isostearamide MIPA	amides, C8-18 and C18-unsatd., N,N-bis(hydroxyethyl)	Cocamide MIPA Isostearamide MIPA	NOAELs = 50 mg/kg bw/day for both systemic and local effects	1,2
DART (dermal, 14-wk, mice)	Isostearamide MIPA	amides, C8-18 and C18-unsatd., N,N-bis(hydroxyethyl	Cocamide MIPA Isostearamide MIPA	Epididymal spermatozoal concentration was significantly increased in 800 mg/kg males	1,2
DART (dermal, 14-wk, rats)	Isostearamide MIPA	amides, C8-18 and C18-unsatd., N,N-bis(hydroxyethyl	Cocamide MIPA Isostearamide MIPA	similar to controls	1,2
DART (oral, OECD TG 414, rats)	Isostearamide MIPA	amides, C12-18 (even-numbered) and C18-unsatd., N,N-bis(hydroxyethyl)	Cocamide MIPA Isostearamide MIPA	NOAELs = 1000 mg/kg bw/day for parental toxicity and developmental toxicity	1,2
Genotox – in vitro (Ames test)	Cocamide MIPA	correct as provided		negative	1
Genotox – in vitro (mutation assay, L5178Y cells)	Cocamide MIPA	correct as provided		negative	1
Genotox – in vitro (chromosome aberration test, human lymphocytes)	Cocamide MIPA	correct as provided		negative	1
Genotox – in vitro (Ames test)	Isostearamide MIPA	correct as provided		negative	2
Genotox – in vitro (chromosomal aberration assay, V79 cells)	Isostearamide MIPA	correct as provided		clastogenic	2
Genotox – in vitro (gene mutation assay, L5178Y cells)	Isostearamide MIPA	amides, C8-18 and C18-unsatd., N,N-bis(hydroxyethyl)	Isostearamide MIPA	negative	2
Genotox – in vivo (UDS, rats)	Isostearamide MIPA	correct as provided		negative	2
Genotox – in vivo (micronucleus test, mouse)	Isostearamide MIPA	correct as provided		negative	2
Carcinogenicity (dermal, mouse)	Cocamide MIPA	amides, C8-18 (even-numbered) and C18-unsatd., N-(2-hydroxypropyl	Cocamide MIPA	LOAEL = 100 mg/mg/day for systemic and local effects; clear evidence of carcinogenic activity in males based on increased incidences of hepatic and renal tubule neoplasms and in females based on increased incidences of hepatic neoplasms	1
Carcinogenicity (dermal, mouse; same protocol as above)		amides, C8-18 and C18-unsatd., N, N-bis(hydroxyethyl)	Isostearamide MIPA	same as above	2
Carcinogenicity (dermal, rats)	Cocamide MIPA	amides, C8-18 and C18-unsatd., N, N-bis(hydroxyethyl)	Cocamide MIPA Isostearamide MIPA	NOAEL = 50 mg/kg/day; no evidence of carcinogenic activity in males at any dose; equivocal evidence of carcinogenic activity in females based on a marginal increase in the incidences of renal tubule neoplasms	1,2
Dermal Irritation – Animal (4-h, semi-occlusive, rabbits)	Cocamide MIPA	Isostearamide MIPA		not irritating	2
Dermal Irritation – Animal (4-h, occlusive, rabbits)	Cocamide MIPA	amides, C8-18 and C18-unsatd., N-(hydroxyethyl)	Cocamide MIPA	moderately irritating	1
Sensitization – Animal (GPMT)	Cocamide MIPA	correct as provided		non-sensitizing	1
Sensitization – Animal (GPMT)	Isostearamide MIPA	correct as provided		non-sensitizing	2
Ocular Irritation - Animal	Cocamide MIPA	amides, C8-18 and C18-unsatd., N-(hydroxyethyl)	Cocamide MIPA	moderately irritating	1
Ocular Irritation - Animal	Isostearamide MIPA	correct as provided		non-irritating	2

1. European Chemical Agency (ECHA). REACH dossier: Amides, C8-18 (even-numbered) and C18 (unsatd.), N-(2-hydroxypropyl) (CAS No. 1335203-30-9). https://echa.europa.eu/registration-dossier/-/registered-dossier/13560. Last Updated: 08/17/2019. Accessed: 08/21/2019.

2. European Chemical Agency (ECHA). REACH dossier: isostearic acid monoisopropanolamide (Isostearamide MIPA). https://echa.europa.eu/en/registration-dossier/-/registered-dossier/2879. Last Updated: 10/10/2017. Accessed: 8/21/2019. Note: The test material was not always clearly defined in the dossier; however, personal communication with the C. Eisenmann (May 6, 2019) provided confirmation that the test article identified as "constituent" with lot number E16734, purity 94.1%, is Isostearamide MIPA.

Summary - List of Read-Across Substances

Read-Across Substance	Corresponding Ingredient(s)	Study Types
amides, C8-18 and C18-unsatd., N-(hydroxyethyl)	Cocamide MIPA	acute - dermal; dermal irritation – animal; ocular irritation - animal
amides, C8-18 (even-numbered) and C18-unsatd., N-(2-hydroxypropyl	Cocamide MIPA	carcinogenicity – dermal (mouse)
amides, C8-18 and C18-unsatd., N,N-bis(hydroxyethyl) **["*N,N*-bis(hydroxyethyl)" is equivalent to DEA, not MIPA]**	Cocamide MIPA; Isostearamide MIPA	subchronic - dermal; DART – dermal; carcinogenicity – dermal (rat)
	Isostearamide MIPA	genotox – in vitro; carcinogenicity – dermal (mouse)
amides, C12-18 and C18-unsatd. N-(hydroxyethyl)	Cocamide MIPA	short-term oral
amides, C12-18 (even-numbered) and C18-unsatd., N,N-bis(hydroxyethyl)	Cocamide MIPA; Isostearamide MIPA	DART - oral

Concentration of Use by FDA Product Category – Alkyl Amide MIPA Ingredients*

Lauramide MIPA
Cocamide MIPA
Coconut Oil MIPA Amides
Hydroxyethyl Stearamide-MIPA
Isostearamide MIPA
Linoleamide MIPA
Myristamide MIPA
Oleamide MIPA
Palmamide MIPA
Palm Kernelamide MIPA
Ricinoleamide MIPA
Stearamide MIPA
MIPA-Myristate

Ingredient	Product Category	Maximum Concentration of Use
Lauramide MIPA	Shampoos (noncoloring)	2%
Lauramide MIPA	Bath soaps and detergents	4.8%
Lauramide MIPA	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	3%
Cocamide MIPA	Bubble baths	2%
Cocamide MIPA	Other bath preparations	1.5%
Cocamide MIPA	Shampoos (noncoloring)	1.3-3.7%
Cocamide MIPA	Tonics, dressings and other hair grooming aids	0.12%
Cocamide MIPA	Hair bleaches	12%
Cocamide MIPA	Bath soaps and detergents	1.1-4%
Cocamide MIPA	Other personal cleanliness products	3%
Cocamide MIPA	Skin cleansing (cold creams, cleansing lotions liquids and pads)	0.1-3.5%
Cocamide MIPA	Body and hand products Not spray, rinse-off	1%
Cocamide MIPA	Other skin care preparations Rinse-off	1.5%
Oleamide MIPA	Face and neck products Not spray	0.4%

*Ingredients included in the title of the table but not found in the table were included in the concentration of use survey, but no uses were reported.

Information collected in 2017
Table prepared: September 27, 2017
Updated August 29, 2019: Cocamide MIPA body and hand product is a rinse-off product

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Memorandum

To: CIR Expert Panel Members and Liaisons
From: Priya Cherian
Scientific Writer/Analyst
Date: September 6, 2019
Subject: Wave 2 Data on Brown Algae

Since the draft final report was issued at mail date, the Council has provided additional information regarding ingredients in the Brown Algae report (*broalg092019wave2_pcpc*). This information includes the manufacturing process, an Ames test, and a cutaneous sensitization test on a trade name mixture containing 1-3% Cystoseira Compressa Extract and 97-99% amilopectine glycerine water. Details regarding this information are presented below. In addition, a study was provided noting that the species *Cystoseria tamariscifolia*, *Cystoseira compressa*, and *Cystoseira baccata* are used as foods in Portugal.[1]

In order to manufacture a trade name mixture consisting of 1-3% Cystoseira Compressa Extract, the algae (*Cystoseira compressa*) is placed in a solvent (water and glycerin), macerated, extracted, and concentrated.[2] The mixture is then combined with preservatives and filtrated. The resulting extract is then injected with a pregel consisting of amilopectine glycerine water.

An Ames test was performed on a trade name mixture consisting of 1-3% Cystoseira Compressa Extract and 97-99% amilopectine glycerine water at doses of 3.25 to 51.95 mg/plate.[3] Five strains of *Salmonella typhimurium* (TA-1535, TA-1537, TA-98, TA-100, and TA-102) were exposed to the test substance with and without metabolic activation. The test substance was considered to be non-mutagenic.

A human repeat insult patch test (HRIPT) was performed on 54 volunteers using a test substance consisting of 1-3% Cystoseira Compressa Extract and 97-99% amilopectine glycerine water.[4] The product, tested at 25%, was applied to the skin, under an occlusive patch, for a total 9 times during the induction phase. After a rest period of 15 days, a challenge patch was applied for 48 hours. No allergic reaction was observed.

An updated table presenting each ingredient, as well as a notation of the presence or absence of systemic toxicity data (repeated dose studies or use in food/as a GRAS substance) and sensitization data, has also been included. This table can be found as *broalg092019wave2_data1*. An alphabetized version of this list has also been included (*broalg092019wave2_data2*).

1. Vizetto-Duarte C, Custódio L, and Barreira L. Proximate biochemical composition and mineral content of edible species from the genus *Cystoseira* in Portugal. *Botanica Marina*. 2016;59(4)

2. Anonymous. 2019. Manufacturing process: Cystoseira Compressa Extract (trade name mixture containing 1-3% Cystoseira Compressa Extract). Unpublished data submitted by Personal Care Products Council on August 29, 2019.

3. Anonymous. 2011. Genetic mutation bacteria in vitro test (Ames Test) (trade name mixture containing 1-3% Cystoseira Compressa Extract). Unpublished data submitted by Personal Care Products Council on August 29, 2019.

4. Anonymous. 2011. Cutaneous sensitization test (trade name mixture containing 1-3% Cystoseira Compressa Extract). Unpublished data submitted by Personal Care Products Council on August 29, 2019.

Ingredient	GRAS	Food	Tox	Sensitization
Alaria Esculenta Extract		✓		✓
Ascophyllum Nodosum			✓ - 4 week oral	✓
Ascophyllum Nodosum Extract		✓	✓ - 4 week oral	✓
Ascophyllum Nodosum Powder		✓		✓
Cystoseira Baccata Extract (synonymous with Phyllacantha Fibrosa)		✓		✓
Cystoseira Compressa Extract		✓		✓
Cystoseira Compressa Powder		✓		✓
Cystoseira Tamariscifolia Extract		✓		✓
Fucus Spiralis Extract		✓		✓
Fucus Vesiculosus		✓		✓
Fucus Vesiculosus Extract		✓	✓ - 4 week oral	✓
Fucus Vesiculosus Powder		✓		✓
Himanthalia Elongata Extract		✓		✓
Himanthalia Elongata Powder		✓		✓
Hydrolyzed Fucus Vesiculosus Extract		✓	✓ - 4 wk oral	✓
Hydrolyzed Fucus Vesiculosus Protein		✓	✓ - 4 wk oral	✓
Laminaria Diabolica Extract (synonymous with Laminaria Japonica Extract, Laminaria Ochroleuca Extract, and Saccharina Japonica Extract)	✓	✓	✓ - 6 week oral	✓
Laminaria Digitata Extract	✓	✓		✓
Laminaria Digitata Powder	✓			✓
Laminaria Japonica Extract (synonymous with Laminaria Diabolica Extract, Laminaria Ochroleuca Extract, and Saccharina Japonica Extract)	✓	✓	✓ - 6 week oral	✓
Laminaria Japonica Powder	✓	✓	✓ - lifetime oral	✓
Laminaria Ochroleuca Extract (synonymous with Laminaria Diabolica Extract, Laminaria Japonica Extract, and Saccharina Japonica Extract)	✓	✓	✓ - 6 week oral	✓
Laminaria Saccharina Extract	✓	✓		✓
Macrocystis Pyrifera (Kelp)	✓	✓		✓
Macrocystis Pyrifera (Kelp) Blade/Pneumatocyst/Stipe Juice Extract	✓	✓		✓
Macrocystis Pyrifera (Kelp) Extract	✓	✓		✓
Macrocystis Pyrifera (Kelp) Juice	✓	✓		✓
Macrocystis Pyrifera (Kelp) Protein	✓	✓		✓
Phyllacantha Fibrosa Extract (synonymous with Cystoseira Baccata Extract)		✓		✓

Saccharina Japonica Extract (synonymous with Laminaria Diabolica Extract, Laminaria Japonica Extract, and Laminaria Ochroleuca Extract)	✓	✓	✓ - 6 week oral	✓
Sargassum Filipendula Extract		✓		✓
Sargassum Muticum Extract		✓		✓
Undaria Pinnatifida Cell Culture Extract	✓	✓		✓
Undaria Pinnatifida Extract	✓	✓	✓ - 32 week oral	✓
Undaria Pinnatifida Leaf/Stem Extract	✓	✓		✓
Undaria Pinnatifida Powder	✓	✓	✓ - 36 week oral	✓
Undaria Pinnatifida Root Powder	✓	✓		✓
Agarum Cribrosum Extract				✓
Cystoseira Amentacea/Caespitosa/Branchycarpa Extract				✓
Dictyopteris Polypodiodes Extract				✓
Halidrys Siliquosa Extract				✓
Halopteris Scoparia Extract (synonymous with Sphacelaria Scoparia Extract)				✓
Pelvetia Canaliculata Extract				✓
Sphacelaria Scoparia Extract (synonymous with Halopteris Scoparia Extract)				✓
Cladosiphon Okamuranus Extract		✓	✓ - 3 month oral	
Ecklonia Cava Extract		✓	✓ - 13 week oral	
Ecklonia Cava Water		✓		
Eisenia Arborea Extract		✓		
Fucus Serratus Extract		✓		
Hizikia Fusiforme Extract (synonymous with Sargassum Fusiforme Extract)	✓	✓		
Hizikia Fusiformis Water	✓	✓		
Hizikia Fusiformis Callus Culture Extract	✓	✓		
Hydrolyzed Ecklonia Cava Extract		✓	✓ - 13 wk oral	
Laminaria Cloustoni Extract (synonymous with Laminaria Hyperborea Extract)	✓			
Laminaria Hyperborea Extract (synonymous with Laminaria Cloustoni Extract)	✓			
Laminaria Longissima Extract	✓	✓		
Nereocystis Leutkeana Extract	✓			
Saccharina Angustata Extract		✓		
Saccharina Longicruris Extract		✓		

Sargassum Fulvellum Extract		✓		
Sargassum Fusiforme Extract (synonymous with Hizikia Fusiforme Extract)	✓	✓		
Sargassum Glaucescens Extract		✓		
Sargassum Horneri Extract		✓		
Sargassum Pallidum Extract		✓		
Sargassum Siliquastrum Extract		✓		
Sargassum Thunbergii Extract		✓		
Sargassum Vulgare Extract		✓		
Undaria Peterseniana Extract		✓		

For the GRAS and Food column, as seen in the report, specific ingredient types were not reported, however, larger ingredient groups were reported. For example, Laminaria digitata since considered GRAS, it was assumed that the related ingredients, Laminaria Digitata Extract and Laminaria Digitata Powder, would also be considered GRAS. Ingredients in green have both GRAS/food/tox and sensitization data.

Remaining Ingredients

Cladosiphon Novae-Caledoniae Extract
Cystoseira Balearica Extract (synonymous with Cystoseira Caespitosa Extract)
Cystoseira Caespitosa Extract (synonymous with Cystoseira Balearica Extract)
Dictyota Coriacea Extract
Durvillaea Antarctica Extract
Ecklonia Kurome Extract
Ecklonia Kurome Powder
Ecklonia/Laminaria Extract
Ecklonia Maxima Extract
Ecklonia Maxima Powder
Ecklonia Radiata Extract
Lessonia Nigrescens Extract
Lessonia Nigrescens Powder
Pelvetia Siliquosa Extract

Ingredient	GRAS	Food	Tox	Sensitization data
Agarum Cribrosum Extract				✓
Alaria Esculenta Extract		✓		✓
Ascophyllum Nodosum			✓ - 4 week oral	✓
Ascophyllum Nodosum Extract		✓	✓ - 4 week oral	✓
Ascophyllum Nodosum Powder		✓		✓
Cladosiphon Okamuranus Extract		✓	✓ - 3 month oral	
Cystoseira Amentacea/Caespitosa/Branchycarpa Extract				✓
Cystoseira Baccata Extract (synonymous with Phyllacantha Fibrosa)		✓		✓
Cystoseira Compressa Extract		✓		✓
Cystoseira Compressa Powder		✓		✓
Cystoseira Tamariscifolia Extract		✓		✓
Dictyopteris Polypodiodes Extract				✓
Ecklonia Cava Extract		✓	✓ - 13 week oral	
Ecklonia Cava Water		✓		
Eisenia Arborea Extract		✓		
Fucus Serratus Extract		✓		
Fucus Spiralis Extract		✓		✓
Fucus Vesiculosus		✓		✓
Fucus Vesiculosus Extract		✓	✓ - 4 week oral	✓
Fucus Vesiculosus Powder		✓		✓
Halidrys Siliquosa Extract				✓
Halopteris Scoparia Extract (synonymous with Sphacelaria Scoparia Extract)				✓
Himanthalia Elongata Extract		✓		✓
Himanthalia Elongata Powder		✓		✓
Hizikia Fusiforme Extract (synonymous with Sargassum Fusiforme Extract)	✓	✓		
Hizikia Fusiformis Water	✓	✓		
Hizikia Fusiformis Callus Culture Extract	✓	✓		
Hydrolyzed Ecklonia Cava Extract		✓	✓ - 13 wk oral	
Hydrolyzed Fucus Vesiculosus Extract		✓	✓ - 4 wk oral	✓

Hydrolyzed Fucus Vesiculosus Protein		✓	✓ - 4 wk oral	✓
Laminaria Cloustoni Extract (synonymous with Laminaria Hyperborea Extract)	✓			
Laminaria Diabolica Extract (synonymous with Laminaria Japonica Extract, Laminaria Ochroleuca Extract, and Saccharina Japonica Extract)	✓	✓	✓ - 6 week oral	✓
Laminaria Digitata Extract	✓	✓		✓
Laminaria Digitata Powder	✓			✓
Laminaria Hyperborea Extract (synonymous with Laminaria Cloustoni Extract)	✓			
Laminaria Japonica Extract (synonymous with Laminaria Diabolica Extract, Laminaria Ochroleuca Extract, and Saccharina Japonica Extract)	✓	✓	✓ - 6 week oral	✓
Laminaria Japonica Powder	✓	✓	✓ - lifetime oral	✓
Laminaria Longissima Extract	✓	✓		
Laminaria Ochroleuca Extract (synonymous with Laminaria Diabolica Extract, Laminaria Japonica Extract, and Saccharina Japonica Extract)	✓	✓	✓ - 6 week oral	✓
Laminaria Saccharina Extract	✓	✓		✓
Macrocystis Pyrifera (Kelp)	✓	✓		✓
Macrocystis Pyrifera (Kelp) Blade/Pneumatocyst/Stipe Juice Extract	✓	✓		✓
Macrocystis Pyrifera (Kelp) Extract	✓	✓		✓
Macrocystis Pyrifera (Kelp) Juice	✓	✓		✓
Macrocystis Pyrifera (Kelp) Protein	✓	✓		✓
Nereocystis Leutkeana Extract	✓			
Pelvetia Canaliculata Extract				✓
Phyllacantha Fibrosa Extract (synonymous with Cystoseira Baccata Extract)		✓		✓
Saccharina Angustata Extract		✓		
Saccharina Japonica Extract (synonymous with Laminaria Diabolica Extract, Laminaria Japonica Extract, and Laminaria Ochroleuca Extract)	✓	✓	✓ - 6 week oral	✓
Saccharina Longicruris Extract		✓		
Sargassum Filipendula Extract		✓		✓
Sargassum Fulvellum Extract		✓		

Sargassum Fusiforme Extract (synonymous with Hizikia Fusiforme Extract)	✓	✓		
Sargassum Glaucescens Extract		✓		
Sargassum Horneri Extract		✓		
Sargassum Muticum Extract		✓		✓
Sargassum Pallidum Extract		✓		
Sargassum Siliquastrum Extract		✓		
Sargassum Thunbergii Extract		✓		
Sargassum Vulgare Extract		✓		
Sphacelaria Scoparia Extract (synonymous with Halopteris Scoparia Extract)				✓
Undaria Peterseniana Extract		✓		
Undaria Pinnatifida Cell Culture Extract	✓	✓		✓
Undaria Pinnatifida Extract	✓	✓	✓ - 32 week oral	✓
Undaria Pinnatifida Leaf/Stem Extract	✓	✓		✓
Undaria Pinnatifida Powder	✓	✓	✓ - 36 week oral	✓
Undaria Pinnatifida Root Powder	✓	✓		✓

For the GRAS and Food column, as seen in the report, specific ingredient types were not reported, however, larger ingredient groups were reported. For example, Laminaria digitata since considered GRAS, it was assumed that the related ingredients, Laminaria Digitata Extract and Laminaria Digitata Powder, would also be considered GRAS. Ingredients in green have both GRAS/food/tox and sensitization data.

Remaining Ingredients

Cladosiphon Novae-Caledoniae Extract
Cystoseira Balearica Extract (synonymous with Cystoseira Caespitosa Extract)
Cystoseira Caespitosa Extract (synonymous with Cystoseira Balearica Extract)
Dictyota Coriacea Extract
Durvillaea Antarctica Extract
Ecklonia Kurome Extract
Ecklonia Kurome Powder
Ecklonia/Laminaria Extract
Ecklonia Maxima Extract
Ecklonia Maxima Powder
Ecklonia Radiata Extract
Lessonia Nigrescens Extract
Lessonia Nigrescens Powder
Pelvetia Siliquosa Extract

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review (CIR)

FROM: Carol Eisenmann, Ph.D.
Personal Care Products Council

DATE: August 29, 2019

SUBJECT: Cystoseira Compressa Extract

Anonymous. 2019. Manufacturing process: Cystoseira Compressa Extract (trade name mixture containing 1-3% Cystoseira Compressa Extract).

Anonymous. 2011. Genetic mutation bacteria in vitro test (Ames Test) (trade name mixture containing 1-3% Cystoseira Compressa Extract).

Anonymous. 2011. Cutaneous sensitization test (trade name mixture containing 1-3% Cystoseira Compressa Extract).

To support lack of systemic toxicity potential, the following published paper, which indicates *Cystoseira compressa* and other *Cystoseira* species are edible, should be obtained and added to the CIR report. (abstract attached)

Vizetto-Duarte C, Custódio L, Barreira L. 2016. Proximate biochemical composition and mineral content of edible species from the genus *Cystoseira* in Portugal. Botanica Marina, 59(4) (published Online: 2016-07-22) DOI: https://doi.org/10.1515/bot-2016-0014.

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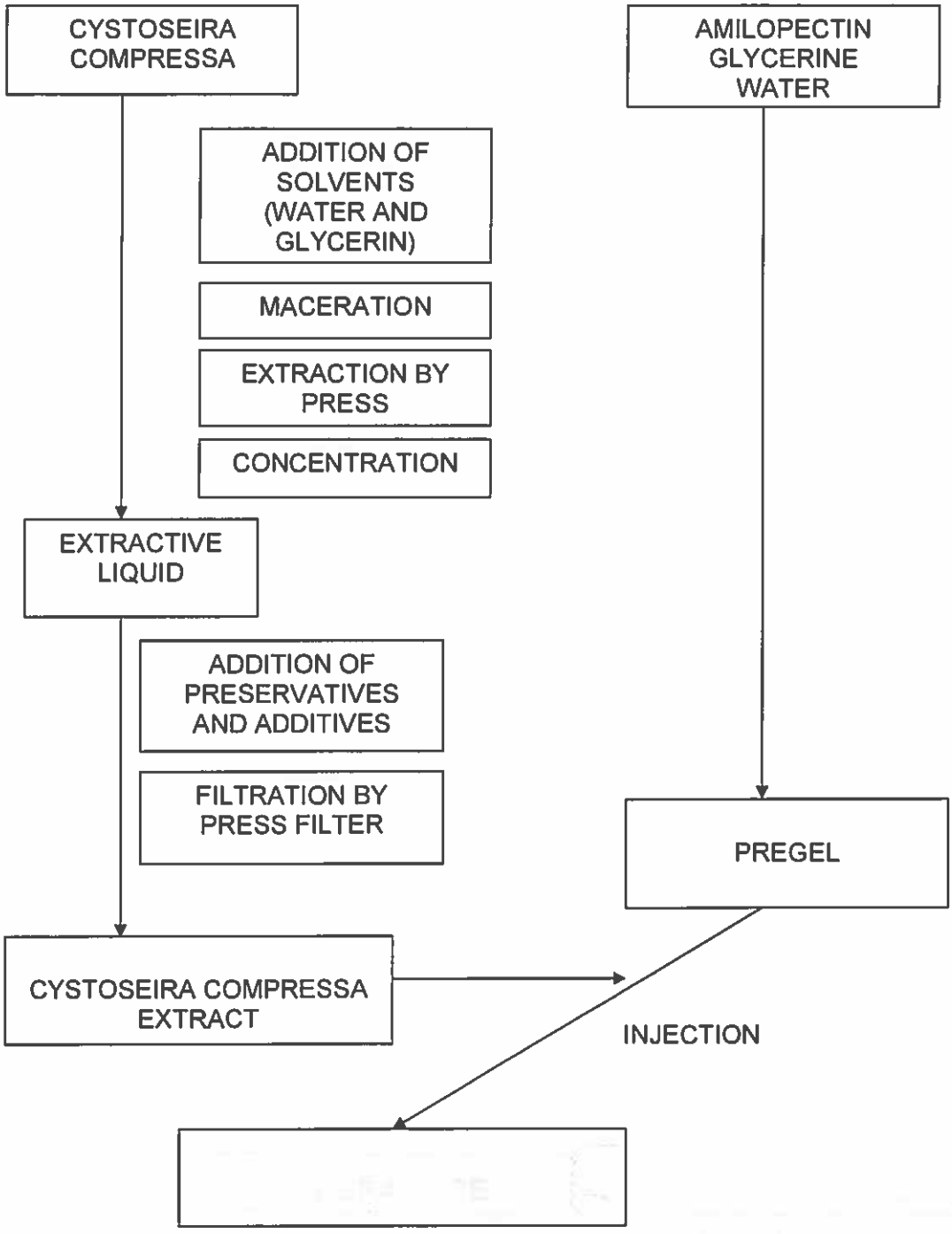
[redacted]

MANUFACTURING PROCESS

Cystoseira Compressa Extract



The trade name mixture contains

1-3% Cystoseira Compressa Extract

STUDY REPORT

FOR.04.06 rev.3

Trade name mixture Containing 1-3% Cystoseira Compressa Extract

STUDY AND METHOD

Genic Mutation Bacteria in vitro Test (Ames Test).

This test uses five strains of Salmonella typhimurium (TA-1535, TA-1537, TA-98, TA-100 and TA-102) to detect point mutations, which involve substitution, addition or deletion of one or a few DNA base pairs. The principle of this bacterial reverse mutation test is that it detects revertant colonies that show a mutation due to the presence of the product, both in the presence and absence of an appropriate metabolic activation system (S-9). The mixing S9 consisted of induced enzymatic systems contained in the post-microsomial fraction (S9) of the rat liver and of the cofactors necessary for their function.

This study has been designated to comply with the following guidelines: OECD Guideline, nº 471, adopted on 21st July 1997; Commission Directive 200/32/EC of 19 May 2000 (Official Journal of the European Communities, 8.6.2000, L 136/1). This study was conducted in compliance with the Good Laboratory Practices.

PRODUCT

was tested at five dose levels between 3.25 and 51.95 mg/plate.

TEST FACILITIES

The study was carried out in the laboratories of Analysis Service and Microbiology, Department of Genetic and Microbiology, Autonomous University of Barcelona, Spain.

STUDY DATE

March 2011

RESULTS

No significant increase in the number of revertants was noted in any of the five tester strains.

CONCLUSION

In the assay conditions, the product does not show any evidence of mutagenicity.

STUDY REPORT

FOR.04.06 rev.3

Trade name mixture containing 1-3% Cystoseira Compressa Extract

STUDY AND METHOD

Cutaneous Sensitisation Test. (Marzulll and Maibach's Method: Human Repeated Insult Patch Test)
The test is based on the occlusive application of the product on 54 volunteers and consists of the following phases: Induction Stage (9 consecutive applications), Rest Period (15 days) and Challenge Stage (patch of 48 hours). Visual evaluatlon of the dermal reactions.

The skln compatibility and possible Irritation reactions are evaluated by the macroscopic examination of skin after removal of each patch of the Induction period. The test raw material could therefore have very good, good, moderate or bad skin compatibility.

The allergenic potential is evaluated by the macroscopic examination of reactions after removal of the patches of the challenge period. The interpretation of the results was based on the allergenicity evaluation scale established by the ICDRG (International Contact Dermatitis Research Group) and took lnto account the visible reactions (clinical signs) and the possible reactions appeared on the control site.

This study was conducted in compliance with the Good Clinlcal Practices.

PRODUCT AND CONCENTRATION

Product tested at 25%

TESTING FACILITIES

The study was carried out In the laboratories of EVIC Romania (15, Constantin Boslanu Street, 040505-Bucharest, Romania)

STUDY DATES

Start of the experlments: February 21^{sl}, 2011
End of the experiments: April 02nd, 2011

RESULTS

- Induction phase. Type of reactivity: None. Number and percentage of reactive volunteers: 0 and 0%
- Challenge phase. Type of reactivity: None. Number and percentage of reactive volunteers: 0 and 0%

CONCLUSION

Under the experimental conditions adopted in the repeated applications, under occlusive patch, induced no reaction of irritation and has very good skin compatibility. Moreover, no allergic reaction was detected. Thus, the product may be considered as hypoallergenic, under thls specific context.

DE GRUYTER Botanica Marina

Volume 59, Issue 4 < Previous Article

Next Article >

Proximate biochemical composition and mineral content of edible species from the genus *Cystoseira* in Portugal

Catarina Vizetto-Duarte / Luísa Custódio / Luísa Barreira / Manuela Moreira da Silva / Amélia P. Rauter / Fernando Albericio / João Varela

Published Online: 2016-07-22 | **DOI**: https://doi.org/10.1515/bot-2016-0014

Abstract

Macroalgae are valuable resources for human consumption in many countries. This work reports for the first time a comparative evaluation of the nutritional properties of five edible macroalgae from the genus *Cystoseira*, namely *C. humilis*, *C. tamariscifolia*, *C. nodicaulis*, *C. compressa* and *C. baccata*. For this purpose, their proximate composition was determined in terms of moisture, ash, and total contents of protein, lipids, carbohydrates and mineral profile. *Cystoseira tamariscifolia* and *C. baccata* were the species that in general had the higher ash, protein and lipid contents, while the highest levels of moisture and total carbohydrates were detected in *C. nodicaulis* and *C. compressa*. *Cystoseira* species had also high amounts of minerals, especially of potassium, calcium and iron, and a favorable Na/K ratio. The present study shows that *Cystoseira* has a balanced nutritional composition, suitable for human consumption, and that its intake can contribute to a healthy and well-balanced diet.

Keywords: brown algae; Cystoseira; minerals; nutritional profile; proximate composition

References

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Memorandum

To: CIR Expert Panel Members and Liaisons
From: Wilbur Johnson, Jr.
Senior Scientific Analyst
Date: September 6, 2019
Subject: Wave 2 Data on Capryloyl Salicylic Acid

In vitro phototoxicity data on Capryloyl Salicylic Acid (*capryl092019data1*) that were received from the Council this month are attached for the Panel's review. These data were submitted in response to the insufficient data announcement (IDA) that was issued at the April Panel meeting. To date, there has been no response to the Panel's request for impurities data, the remaining data request in the IDA.

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Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review (CIR)

FROM: Carol Eisenmann, Ph.D.
Personal Care Products Council

DATE: September 4, 2019

SUBJECT: Capryloyl Salicylic Acid

Anonymous. 2000. Evaluation of *in vitro* phototoxicity on Balb/c3T3 fibroblasts using the neutral red uptake (NRU) Assay (Capryloyl Salicylic Acid).

Final Report

[redacted] Evaluation of *in vitro* Phototoxicity on Balb/c 3T3 fibroblasts using the Neutral Red Uptake (NRU) Assay

Capryloyl Salicylic Acid

[redacted]

June 2000

STUDY DIRECTOR AUTHENTICATION AND GLP COMPLIANCE STATEMENT

[redacted] Evaluation of *in vitro* Phototoxicity on Balb/c 3T3 fibroblasts using the Neutral Red Uptake (NRU) Assay

I, the undersigned, hereby declare that the work described in this report was performed under my supervision, as Study Director, and that the report provides a true and accurate record of the results obtained.

The study was performed in accordance with the agreed protocol and with [redacted] unless otherwise stated, and the study objectives were achieved. The study was conducted in compliance with the United Kingdom Statutory Instrument 1999 No. 3106, The Good Laboratory Practice Regulations 1999 and the OECD Principles on Good Laboratory Practice (revised 1997, issued January 1998) ENV/MC/CHEM(98)17. With the exception of the curve fitting program Ratefit97.XLS V2. However, this program used the same formulae as validated program Ratefit97.XLS V1.

[redacted]

Study Director

[redacted]

REVIEWING SCIENTIST'S STATEMENT

[redacted] Evaluation of *in vitro* Phototoxicity on Balb/c 3T3 fibroblasts using the Neutral Red Uptake (NRU) Assay

I, the undersigned, hereby declare that I have reviewed this report in conjunction with the Study Director and that the interpretation and presentation of the data in the report are consistent with the results obtained.

[redacted]

[redacted]: 15 June 2000

[redacted]

RESPONSIBLE PERSONNEL

Vice President, Consultancy and Regulatory Services	[redacted]
Head of Genetic and Molecular Toxicology	[redacted]
Head of Quality Assurance	[redacted]
Study Director	[redacted]
Experimental Officer	[redacted]

* The person responsible for Quality Assurance up to 10 May 2000 was [redacted], Head of Quality Assurance. From 11 May 2000 this responsibility transferred to [redacted], Vice President of Consultancy and Regulatory Services

Sponsor's Monitor	[redacted]
Date of initiation of study	14 March 2000
Date of Sponsor's approval of study	16 March 2000
Date of start of experimental work	30 March 2000
Date of completion of experimental work	11 May 2000
Date of study completion	15 June 2000

QUALITY ASSURANCE RECORD AND AUTHENTICATION STATEMENT

[redacted] Evaluation of *in vitro* Phototoxicity on Balb/c 3T3 fibroblasts using the Neutral Red Uptake (NRU) Assay

The study described in this report was subject to audit by the independent Quality Assurance Department as indicated below. The findings of each audit were reported to the Study Director and management as prescribed by Standard Operating Procedures.

The report audit was designed to confirm that the methods described and results incorporated in the report accurately reflect the raw data produced during the study.

Inspection programme	Inspection date	Report date
Protocol review	16 March 2000	16 March 2000
Lamp calibration	30 March 2000	30 March 2000
Data review	June 2000	2 June 2000
Draft study report	June 2000	2 June 2000

[redacted]

[redacted]

Section Head, Quality Assurance

15 June 2000

Date:

ARCHIVE STATEMENT

All primary data, or authenticated copies thereof, specimens and the final report will be retained in the [redacted] archives for one year after the submission of the final report. At this time the Sponsor will be contacted to determine whether data should be returned, retained or destroyed on their behalf.

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1 SUMMARY

[redacted] was assayed for phototoxicity to Balb/c 3T3 fibroblast cells using the neutral red uptake (NRU) assay.

Balb/c 3T3 fibroblast cells seeded into 96 well microtitre plates were treated with a range of concentrations of the test article in two independent experiments. Doses tested in Experiment 1 ranged from 0.316 to 1000 µg/mL in the absence of UV light and from 0.0316 to 100 µg/mL in the presence of UV light. Doses tested in Experiment 2 ranged from 5 to 100 µg/mL in the absence of UV light and from 1.25 to 30 µg/mL in the presence of UV light. Positive control (chlorpromazine) and solvent control (1% v/v DMSO) treatments were also included. Test plates were exposed to 5 J/cm^2 Ultraviolet A (UVA) light. A second set of plates was kept in the dark. Cytotoxicity was assessed by the NRU assay. Where possible, Inhibitory Concentrations 50% (IC_{50}) values were calculated for the positive control and test article, and a Photo Irritation Factor (PIF) value (IC_{50} absence UVA / IC_{50} presence UVA) was calculated. Two experiments were performed. The following table summarises the results:

Experiment 1

Test Article	IC_{50} absence of UVA (µg/mL)	IC_{50} presence of UVA (µg/mL)	PIF Value
[redacted]	66.5	16.7	4
Chlorpromazine	38.4	3.2	12*

Experiment 2

Test Article	IC_{50} absence of UVA (µg/mL)	IC_{50} presence of UVA (µg/mL)	PIF Value
[redacted]	51.4	20-30	2.6-1.7
Chlorpromazine	29.0	1.4	21*

* = PIF > 6, positive control response was acceptable

Negative and positive controls gave acceptable responses and the study was considered valid.

When [redacted] was tested in this *in vitro* phototoxicity assay, dose-related decreases in survival were obtained in the presence and absence of UVA light in two independent experiments. However, the PIF value obtained for [redacted] was less than 5 in both experiments. Accordingly [redacted] did not fulfil the criteria for a test article to be considered an *in vitro* phototoxin in this test system.

It is concluded that, under the conditions employed in this study, [redacted] was not phototoxic in this *in vitro* test system, according to the proposed OECD guideline evaluation criteria.

2 INTRODUCTION

The *in vitro* 3T3 Neutral Red Uptake (NRU) phototoxicity test is designed to identify the phototoxic potential of a test substance which may be likely to arise in association with exposure to Ultraviolet A (UVA) and visible light.

Phototoxicity, or photo-irritation, is a toxic response which is elicited after the initial exposure of skin to certain chemicals followed by subsequent exposure to light, or which may be induced by skin irradiation after systemic administration of a chemical.

The mechanisms of phototoxic reaction may include the formation of free radicals or oxygen singlets, the covalent binding to DNA in skin proteins and/or the formation of toxic photo-products. All of these mechanisms may result in cell damage which can be assessed in this assay.

The assay is a rapid sensitive and economical *in vitro* screen. After exposure of the test article and cells, to UVA, toxicity is measured by NRU. Neutral red is a weak cationic dye which may penetrate cell membranes and accumulate in the lysosomes of viable cells (1,2).

The objective of this study was to evaluate whether the test substance induces an *in vitro* phototoxic effect when applied to Balb/c 3T3 fibroblasts using the Neutral Red Uptake (NRU) assay as the endpoint. The study was performed in accordance with OECD Guideline For Testing Of Chemicals Draft Proposal for a New Guideline, *In Vitro* 3T3 NRU phototoxicity test (Draft Document, February 2000).

This study was performed according to the protocol and one amendment.

3 MATERIALS

3.1 Test material

The test material was [redacted] batch number [redacted]. Its appearance was as bright white to slightly pink scales. The test article was received from the Sponsor on 1 December 1999 and stored at room temperature in the dark. Determination of the stability and characteristics of the test material, where defined in GLP regulations, were the responsibility of the Sponsor. The Sponsor's Certificate of Analysis is included in Appendix 3. The purity of [redacted] was ~ 100%. The Sponsor did not supply an expiry date.

Immediately prior to assay, test article solutions were prepared under yellow light in sterile anhydrous analytical grade dimethyl sulphoxide (DMSO). Further dilutions were prepared with DMSO. For treatment, 1% (v/v) additions were made in phosphate buffered saline (PBS). Formulations were protected from light and used as follows, within approximately 5 hours of preparation:

Experiment	Absence UVA Concentration of treatment solution (mg/mL)	Absence UVA Final concentration (μg/mL)	Presence UVA Concentration of treatment solution (mg/mL)	Presence UVA Final concentration (μg/mL)
1	0.0316	0.316	0.00316	0.0316
	0.1	1	0.01	0.1
	0.316	3.16	0.0316	0.316
	1.0	10	0.1	1
	3.16	31.6	0.316	3.16
	10.0	100	1.0	10
	31.6	316	3.16	31.6
	100	1000	10.0	100
2	0.5	5	0.125	1.25
	1.0	10	0.25	2.5
	2.0	20	0.5	5
	4.0	40	1.0	10
	6.0	60	1.25	12.5
	8.0	80	1.5	15
	10.0	100	1.75	17.5
			2.0	20
			3.0	30

It may be noted that two other experiments were initially performed. However, due to problems with toxicity in the presence of UV and variability in the data, data from these experiments were not considered to be valid and are not reported.

3.2 Cell line

Balb/c 3T3 mouse fibroblast cells were provided by the European Collection of Cell Cultures (Salisbury UK). These were a new cell stock and differed from the supply originally stated in the protocol (American Tissue Culture Collection). This minor deviation from protocol did not prejudice the validity of the study in any way. These cells were supplied mycoplasma free.

Frozen stocks were stored in liquid nitrogen. For assay, at least one vial was removed from freeze and grown in tissue culture medium (Dulbecco's Modified Eagle Medium supplemented with 10% newborn calf serum [DMEM complete]). The cells were maintained at 37°C +/- 1°C in an atmosphere of 5% CO_2 in air and were passaged regularly to avoid overgrowth. The passage number of the cells used was lower than 100.

3.3 Controls

The negative control consisted of DMSO diluted in PBS to the same level as test article treatment solutions (1% v/v). The positive control was Chlorpromazine (supplied by Sigma Aldrich Chemical Company, Gillingham UK) freshly prepared in PBS at final treatment concentrations of 1, 10, 100 and 1000 µg/mL for treatment in the absence of UVA and 0.1, 1, 10 and 100 µg/mL for treatment in the presence of UVA.

3.4 Light source

An Heraeus Suntest CPS Solar lamp, fitted with a filter against UV-B emission (Alplas Technologies), was used to produce UV-A light. A UV meter was used to calibrate the lamp for UV emission and intensity prior to UV exposure of the cells.

4 METHODS

4.1 Cell culture preparation

Balb/c 3T3 mouse fibroblasts were maintained in DMEM complete with appropriate re-feeding with medium and subculturing until required for assay treatment. Cultures were incubated at 37°C +/- 1°C in a humidified atmosphere of 5% CO_2 in air.

Near confluent cultures were trypsinized and resuspended in supplemented DMEM. The cell number in the suspension prepared was determined using an haemocytometer. Aliquots (100 μL) of supplemented DMEM were dispensed into all peripheral wells of four 96-well plates. The first column of each plate was used as the assay blank. The cell suspension was diluted to give a final concentration of 1×10^5 cells/ mL and 100 μL was pipetted into the appropriate number of wells (10^4 cells/ well). Two plates were set up for the test article and the positive control. 6-12 wells were seeded on each plate for negative controls, and 6 wells were seeded for each dose of test article or positive control. Plates were incubated at 37°C +/- 1°C for 1 day in a humidified atmosphere of 5% (v/v) CO_2 in air to achieve approximately half-confluent monolayers.

4.2 Treatment

Final treatment concentrations in PBS were prepared as detailed in Section 3.1 for treatments in the absence and presence of UVA. Media was removed from appropriate wells of the 96 well plates, wells were washed with 100 µL PBS, then 100 µL of test article, solvent or positive control solution was added to appropriate wells. Plates were labelled to distinguish cultures to be tested in the presence of UVA (+UVA) and those to be tested in the absence of UVA (-UVA). All plates were incubated at 37°C +/- 1°C in the dark for 1 hour.

On completion of the 1 hour incubation, the +UVA plates were exposed to UVA for approximately 40 minutes to achieve a UVA dose of 5 J/cm^2. The -UVA plates were kept at room temperature in the dark for the same time period. Following treatment, test solutions were removed from the wells, cells were washed with 150 µL PBS and 200 µL DMEM complete was added to each well. The plates were then incubated at 37°C +/- 1°C in a humidified atmosphere of 5% CO_2 in air for 19 to 21 hours.

4.3 Evaluation of cytotoxic/ phototoxic effects

4.3.1 Microscopic evaluation

At the end of the incubation, cells were examined microscopically for evidence of cytotoxicity.

4.3.2 Quantitative evaluation of cytotoxic effects- NRU assay

Immediately following microscopic evaluation, medium was removed and the cells were washed with 150 μL of PBS. After removal of the PBS, 100 μL of neutral red solution (50 μg/mL in PBS) was added to each well. The plates were then incubated at 37°C +/- 1°C in a humidified atmosphere of 5% (v/v) CO_2 in air for 3 hours. After incubation, the neutral red solution was removed and the cells were washed twice with 100 μL PBS. PBS was removed and 100 μL of neutral red destain solution (1:50:49, acetic acid: ethanol: distilled water) was added. Plates were shaken for 10 minutes to allow extraction of neutral red from the cells.

Optical densities (OD) of each well were read on a THERMOmax plate reader, at a wavelength of 540 nm. Final OD's were expressed after subtracting the mean blank reading. Mean OD for each test article dose and controls were calculated, along with the coefficient of variance (CV) for the solvent control on each plate. Where possible, IC_{50} values were then calculated for the test article and the positive control, using a curve fitting program ([redacted] modified Excel spreadsheet [redacted] version 2.0).

Where possible, for the test article and the positive control, the Photo-Irritation Factor (PIF) was calculated. This was given by the following equation:

$$PIF = \frac{IC_{50} \text{ in the absence of UVA}}{IC_{50} \text{ in the presence of UVA}}$$

5 DATA

5.1 Acceptance criteria

The assay was considered valid if the following criteria were met:

1) In the negative controls there was a low variability in OD values between the treatment replicates (Coefficient of Variance (CV) < 30%),
2) The positive control showed a clear cytotoxic response in the presence of UVA, compared to the response seen in the absence of UVA, such that the PIF for the positive control was ≥ 6

5.2 Evaluation criteria

1) A test article was considered to be phototoxic in this assay if a marked decrease in cell viability (as measured by OD_{540} in the NRU) was seen in the presence of UVA, by comparison with the viability seen in the absence of UVA, such that PIF values of ≥ 5 were obtained.
2) A test article was considered to be non-phototoxic in this assay if there was no marked decrease in cell viability when cells were exposed to the test article in the absence and presence of UVA, or if similar toxic profiles were observed in the absence and presence of UVA (PIF < 5).

6 RESULTS

A summary of the results are presented in Table 1. The raw data, mean OD's and percentage relative viability (for each dose of test article and positive control) and the SD, mean and %CV for the negative controls are presented in Appendix 1. Where appropriate, data from curve fitting analysis are presented in Appendix 2. The assay acceptance criteria as detailed in Section 5.1 were met (see Table 1 and Appendix 1).

6.1 Limit doses

[redacted] was tested up to toxic doses in the absence and presence of UVA. Doses tested are detailed in Section 3.1 and Appendix 1.

6.2 Visual evaluation

Approximately 20 hours after the end of UVA exposure, cell monolayers were examined microscopically. No unexpected effects were seen, confluent monolayers observed in solvent controls and cytotoxicity observed in positive controls.

6.3 NRU assay and phototoxicity

When [redacted] was tested in this *in vitro* phototoxicity assay, dose-related decreases in survival were obtained in the presence and absence of UVA light in two independent experiments. However, the PIF value obtained for [redacted] was less than 5 in both experiments. Accordingly [redacted] did not fulfil the criteria for a test article to be considered an *in vitro* phototoxin in this test system.

It may be noted that in Experiment 2, no doses of extreme toxicity were available for analysis in the presence of UVA. Accordingly no toxicity curve could be drawn. The calculated IC_{50} value and PIF value is therefore a range from the highest dose that yielded more than 50% relative survival to the next dose that yielded less than 50% survival (doses of 20 and 30 µg/mL respectively [see Appendix 1]).

TABLE 1: Summary of Results

Experiment 1

Test Article	IC_{50} absence of UVA (µg/mL)	IC_{50} presence of UVA (µg/mL)	PIF Value
[redacted]	66.5	16.7	4
Chlorpromazine	38.4	3.2	12*

Experiment 2

Test Article	IC_{50} absence of UVA (µg/mL)	IC_{50} presence of UVA (µg/mL)	PIF Value
[redacted]	51.4	20-30	2.6-1.7
Chlorpromazine	29.0	1.4	21*

* = PIF > 6, positive control response was acceptable

Negative and positive controls gave acceptable responses and the study was considered valid.

7 CONCLUSION

It is concluded that, under the conditions employed in this study, [redacted] was not phototoxic in this *in vitro* test system, according to the proposed OECD guideline evaluation criteria (3).

Cosmetic Ingredient Review

Commitment & Credibility since 1976

Memorandum

To: CIR Expert Panel Members and Liaisons
From: Christina L. Burnett, Senior Scientific Analyst/Writer
Date: September 6, 2019
Subject: Draft Final Amended Safety Assessment of Amorphous Silica and Synthetically-Manufactured Amorphous Silicates – Wave 2

The Council has provided production information on Sodium Silver Aluminum Silicate, which you will find in this Wave 2 package (*silica092019wave2_data*). The information includes chemical characterization and method of manufacturing of Sodium Silver Aluminum Silicate.

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Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review (CIR)

FROM: Carol Eisenmann, Ph.D.
Personal Care Products Council

DATE: August 2, 2019

SUBJECT: Sodium Silver Aluminum Silicate

Anonymous. 2019. Product information: Sodium Silver Aluminum Silicate.

1620 L Street, N.W., Suite 1200 | Washington, D.C. 20036 | 202.331.1770 | 202.331.1969 (fax) | www.personalcarecouncil.org

Product Information (Ver-1. 30 July 2019)
INCI Name: Sodium Silver Aluminum Silicate

- INCI Monograph ID: 19713
- Definition: Sodium Silver Aluminum Silicate is the complex silicate obtained by the reaction of sodium silicate with sodium aluminate in an aqueous solution of sodium nitrate, sodium hydroxide and silver nitrate.

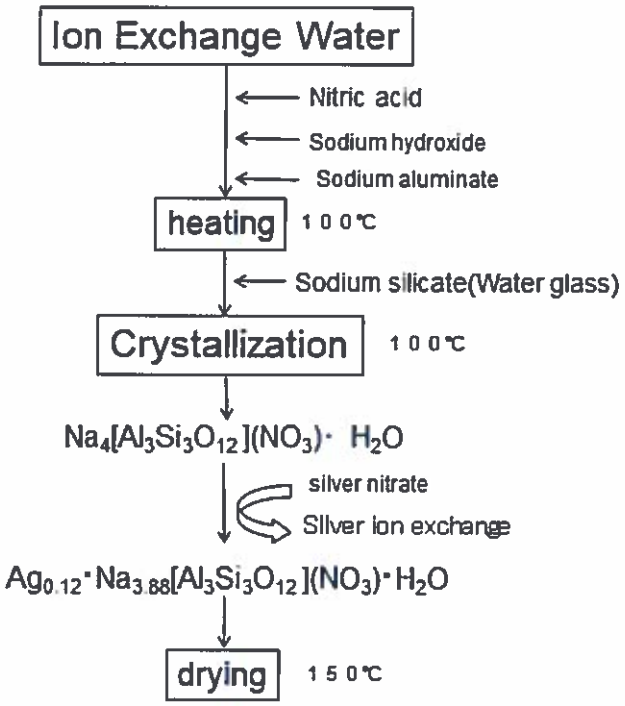
1. Chemical characterization

<Chemical structure>

$Ag_{0.12} \cdot Na_{3.88}[Al_3Si_3O_{12}](NO_3) \cdot H_2O$

$Ag_{0.12} \cdot Na_{3.88}[Al_3Si_3O_{12}](NO_3) \cdot H_2O$

2. Manufacturing Process



Cosmetic Ingredient Review

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Memorandum

To: CIR Expert Panel Members and Liaisons
From: Priya Cherian
Scientific Writer/Analyst
Date: September 6, 2019
Subject: Wave 2 Data on Xylitol

A summary of a human repeated insult patch test (HRIPT) on a product containing 0.115% Xylitol, that was received from the Council, is summarized below and attached (*xylito092019wave2_data1*) for the Panel's review.

An HRIPT involving a product containing 0.115% Xylitol was performed using 119 subjects.[1] During induction, the product was applied neat, under an occlusive patch for 48-72 h. The amount of material used for testing was not specified. This procedure was repeated for a total of 9 induction applications. The 9th application was followed by a 2-wk rest period, after which, the challenge phase was initiated. A challenge patch was applied to a new test site, and reactions were scored at 48 h and 96 h after patch application. Three individuals displayed low-level reactions (mild erythema) during the induction phase, and one individual displayed a low-level reaction in the challenge phase. The authors concluded that there was no evidence of sensitization to the product tested in this study.

1. Anonymous. 2019. Summary of an HRIPT of a product containing 0.115% Xylitol. Unpublished data submitted by the Personal Care Products Council on August 26, 2019.

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Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - Cosmetic Ingredient Review (CIR)

FROM: Carol Eisenmann, Ph.D.
Personal Care Products Council

DATE: August 26, 2019

SUBJECT: Xylitol

Anonymous. 2019. Summary of an HRIPT of a product containing 0.115% Xylitol.

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Product Number	% Xylitol	Product Type	HRIPT Test Yes/No	Occlusivity	Completed Subjects	Did formula induce an allergic response	Number of Subjects Exhibiting Low Level Reaction During Induction	Number of Subjects Exhibiting High Level Reaction During Induction	Number of Subjects Exhibiting Low Level Reaction During Challenge	Number of Subjects Exhibiting High Level Reaction During Challenge	pass/fail	comments
1	0.115	LEAVE ON	YES	OCCLUSIVE	119	NO	3	0	1	0	PASS	Did not induce Allergic Contact Sensitizati on

Product Number 1	
Induction Phase Grading Scale	
Grade	**Response**
Erythema and Elevated Responses	
0	No evidence of Irritation
1	Minimal erythema, barely percpetible
2	Definitely Erythema, readily visible;or minimal edema;or minimal papular response
3	Erythema and Papules
4	Definite Edema
5	Erythema, Edema and Papules
6	Vesicular Eruption
7	Strong reactions spreading beyond site
Effects on Superficail layer of Skin	
A	Slight gazed appearance
B	Marked glazing
C	Glazing wit peeling and cracking
D	Glazing with fissures
E	Film of dried serrous exudatecovering all or portion of patch site
F	Small petechial ersion or scabs

Challenge Phase Grading Scale	
	Erythema Scale:
Score	**Interpretation**
0	No Visible erythema
1	Mild erythema (faint pink to definite erythema)
2	Moderate erythema (definite redness)
3	Severe erythema (very intense redness)
Designation for Elevated Responses:	
E	Edema-Definite swelling
P	Papules-small, red, solid elevations; surface of reaction has granular feeling
V	Vesicles-small, circumscribed elevations having translucent surfaces so that fluid is visible (blister-like); vesicles are no larger than 0.5 cm in diameter

B	Bullae- vesicles with diameter >0.5cm; vesicles may coalesce to form one or a few large blisters that fill the patch size
Other Responses Characteristics	
S	Spreading- evidence of the reaction beyond the chamber area (does not include obvious signs of leakage of the test material away from chamber
W	Weeping-evidence of release of fluid from a vesicular or bullos reaction

Details of Test Methodology and Results	
0	panelist discontinued due to reactions
48 to 72 hrs	patch duration
9	induction patches
3	weeks induction
2	week rest period
Inducted/orginial and virgin site	challenge Patch
48 hrs and 96 hrs	challenge readings
Test Material Concentration/Dilution	As is /Neat

Grading Scale Interpretation	
Low Level Reactions	0 or 1
High Level Reaction	2 and above