Safety Assessment of Brown Algae-Derived Ingredients as Used in Cosmetics

Status:	Draft Report for Panel Review
Release Date:	August 29, 2018
Panel Meeting Date:	September 24-25, 2018

The 2018 Cosmetic Ingredient Review Expert Panel members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Ronald A. Hill, Ph.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; James G. Marks, Jr., M.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Executive Director is Bart Heldreth, Ph.D. This report was prepared by Lillian C. Becker, former Scientific Analyst/Writer and Priya Cherian, Scientific Analyst/Writer.

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Cosmetic Ingredient Review

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Memorandum

To: CIR Expert Panel Members and Liaisons
From: Priya Cherian, Scientific Analyst/Writer
Date: August 29, 2018
Subject: Safety Assessment of Brown Algae as Used in Cosmetics

Enclosed is the Draft Report of 83 brown algae-derived ingredients as used in cosmetics. (It is identified as *broalg092018rep* in this pdf.) This is the first time the Panel is reviewing this document. The ingredients in this review are extracts, powders, juices, or waters derived from one or multiple species of brown algae.

Information received from the Personal Care Products Council (Council) are attached:

- use concentration data of brown algae and algae-derived ingredients (*broalg092018data1, broalg092018data2, broalg092018data3*);
- Information regarding hydrolyzed fucoidan extracted from *Laminaria digitata* has been included in the report. Although fucoidan is a not one of the ingredients being reviewed in the report, data regarding fucoidan has been included in the report as it is a primary constituent in many brown algae species (*broalg092018data4*).
- information regarding a trade name mixture containing Ascophyllum Nodosum Extract (*broalg092018data5*);
- ocular irritation and sensitization data of products containing Sargassum Muticum Extract (*broalg092018data6*);
- sensitization data of a night cream containing Alaria Esculenta Extract (*broalg092018data7*).

Additionally, Council comments on the SLR were received (*broalg092018pcpc*), and have been addressed. The presentation made for the Panel on Algal diversity and application, given by Rex L. Lowe, is available at the (June 2014) meeting page, https://www.cir-safety.org/sites/default/files/broalg092018data8.pdf.

The following are also included in this package for your review:

- *broalg092018flow*: report flowchart
- *broalg092018hist:* history
- *broalg092018prof:* data profile
- *broalg092018strat:* search strategy
- *broalg092018FDA*: 2018 VCRP data

After reviewing these documents, if the available data are deemed sufficient to make a determination of safety the Panel should identify matters to be addressed in the Discussion, and then issue a Tentative Report with a safe as used, safe with qualifications, or unsafe conclusion. If the available data are insufficient, the Panel should issue an Insufficient Data Announcement (IDA), specifying the data needs therein.

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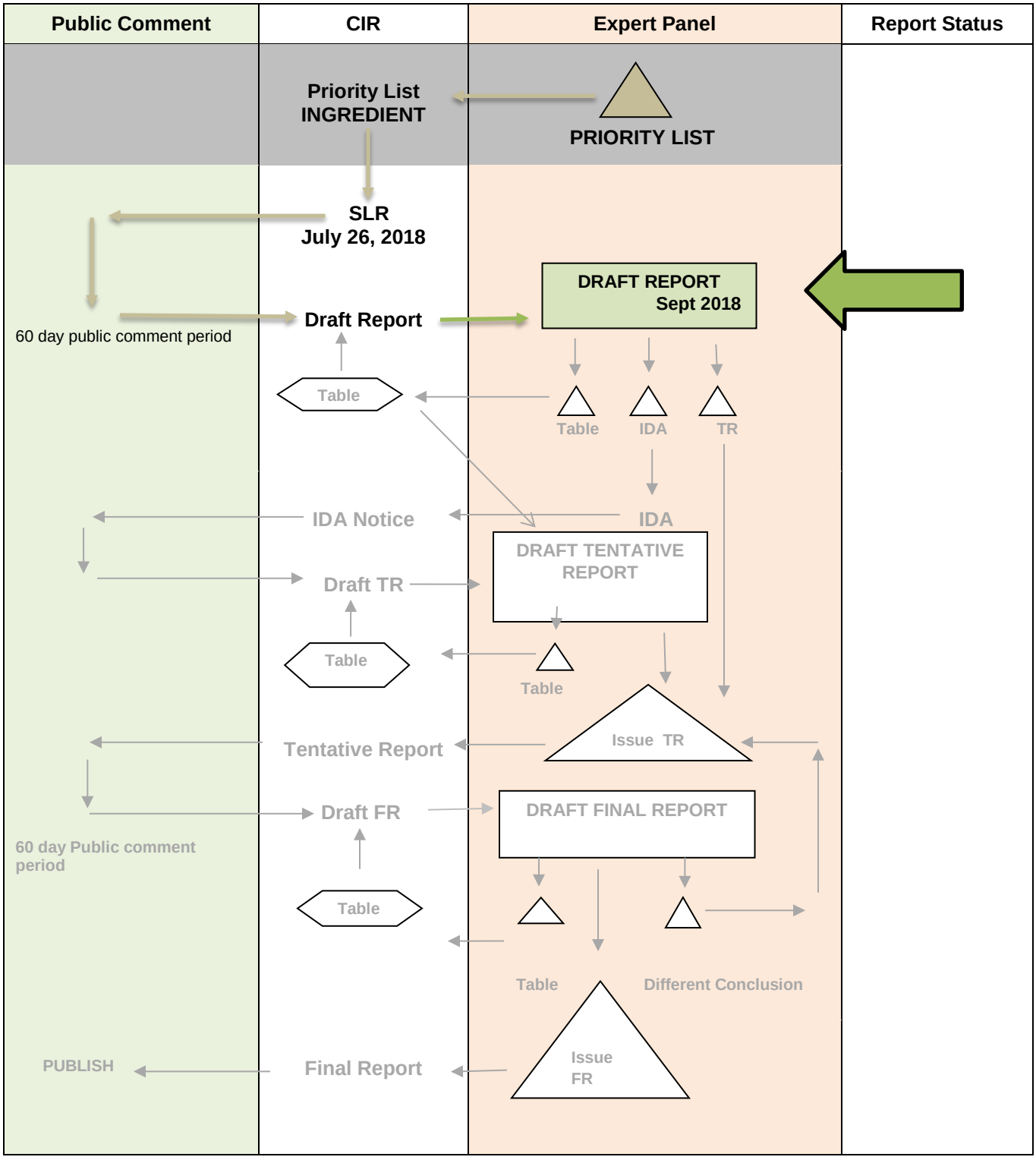
SAFETY ASSESSMENT FLOW CHART

INGREDIENT/FAMILY Brown Algae-derived ingredients

MEETING Sept 2018



History of Brown Algae

August 2018: SLR announced for public comment

September 2018: draft report reviewed by Panel

Brown Algae Data Profile for ***September*** **2018**. Writer – Priya Cherian																					
		ADME		Acute toxicity			Repeated dose toxicity			Irritation					Sensitization						
	Use	Log K_{ow}	Dermal Penetration	Oral	Dermal	Inhale	Oral	Dermal	Inhale	Ocular Animal	Ocular In Vitro	Dermal Animal	Dermal Human	Dermal In Vitro	Animal	Human	In Vitro	Repro/Devel	Genotoxicity	Carcinogenicity	Phototoxicity
1. Agarum Cribrosum Extract	x																				
2. Alaria Esculenta Extract	x																				
3. Ascophyllum Nodosum							x														
4. Ascophyllum Nodosum Extract	x									x		x							x		
5. Ascophyllum Nodosum Powder	x	x																			
6. Cladosiphon Novae-Caledoniae Extract																					
7. Cladosiphon Okamuranus Extract	x																				
8. Cystoseira Amentacea/Caespitosa/ Branchycarpa Extract																					
9. Cystoseira Baccata Extract																					
10. Cystoseira Balearica Extract																					
11. Cystoseira Caespitosa Extract																					
12. Cystoseira Compressa Extract				x															x		
13. Cystoseira Compressa Powder																					
14. Cystoseira Tamariscifolia Extract																					
15. Dictyopteris Membranacea Extract (Retired)																					
16. Dictyopteris Polypodioides Extract	x																				
17. Dictyota Coriacea Extract																					
18. Durvillea Antarctica Extract	x																				
19. Ecklonia Cava Extract				x			x												x		
20. Ecklonia Cava Water							x														
21. Ecklonia Kurome Extract																					
22. Ecklonia Kurome Powder																					
23. Ecklonia/Laminaria Extract																					
24. Ecklonia Maxima Extract																					
25. Ecklonia Maxima Powder																					
26. Ecklonia Radiata Extract	x																				
27. Eisenia Arborea Extract																					
28. Fucus Serratus Extract	x																				
29. Fucus Spiralis Extract																					
30. Fucus Vesiculosus	x																				
31. Fucus Vesiculosus Extract	x			x			x												x		
32. Fucus Vesiculosus Powder	x																				
33. Halidrys Siliquosa Extract																					
34. Halopteris Scoparia Extract																					
35. Himanthalia Elongata Extract	x																				
36. Himanthalia Elongata Powder																					
37. Hizikia Fusiforme Extract																				x	
38. Hizikia Fusiformis Water																					
39. Hizikia Fusiformis Callus Culture Extract																					
40. Hydrolyzed Ecklonia Cava Extract																					

Brown Algae Data Profile for ***September*** **2018**. Writer – Priya Cherian																					
		ADME		Acute toxicity			Repeated dose toxicity			Irritation					Sensitization						
	Use	Log K_{ow}	Dermal Penetration	Oral	Dermal	Inhale	Oral	Dermal	Inhale	Ocular Animal	Ocular In Vitro	Dermal Animal	Dermal Human	Dermal In Vitro	Animal	Human	In Vitro	Repro/Devel	Genotoxicity	Carcinogenicity	Phototoxicity
41. Hydrolyzed Fucus Vesiculosus Extract																					
42. Hydrolyzed Fucus Vesiculosus Protein																					
43. Kappaphycus Alvarezii Extract																					
44. Laminaria Angustata Extract (Retired)																					
45. Laminaria Cloustoni Extract	x																				
46. Laminaria Diabolica Extract																					
47. Laminaria Digitata Extract	x																				
48. Laminaria Digitata Powder	x																				
49. Laminaria Hyperborea Extract	x																				
50. Laminaria Japonica Extract	x						x						x								
51. Laminaria Japonica Powder							x														
52. Laminaria Longissima Extract																					
53. Laminaria Ochotensis Extract (Retired)																					
54. Laminaria Ochroleuca Extract	x																				
55. Laminaria Saccharina Extract																					
56. Lessonia Nigrescens Extract	x																				
57. Lessonia Nigrescens Powder																					
58. Macrocystis Pyrifera (Kelp)	x																				
59. Macrocystis Pyrifera (Kelp) Blade/Pneumatocyst/Stipe Juice Extract																					
60. Macrocystis Pyrifera (Kelp) Extract	x																				
61. Macrocystis Pyrifera (Kelp) Juice																					
62. Macrocystis Pyrifera (Kelp) Protein	x																				
63. Nereocystis Luetkeana Extract																					
64. Pelvetia Canaliculata Extract	x																				
65. Pelvetia Siliquosa Extract																					
66. Phyllacantha Fibrosa Extract																					
67. Saccharina Angustata Extract																				x	
68. Saccharina Japonica Extract																					
69. Saccharina Longicruris Extract																					
70. Sargassum Filipendula Extract	x																				
71. Sargassum Fulvellum Extract				x																	
72. Sargassum Fusiforme Extract																					

Brown Algae Data Profile for ***September*** **2018**. Writer – Priya Cherian																				
		ADME		Acute toxicity			Repeated dose toxicity			Irritation					Sensitization						
	Use	Log K_{ow}	Dermal Penetration	Oral	Dermal	Inhale	Oral	Dermal	Inhale	Ocular Animal	Ocular In Vitro	Dermal Animal	Dermal Human	Dermal In Vitro	Animal	Human	In Vitro	Repro/Devel	Genotoxicity	Carcinogenicity	Phototoxicity
73. Sargassum Glaucescens Extract																					
74. Sargassum Horneri Extract																					
75. Sargassum Muticum Extract	x																				
76. Sargassum Pallidum Extract																				x	
77. Sargassum Siliquastrum Extract																					
78. Sargassum Thunbergii Extract																					
79. Sargassum Vulgare Extract	x																				
80. Sphacelaria Scoparia Extract	x																				
81. Undaria Peterseniana Extract																					
82. Undaria Pinnatifida Extract	x						x														
83. Undaria Pinnatifida Cell Culture Extract																					
84. Undaria Pinnatifida Leaf/Stem Extract																				x	
85. Undaria Pinnatifida Powder	x						x													x	
86. Undaria Pinnatifida Root Powder																					

Brown Algae

Ingredient	CAS #	InfoBase	SciFinder	PubMed	TOXNET	FDA	EU	ECHA	IUCLID	SIDS	HPVIS	NICNAS	NTIS	NTP	WHO	FAO	FEMA	Web
1. Agarum Cribrosum Extract	-	-	X	X	X	X	X	X					N	N	N	n	n	√
2. Alaria Esculenta Extract	-	-	X	X	X	X	X	X										√
3. Ascophyllum Nodosum	-	-	√	X	√	X	X	X										√
4. Ascophyllum Nodosum Extract	84775-78-0	√	√	X	√	X	X	C										√
5. Ascophyllum Nodosum Powder	-	-	√	X	X	X	X	X										√
6. Asterionellopsis Glacialis Extract	-	-	X	X	X	X	X	X										X
7. Cladosiphon Novae-Caledoniae Extract	-	-	X	X	X	X	X	X										X
8. Cladosiphon Okamuranus Extract	-	-	X	X	X	X	X	X										
9. Cystoseira Amentacea/ Caespitosa/ Branchycarpa Extract	-	-	X	X	X	X	X	X										
10. Cystoseira Baccata Extract	-	-	X	X	X	X	X	X										
11. Cystoseira Balearica Extract	-	-	X	X	X	X	X	X										
12. Cystoseira Caespitosa Extract	-	-	X	X	X	X	X	X										
13. Cystoseira Compressa Extract	-	-	X	√	X	X	X	X										
14. Cystoseira Compressa Powder	-	-	X	X	X	X	X	X										
15. Cystoseira Tamariscifolia Extract	-	-	X	X	X	X	X	X										
16. Dictyopteris Membranacea Extract (Retired)	-	-	X	√	X	X	X	X										
17. Dictyopteris Polypodioides Extract	-	-	X	X	X	X	X	X										
18. Dictyota Coriacea Extract	-	-	X	X	X	X	X	X										
19. Durvillea Antarctica Extract	-	-	X	X	X	X	X	X										

Ingredient	CAS #	InfoBase	SciFinder	PubMed	TOXNET	FDA	EU	ECHA	IUCLID	SIDS	HPVIS	NICNAS	NTIS	NTP	WHO	FAO	FEMA	Web
20. Ecklonia Cava Extract	-	-	X	√	X	X	X	X										
21. Ecklonia Cava Water	-	-	X	X	X	X	X	X										
22. Ecklonia Kurome Extract	-	-	X	X	X	X	X	X										
23. Ecklonia Kurome Powder	-	-	X	X	X	X	X	X										
24. Ecklonia/Laminaria Extract	-	-	X	X	X	X	X	X										
25. Ecklonia Maxima Extract	-	-	X	X	X	X	X	X										
26. Ecklonia Maxima Powder	-	-	X	X	X	X	X	X										
27. Ecklonia Radiata Extract	-	-	X	X	X	X	X	X										
28. Eisenia Arborea Extract	-	-	X	X	X	X	X	X										
29. Fucus Serratus Extract	94167-02-9	-	√	√	X	X	X	X										
30. Fucus Spiralis Extract	-	-	√	X	X	X	X	X										
31. Fucus Vesiculosus	-	-	X	√	√	X	X	X										
32. Fucus Vesiculosus Extract	283-633-7	√	X	X	X	X	X	X										
33. Fucus Vesiculosus Powder	-	√	X	√	X	X	X	X										
34. Halidrys Siliquosa Extract	-	-	X	X	X	X	X	X										
35. Halopteris Scoparia Extract	-	-	X	X	X	X	X	X										
36. Himanthalia Elongata Extract	-	-	X	X	√	X	X	X										
37. Himanthalia Elongata Powder	-	-	X	X	X	X	X	X										
38. Hizikia Fusiforme Extract	-	-	X	X	√	X	X	X										
39. Hizikia Fusiformis Water	-	-	X	X	X	X	X	X										
40. Hizikia Fusiformis Callus Culture Extract	-	-	X	X	X	X	X	X										
41. Hydrolyzed Ecklonia Cava Extract	-	-	X	X	X	X	X	X										
42. Hydrolyzed Fucus Vesiculosus Extract	84696-13-9	-	√	X	X	X	X	X										

Ingredient	CAS #	InfoBase	SciFinder	PubMed	TOXNET	FDA	EU	ECHA	IUCLID	SIDS	HPVIS	NICNAS	NTIS	NTP	WHO	FAO	FEMA	Web
43. Hydrolyzed Fucus Vesiculosus Protein	-	-	X	X	X	X	X	X										
44. Kappaphycus Alvarezii Extract	1220882-73-4 (generic)	-	X	X	X	X	X	X										
45. Laminaria Angustata Extract (Retired)	-	√	X	X	X	X	X	X										
46. Laminaria Cloustoni Extract	90046-11-0 92128-82-0	-	X	X	X	X	X	X										
47. Laminaria Diabolica Extract	-	-	X	X	X	X	X	X										
48. Laminaria Digitata Extract	90046-12-1 92128-82-0	√	√	X	√	√	X	X										
49. Laminaria Digitata Powder	-	√	X	X	X	√	X	X										
50. Laminaria Hyperborea Extract	90046-13-2 92128-82-0	√	√	X	√	√	X	X										
51. Laminaria Japonica Extract	92128-82-0	√	√	√	√	√	X	X										
52. Laminaria Japonica Powder	-	-	X	X	X	X	X	X										
53. Laminaria Longissima Extract	-	-	X	X	X	X	X	X										
54. Laminaria Ochotensis Extract (Retired)	-	√	X	X	X	√	X	X										
55. Laminaria Ochroleuca Extract	92128-82-0	-	√	X	X	X	X	X										
56. Laminaria Saccharina Extract	90046-14-3 92128-82-0	√	√	X	X	√	X	X										
57. Lessonia Nigrescens Extract	-	-	X	X	X	X	X	X										
58. Lessonia Nigrescens Powder	-	-	X	X	X	X	X	X										
59. Macrocystis Pyrifera (Kelp)	-	√	√	X	X	X	X	X										
60. Macrocystis Pyrifera (Kelp) Blade/Pneumatocyst/ Stipe Juice Extract	-	-	X	X	X	X	X	X										
61. Macrocystis Pyrifera (Kelp) Extract	347174-92-9	√	√	X	X	√	X	X										
62. Macrocystis Pyrifera (Kelp) Juice	-	-	X	X	X	X	X	X										
63. Macrocystis Pyrifera (Kelp) Protein	-	-	X	X	X	X	X	X										

Ingredient	CAS #	InfoBase	SciFinder	PubMed	TOXNET	FDA	EU	ECHA	IUCLID	SIDS	HPVIS	NICNAS	NTIS	NTP	WHO	FAO	FEMA	Web
64. Nereocystis Luetkeana Extract	-	√	X	X	X	√	X	X										
65. Pelvetia Canaliculata Extract	223751-75-5	-	√	X	X	X	X	X										
66. Pelvetia Siliquosa Extract	-	-	X	X	X	X	X	X										
67. Phyllacantha Fibrosa Extract	-	-	X	X	X	X	X	X										
68. Rissoella Verruculosa Extract	-	-	X	X	X	X	X	X										
69. Saccharina Angustata Extract	-	-	X	X	X	X	X	X										
70. Saccharina Japonica Extract	-	-	X	X	X	X	X	X										
71. Saccharina Longicruris Extract	-	-	X	X	X	X	X	X										
72. Sargassum Filipendula Extract	-	-	X	X	X	X	X	X										
73. Sargassum Fulvellum Extract	-	-	X	X	X	X	X	X										
74. Sargassum Fusiforme Extract	-	-	X	X	X	X	X	X										
75. Sargassum Glaucescens Extract	-	-	X	X	X	X	X	X										
76. Sargassum Horneri Extract	-	-	X	X	X	X	X	X										
77. Sargassum Muticum Extract	-	-	X	X	√	X	X	X										
78. Sargassum Pallidum Extract	-	-	X	X	X	X	X	X										
79. Sargassum Siliquastrum Extract	-	-	X	X	√	X	X	X										
80. Sargassum Thunbergii Extract	-	-	X	X	X	X	X	X										
81. Sargassum Vulgare Extract	-	-	X	X	X	X	X	X										
82. Sahel Scenedesmus Extract	-	-	X	X	X	X	X	X										
83. Sphacelaria Scoparia Extract	-	-	X	X	X	X	X	X										
84. Undaria Peterseniana Extract	-	-	X	X	X	X	X	X										
85. Undaria Pinnatifida Extract	-	-	X	√	X	X	X	X										
86. Undaria Pinnatifida Cell Culture Extract	-	-	X	X	X	X	X	X										

Ingredient	CAS #	InfoBase	SciFinder	PubMed	TOXNET	FDA	EU	ECHA	IUCLID	SIDS	HPVIS	NICNAS	NTIS	NTP	WHO	FAO	FEMA	Web
87. Undaria Pinnatifida Leaf/Stem Extract	-	-	X	X	X	X	X	X										
88. Undaria Pinnatifida Powder	-	√	X	X	X	√	X	X										
89. Undaria Pinnatifida Root Powder	-	√	X	X	X	√	X	X	N	N	N							

Botanical and/or Fragrance Websites (if applicable)

Ingredient	CAS #	Dr. Duke's	Taxonomy	GRIN	Sigma-Aldrich	IFRA	RIFM
1. Agarum Cribrosum Extract	-						
2. Alaria Esculenta Extract	-						
3. Ascophyllum Nodosum	-						
4. Ascophyllum Nodosum Extract	-						
5. Ascophyllum Nodosum Powder	84775-78-0						
6. Asterionellopsis Glacialis Extract	-						
7. Cladosiphon Novae-Caledoniae Extract	-						
8. Cladosiphon Okamuranus Extract	-						
9. Cystoseira Amentacea/Caespitosa/ Branchycarpa Extract	-						
10. Cystoseira Baccata Extract	-						
11. Cystoseira Balearica Extract	-						
12. Cystoseira Caespitosa Extract	-						
13. Cystoseira Compressa Extract	-						
14. Cystoseira Compressa Powder	-						

Ingredient	CAS #	Dr. Duke's	Taxonomy	GRIN	Sigma-Aldrich	IFRA	RIFM
15. Cystoseira Tamariscifolia Extract	-						
16. Dictyopteris Membranacea Extract (Retired)	-						
17. Dictyopteris Polypodioides Extract	-						
18. Dictyota Coriacea Extract	-						
19. Durvillea Antarctica Extract	-						
20. Ecklonia Cava Extract	-						
21. Ecklonia Cava Water	-						
22. Ecklonia Kurome Extract	-						
23. Ecklonia Kurome Powder	-						
24. Ecklonia/Laminaria Extract	-						
25. Ecklonia Maxima Extract	-						
26. Ecklonia Maxima Powder	-						
27. Ecklonia Radiata Extract	-						
28. Eisenia Arborea Extract	-						
29. Fucus Serratus Extract	94167-02-9						
30. Fucus Spiralis Extract	-						
31. Fucus Vesiculosus	-						
32. Fucus Vesiculosus Extract	-						
33. Fucus Vesiculosus Powder	-						
34. Halidrys Siliquosa Extract	-						
35. Halopteris Scoparia Extract	-						
36. Himanthalia Elongata Extract	-						

Ingredient	CAS #	Dr. Duke's	Taxonomy	GRIN	Sigma-Aldrich	IFRA	RIFM
37. Himanthalia Elongata Powder	-	X	X	X	X	X	X
38. Hizikia Fusiforme Extract	-						
39. Hizikia Fusiformis Water	-						
40. Hizikia Fusiformis Callus Culture Extract	-						
41. Hydrolyzed Ecklonia Cava Extract	-						
42. Hydrolyzed Fucus Vesiculosus Extract	84696-13-9						
43. Hydrolyzed Fucus Vesiculosus Protein	-						
44. Kappaphycus Alvarezii Extract	1220882-72-4 (generic)						
45. Laminaria Angustata Extract (Retired)	-						
46. Laminaria Cloustoni Extract	90046-11-0 92128-82-0						
47. Laminaria Diabolica Extract	-						
48. Laminaria Digitata Extract	90046-12-1 92128-82-0						
49. Laminaria Digitata Powder	-						
50. Laminaria Hyperborea Extract	90046-13-2 92128-82-0						
51. Laminaria Japonica Extract	92128-82-0						
52. Laminaria Japonica Powder	-						
53. Laminaria Longissima Extract	-						
54. Laminaria Ochotensis Extract (Retired)	-						
55. Laminaria Ochroleuca Extract	92128-82-0						
56. Laminaria Saccharina Extract	90046-14-3 92128-82-0						

Ingredient	CAS #	Dr. Duke's	Taxonomy	GRIN	Sigma-Aldrich	IFRA	RIFM
57. Lessonia Nigrescens Extract	-						
58. Lessonia Nigrescens Powder	-						
59. Macrocystis Pyrifera (Kelp)	-						
60. Macrocystis Pyrifera (Kelp) Blade/Pneumatocyst/Stipe Juice Extract	-						
61. Macrocystis Pyrifera (Kelp) Extract	347174-92-9						
62. Macrocystis Pyrifera (Kelp) Juice	-						
63. Macrocystis Pyrifera (Kelp) Protein	-						
64. Nereocystis Luetkeana Extract	-						
65. Pelvetia Canaliculata Extract	223751-75-5						
66. Pelvetia Siliquosa Extract	-						
67. Phyllacantha Fibrosa Extract	-						
68. Rissoella Verruculosa Extract	-						
69. Saccharina Angustata Extract	-						
70. Saccharina Japonica Extract	-						
71. Saccharina Longicruris Extract	-						
72. Sargassum Filipendula Extract	-						
73. Sargassum Fulvellum Extract	-						
74. Sargassum Fusiforme Extract	-						
75. Sargassum Glaucescens Extract	-						
76. Sargassum Horneri Extract	-						

Ingredient	CAS #	Dr. Duke's	Taxonomy	GRIN	Sigma-Aldrich	IFRA	RIFM
77. Sargassum Muticum Extract	-						
78. Sargassum Pallidum Extract	-						
79. Sargassum Siliquastrum Extract	-						
80. Sargassum Thunbergii Extract	-						
81. Sargassum Vulgare Extract	-						
82. Sahel Scenedesmus Extract	-						
83. Sphacelaria Scoparia Extract	-						
84. Undaria Peterseniana Extract	-						
85. Undaria Pinnatifida Extract	-						
86. Undaria Pinnatifida Cell Culture Extract	-						
87. Undaria Pinnatifida Leaf/Stem Extract	-						
88. Undaria Pinnatifida Powder	-						
89. Undaria Pinnatifida Root Powder	-						
90.							
91.							
92.							
93.							
94.							
95.							
96.							
97.							
98.							
99.							

Search Strategy

[*document search strategy used for SciFinder, PubMed, and Toxnet*]

SciFinder

INCI names and CAS No.

Ascophyllum Nodosum – 33 substance hits; 0 useful
Ascophyllum Nodosum Extract – 1 substance hits; 0 useful
Ascophyllum Nodosum Powder – 1 substance hit; 0 useful
Fucus Serratus Extract – 1 substance hit; 0 useful
Fucus Spiralis Extract – 1 substance hit; 0 useful
Hydrolyzed Fucus Vesiculosus Extract – 1 substance hit; 0 useful
Kappaphycus Alvarezii Extract – 1 substance hit; 0 useful
Laminaria Cloustoni Extract – 2 substance hits; 0 useful
Laminaria Digitata Extract – 2 substance hits; 0 useful
Laminaria Hyperborea Extract – 2 substance hits; 0 useful
Laminaria Japonica Extract – 1 substance hit; 0 useful
Laminaria Saccharina Extract – 2 substance hits; 0 useful
Laminaria Ochroleuca Extract – 1 substance hit; 0 useful
Macrocystis Pyrifera – 79 substance hits; 0 useful
Macrocystis Pyrifera (Kelp) Extract – 1 substance hit; 0 useful
Pelvetia Canaliculata Extract – 1 substance hit; 0 useful
Saccharina Angustata Extract – 1 substance hit; 0 useful

PubMed

((((((((((((((Agarum Cribrosum Extract) OR Alaria Esculenta Extract) OR Ascophyllum Nodosum) OR Ascophyllum Nodosum Extract) OR Ascophyllum Nodosum Powder) OR Asterionellopsis Glacialis Extract) OR Cystoseira Tamariscifolia Extract) OR Cladosiphon Novae-Caledoniae Extract) OR Cladosiphon Okamuranus Extract) OR Cystoseira Amentacea/Caespitosa/ Branchycarpa Extract) OR Cystoseira Baccata Extract) OR Cystoseira Balearica Extract) OR Cystoseira Caespitosa Extract) OR Cystoseira Compressa Extract) OR Cystoseira Compressa Powder) OR 84775-78-0 AND (tox[sb]) = 55 hits, 5 possibly useful.

((((((((((((((Cystoseira Tamariscifolia Extract) OR Dictyopteris Membranacea Extract) OR Dictyopteris Polypodioides Extract) OR Dictyota Coriacea Extract) OR Durvillea Antarctica Extract) OR Ecklonia Cava Extract) OR Ecklonia Cava Water) OR Ecklonia Kurome Extract) OR Ecklonia Kurome Powder) OR Ecklonia/Laminaria Extract) OR Ecklonia Maxima Extract) OR Ecklonia Maxima Powder) OR Ecklonia Radiata Extract) OR Eisenia Arborea Extract) OR Fucus Serratus Extract) OR **94167-02-9** AND (tox[sb]) = 41 hits, 4 possibly useful.

((((((((((((((Fucus Spiralis Extract) OR Fucus Vesiculosus) OR Fucus Vesiculosus Extract) OR Fucus Vesiculosus Powder) OR Halidrys Siliquosa Extract) OR Halopteris Scoparia Extract) OR Himanthalia Elongata Extract) OR Himanthalia Elongata Powder) OR Hizikia Fusiforme Extract) OR Hizikia Fusiformis Water) OR Hizikia Fusiformis Callus Culture Extract) OR Hydrolyzed Ecklonia Cava Extract) OR Hydrolyzed Fucus Vesiculosus Extract) OR 84696-13-9) OR Hydrolyzed Fucus Vesiculosus Protein) OR Kappaphycus Alvarezii Extract OR 1220882-73-4) AND (tox[sb]) = 231 hits, 4 possibly useful.

((((((((((((((Laminaria Angustata Extract) OR Laminaria Cloustoni Extract) OR 90046-11-0) OR 92128-82-0) OR Laminaria Diabolica Extract) OR Laminaria Digitata Extract) OR Laminaria Digitata Powder) OR 90046-12-1) OR 92128-82-0) OR Laminaria Hyperborea Extract) OR 90046-13-2) OR 92128-82-0) OR Laminaria Japonica Extract) OR 92128-82-0) OR Laminaria Japonica Powder) OR Laminaria Longissima Extract) OR Laminaria Ochotensis Extract) AND (tox[sb]) = 31 hits, 1 possibly useful.

((((((((((((((Laminaria Ochroleuca Extract) OR Laminaria Saccharina Extract) OR Lessonia Nigrescens Extract) OR Lessonia Nigrescens Powder) OR Macrocystis Pyrifera) OR kelp) OR Macrocystis Pyrifera (Kelp) Blade/Pneumatocyst/Stipe Juice Extract) OR Macrocystis Pyrifera (Kelp) Extract) OR Macrocystis Pyrifera (Kelp) Juice) OR Macrocystis Pyrifera (Kelp) Protein) OR Nereocystis Luetkeana Extract) OR **92128-82-0**) OR **90046-14-3**) OR **92128-82-0**) OR **347174-92-9**) OR **223751-75-5** AND (tox[sb]) = 1 hit, not useful

((((((((((((((Pelvetia Canaliculata Extract) OR **223751-75-5**) OR Pelvetia Siliquosa Extract) OR Phyllacantha Fibrosa Extract) OR Rissoella Verruculosa Extract) OR Saccharina Angustata Extract) OR Saccharina Japonica Extract) OR Saccharina Longicruris Extract) OR Sargassum Filipendula Extract) OR Sargassum Fulvellum Extract) OR Sargassum Fusiforme Extract) OR Sargassum Glaucescens Extract) OR Sargassum Horneri Extract) OR Sargassum Muticum Extract) OR Sargassum Pallidum Extract) OR Sargassum Siliquastrum Extract AND (tox[sb]) 40 hits, 5 possibly useful

((((((((((Sargassum Thunbergii Extract) OR Sargassum Vulgare Extract) OR Sahel Scenedesmus Extract) OR Sphacelaria Scoparia Extract) OR Undaria Peterseniana Extract) OR Undaria Pinnatifida Extract) OR Undaria Pinnatifida Cell Culture Extract) OR Undaria Pinnatifida Leaf/Stem Extract) OR Undaria Pinnatifida Powder) OR Undaria Pinnatifida Root Powder) AND (tox[sb]) = 21 hits, 3 possibly useful

LINKS

InfoBase (self-reminder that this info has been accessed; not a public website) - http://www.personalcarecouncil.org/science-safety/line-infobase
ScfFinder (usually a combined search for all ingredients in report; list # of this/# useful) - https://scifinder.cas.org/scifinder
PubMed (usually a combined search for all ingredients in report; list # of this/# useful) - http://www.ncbi.nlm.nih.gov/pubmed
Toxnet databases (usually a combined search for all ingredients in report; list # of this/# useful) – https://toxnet.nlm.nih.gov/ (includes Toxline; HSDB; ChemIDPlus; DAR; IRIS; CCRIS; CPDB; GENE-TOX)

FDA databases – http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm (CFR); then,
list of all databases: http://www.fda.gov/ForIndustry/FDABasicsforIndustry/ucm234631.htm; then,
http://www.accessdata.fda.gov/scripts/fcn/fcnnavigation.cfm?rpt=eafuslisting&displayall=true (EAFUS);
http://www.fda.gov/food/ingredientspackaginglabeling/gras/default.htm (GRAS);
http://www.fda.gov/food/ingredientspackaginglabeling/gras/scogs/ucm2006852.htm (SCOGS database);
http://www.accessdata.fda.gov/scripts/fdcc/?set=IndirectAdditives (indirect food additives list);
http://www.fda.gov/Drugs/InformationOnDrugs/default.htm (drug approvals and database);
http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/UCM135688.pdf (OTC ingredient list);
http://www.accessdata.fda.gov/scripts/cder/iig/ (inactive ingredients approved for drugs)

EU (European Union); check CosIng (cosmetic ingredient database) for restrictions and SCCS (Scientific Committee for Consumer Safety) opinions - http://ec.europa.eu/growth/tools-databases/cosing/
ECHA (European Chemicals Agency – REACH dossiers) – http://echa.europa.eu/information-on-chemicals;jsessionid=A978100B4E4CC39C78C93A851EB3E3C7.live1
IUCLID (International Uniform Chemical Information Database) - https://iuclid6.echa.europa.eu/search
OECD SIDS documents (Organisation for Economic Co-operation and Development Screening Info Data Sets)- http://webnet.oecd.org/hpv/ui/Search.aspx
HPVIS (EPA High-Production Volume Info Systems) - https://ofmext.epa.gov/hpvis/HPVISlogon https://java.epa.gov/oppt_chemical_search/
https://java.epa.gov/oppt_chemical_search/
NICNAS (Australian National Industrial Chemical Notification and Assessment Scheme)- https://www.nicnas.gov.au/
NTIS (National Technical Information Service) - http://www.ntis.gov/
NTP (National Toxicology Program) - http://ntp.niehs.nih.gov/
WHO (World Health Organization) technical reports - http://www.who.int/biologicals/technical_report_series/en/
FAO (Food and Agriculture Organization of the United Nations) - http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/jecfa-additives/en/ (FAO);
FEMA (Flavor & Extract Manufacturers Association) - http://www.femaflavor.org/search/apachesolr_search/
Web – perform general search; may find technical data sheets, published reports, etc

Botanical Websites, if applicable
Dr. Duke's https://phytochem.nal.usda.gov/phytochem/search
Taxonomy database - http://www.ncbi.nlm.nih.gov/taxonomy
GRIN (U.S. National Plant Germplasm System) - https://npgsweb.ars-grin.gov/gringlobal/taxon/taxonomysimple.aspx
Sigma Aldrich plant profiler http://www.sigmaaldrich.com/life-science/nutrition-research/learning-center/plant-profiler.html

Fragrance Websites, if applicable
IFRA (International Fragrance Association) – http://www.ifraorg.org/
the Research Institute for Fragrance Materials (RIFM) should be contacted

Safety Assessment of Brown Algae-Derived Ingredients as Used in Cosmetics

Status:	Draft Report for Panel Review
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The 2018 Cosmetic Ingredient Review Expert Panel members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Ronald A. Hill, Ph.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; James G. Marks, Jr., M.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Executive Director is Bart Heldreth, Ph.D. This report was prepared by Lillian C. Becker, former Scientific Analyst/Writer and Priya Cherian, Scientific Analyst/Writer.

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INTRODUCTION

This is a review of the safety of 83 brown algae-derived ingredients as used in cosmetics (Table 1). The ingredients in this review are extracts, powders, juices, or waters derived from one or multiple species of brown algae. According to the web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI; *Dictionary*), these brown algae-derived ingredients are most commonly used as skin conditioning agents (Table 2).[1,1] These ingredients are also reported to be used as absorbents, antioxidants, binders, hair conditioning agents, oxidizing agents, pH adjusters, and viscosity increasing agents.

There are several major groups of algae (as described in "Algae Identification" section). However, this safety assessment focuses only on brown algae. The names of the ingredients in this report are written in accordance with the INCI naming conventions, i.e., capitalized without italics or abbreviations. When referring to the algae from which these ingredients are derived, the standard taxonomic practice of using *italics* is followed (e.g., *Agarum cribrosum*). The term "kelp" is commonly used when referring to brown algae. Kelp are large brown algae that belong to the order Laminariales.[2]

Several brown algae constituents, such as phytosterols,[3] phytosteryl ingredients,[3] and alginic acid[4] were found to be safe as used by the Cosmetic Ingredient Review (CIR) Expert Panel (Panel). The full reports on these ingredients can be accessed on the CIR website (https://www.cir-safety.org/ingredients); therefore, information regarding these ingredients will not be included in this report.

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

The European Chemical Agency (ECHA)[5,6] website provides summaries of data generated by industry, and is cited throughout the report as appropriate. Also referenced in this safety assessment are summary data found in other reports, including those published by the European Medicines Agency (EMA),[7,8] the European Food Safety Authority (EFSA) Panel on Dietetic Products, Nutrition and Allergies (NDA),[9] and Food Standards Australia New Zealand (FSANZ).[10,11]

CHEMISTRY

Definitions

The ingredients in this safety assessment are derived from various species of brown algae. "Algae" is not a taxonomic group, but a functional group of convenience.[12] Not all algae should be considered to be plant-like (seaweed; macroalgae). While some algae are seaweed, some are protozoa, and some are unique and belong in other kingdoms. However, these aquatic and oxygenic organisms are all part of the eclectic group called "algae."

Algae Identification

There are several major groups of algae, and they are commonly referred to as brown algae (*Phaeophyceae)*, green algae (*Chlorophyta*), diatoms (*Bacillariophyceae*), chrysophytes (*Chrysophyta*), blue-green algae (*Cyanophyta*), red algae (*Rhodophyta*), dinoflagellates (*Pyrrhophyta*), and euglenoids (*Euglenophyta*). The different algal phyla are differentiated by storage products, pigmentation, and cell wall composition Table 3. A list of the brown algae-derived ingredients based on their subclass, order, family and genus is presented in Table 4.

Brown algae are mostly comprised of large, leathery seaweeds and are classified in about 265 genera with more than 1500 species.[12,13] The actual color varies depending on the proportion of brown pigment (fucoxanthin) to green pigment (chlorophyll). This algal group contains alginic acid and fucoidan in its complex cell walls. General characteristics and the geographic distribution of the specific species of brown algae in this report are presented in Table 5**.**

As with plant-derived ingredients, the constituent composition of these seaweed ingredients can vary widely depending on growing conditions, age of the organisms, local environmental aspects, harvesting conditions, methods of extraction, and many other variables. For example, the concentration of the most abundant carotenoid pigment in brown algae, fucoxanthin, varies remarkably depending on the age of the alga, and the protein content in brown algae varies considerably depending on the season in which it is harvested.[14,15]

Harvesting

Originally, the only source of brown algae was in the wild; but since the mid-twentieth century, demand has exceeded the supply that could be harvested from wild sources, and methods for cultivation have been developed.[16] Consequently, today, commercial brown seaweed comes mainly from farming rather than wild sources. *Laminaria japonica* and *Undaria pinnatifida* are among the most cultivated species of brown algae.[17] Several species, such as *Laminaria japonica*, are grown on suspended ropes in the ocean.[16] Repeated harvesting of *Macrocystis pyrifera* over a 3-month period did not significantly impact tissue chemical properties (i.e. alginate yield; viscosity and strength; nutritional quality, such as protein, carbohydrate, lipid, crude fiber, ash, and energy content; and tissue carbon/nitrogen ratios).[18]

Physical and Chemical Properties

Physical and chemical properties of Ascophyllum Nodosum Extract, Ascophyllum Nodosum Powder, and Ecklonia Cava Extract are presented in Table 6. Using the sieve method, 93.5% of the particle sizes of Ascophyllum Nodosum Extract, as a fully dried extract, were less than 0.250 mm and greater than 0.045 mm.[6]

Method of Manufacture

Numerous methods of manufacture are provided in Table 7.[9,19-31] Several of these methods have a target constituent or composition (e.g., high in fucoidan). The characterization of the final extract is provided in the table.

Arsenic is a constituent of concern in certain brown algae [see Constituents of Concern].[10,11,32,33] There are methods to remove the arsenic, including extraction with water, methanol, or water/methanol mixtures accompanied with sonication or mechanical agitation.[34] Extraction with microwave-assisted heating and accelerated solvent extraction systems are described in the literature.[34] Soaking the algae in water at room temperature followed by simmering in the water is shown to be effective for removing inorganic arsenic.[35] Another variation entails repeated boiling in seawater, replacing the water three times, after initial soaking.[32] Soaking the algae in a simmering 4% acetic acid or a 4% sodium hydrogen carbonate aqueous solution has also been shown to remove arsenic.[36]

Composition

There have been no data found or submitted on the composition of any of the ingredients in this report as used in cosmetics specifically. However, some constituents and constituent groups that are found in brown algae in general are presented in Table 8; included are alkaloids, laminarins, pheromones, phytohormones, and terpenoids, amino acids, betaines, and characteristic pigments such as chlorophyll a and c, β-carotene, fucoxanthin, and several other xanthophylls.[37] The compositions of *Ascophyllum nodosum*, *Laminaria digitata* and two samples of *Fucus vesiculosus* are provided in Table 9.

Sterols are also found in brown algae.[38,39] Sterols reported to be in *Cystoseira tamariscifolia*, *Fucus spiralis*, and *Sargassum vulgare* are provided in Table 10.

Methanol, hexane, and chloroform extracts from *Cystoseira compressa* were examined for flavonoid and phenolic content.[40] The flavonoid content of the methanol, hexane, and chloroform extract were 0.291 ± 0.02, 0.88 ± 0.07 and 0.804 ± 0.07 mg/g, respectively. The phenolic content of hexane (1.541 ± 0.09 mg/g) was considerably higher than the phenolic content of the methanol (0.161 ± 0.08 mg/g) and chloroform (0.45 ± 0.04 mg/g) extracts.

Constituents of ethanolic extracts of *Fucus spiralis* and *Sargassum vulgare* are presented in Table 11. The constituent with the highest concentration in both extracts is vaccenic acid (21,690 and 2848 ppm, respectively).[41]

The composition of a water/propylene glycol extract of *Laminaria japonica* is provided in Table 12.[28] The compositions of extracts of *Laminaria japonica*[26] that are produced via enzyme hydrolysis are presented in Table 13.

The specifications for an alcohol extract of *Ecklonia cava*, as a food/dietary supplement, include a combined phlorotannin content of 90.0 ± 5.0%; the content of dieckol, a specific phlorotannin, is 6.6% to 9.9% (Table 14).[9] The extract is to contain no insoluble substances, and it is reported to contain calcium (4800 ± 400 mg/kg), magnesium (1300 mg/kg), potassium (700 ± 200 mg/kg), and iodine (220 ± 40 mg/kg).

An *Undaria pinnatifida* extract rich in fucoidan (extraction method presented in Table 7) was characterized as having 27% uronic acid, 53% monosaccharides, and 7.4% sulfate.[31] Major monosaccharides included 54% fucose and 35% galactose. The minor monosaccharides were 3% rhamnose, 4% arabinose, and 1% xylose, glucose, and mannose.

A desalinated *Undaria pinnatifida* powder was reported to consist of 532 mg/g dietary fiber, mostly in the form of alginates, and 209 mg/g protein.[42] The composition profile is presented in Table 15.

Impurities/Constituents of Concern

Arsenic – Inorganic

Arsenic, usually in the form of arsenosugars, is a natural constituent of some brown algae, including *Ecklonia radiate*, *Laminaria japonica*, and *Sargassum fusiforme*.[10,11,26,33,43] The amount of arsenic is inconsistent due to varied uptake of inorganic arsenic by brown algae varieties and the influence of external factors (e.g., temperature, season, and pH) on the degree of uptake. Compared to many other foods, algae contain greater inorganic arsenic levels as a proportion of the total arsenic (e.g., 60% to 73%). A trade name mixture containing 4.7% Ascophyllum Nodosum Extract in 94.5% water was reported to have ≤ 2 ppm arsenic.[44] The amounts of arsenic that have been measured in various brown algae are presented in Table 16. The different arsenic-containing moieties found in four brown algae species are presented in Table 17. A comparison of the amount of arsenic found in *Laminaria japonica* and a *Laminaria japonica* extract (equivalence to cosmetic ingredients not confirmed) is presented in Table 18.

Heavy Metals Brown algae exhibit an affinity for heavy metals, which are believed to be absorbed from the water column.[37,45] Heavy metal concentrations in algae are strongly dependent on environmental parameters of the sampling sites (e.g., salinity, temperature, pH, light, nutrient concentrations, oxygen, etc.) and the structural differences among the algae.

The seaweeds also absorb heavy metals from the sediment.[46,47] A trade name mixture containing 4.7% Ascophyllum Nodosum Extract in 94.5% water was reported to have ≤ 20 ppm heavy metals.[44] An overview of the amount of heavy metals found in brown algae species is provided in Table 19.

An edible, phlorotannin-rich, ethanol extract of *Ecklonia cava* has specifications issued by the European Commission.[9] According to the Commission, this extract must contain < 3 mg/kg lead, < 0.1 mg/kg mercury, < 3 mg/kg cadmium, < 25 mg/kg arsenic, and 150 - 650 mg/kg iodine.

Phthalates

Dibutyl phthalate (DBP) and di-(2-ethylhexyl) phthalate (DEHP) was shown to occur naturally in *Laminaria japonica* at concentrations of 60 and 70%, respectively.[48] These phthalates were also present in *Undaria pinnatifida* (concentrations not given).

USE

Cosmetic

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

According to VCRP survey data received in 2018, Fucus Vesiculosus Extract is reported to be used in 287 formulations (201 in leave-on formulations, 75 in rinse-off formulations, and 11 diluted for the bath; Table 20).[49] Laminaria Digitata Extract is reported to be used in 235 formulations, Macrocystis Pyrifera (Kelp) Extract in 188 formulations, and Laminaria Saccharina Extract is used in 132 formulations. All other in-use ingredients are reported to be used in 77 formulations or fewer.

Ascophyllum Nodosum Extract was reported in the VCRP as Ascophyllum Nodosum (Seaweed) Extract and Fucus Vesiculosus Extract was reported as Fucus Vesiculosus (Bladderwrack) Extract. Laminaria Saccharina Extract is reported in the VCRP as Saccharina Latissima (Kelp) Extract; the accepted scientific name for *Laminaria saccharina* is *Saccharina latissima*. There were also entries in the VCRP for ingredients that may be related to the listed brown algae-derived ingredients: kelp (24 uses), kelp extract (15 uses), Laminaria extract (4 uses), Phaeophyceae (brown algae; 4 uses), and seaweed extract (82 uses). It is not known to what extent these erroneous names are connected to any of the ingredients in this report.

The results of the concentration of use surveys conducted by the Council in 2015 and 2016 indicate Laminaria Digitata Powder has the highest reported maximum concentration of use; it is used at up to 40% in face and neck formulations.[50,51] Macrocystis Pyrifera (Kelp) Extract is reported to be used at up to 36.4% in eye lotions. The other ingredients are reported to be used at 6% or less.

In some cases, reports of uses were received in the VCRP, but concentration of use data were not provided. For example, Ascophyllum Nodosum Powder is reported to be used in 4 cosmetic formulations, but no use concentration data were reported. In other cases, no uses were reported in the VCRP, but concentration of use data were reported in the industry survey; Fucus Vesiculosus had no reported uses in the VCRP, but a use concentration in shampoos, moisturizing formulations, and suntan formulations was provided in the industry survey. Therefore, it should be presumed there is at least one use in every category for which a concentration is reported. The ingredients not in use according to 2018 VCRP data and the 2015 and 2016 Council surveys are listed in Table 21.

Several of these ingredients are used in formulations that are used near the eye (e.g., Macrocystis Pyrifera (Kelp) Extract at up to 36.4% in eye lotion and Fucus Vesiculosus Extract in mascara at up to 6%), incidentally ingested (e.g., Macrocystis Pyrifera (Kelp) Extract in lipsticks at up to 0.079%), and in formulations that come in contact with mucous membranes (e.g., Fucus Vesiculosus Extract and Laminaria Digitata Extract at up to 5% in bubble baths and Laminaria Japonica Extract and Macrocystis Pyrifera (Kelp) Extract at up to 5% in bath oils, tablets and salts).

Additionally, some of the brown algae-derived ingredients are used in cosmetic sprays and could possibly be inhaled; for example, Macrocystis Pyrifera (Kelp) Extract is reported to be used at up to 0.79% in spray face and neck products. In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters > 10 µm, with propellant sprays yielding a greater fraction of droplets/particles < 10 µm compared with pump sprays.[52,53] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and thoracic regions of the respiratory tract and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.[54,55] Laminaria Japonica Extract and Macrocystis Pyrifera (Kelp) Extract were reported to be used in face powders at concentrations up to 0.0035%. Conservative estimates of inhalation exposures to respirable particles during the use of loose-powder cosmetic products are 400- to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace.[56-58]

None of the brown algae-derived ingredients named in this report are restricted from use in any way under the rules governing cosmetic products in the European Union.[59]

Non-Cosmetic

Brown seaweeds are consumed around the world and come mostly, but not only, from the *Laminaria*, *Undaria*, and *Hizikia* species.[16] According to the US FDA, brown algae (i.e., several species of seaweeds that are harvested principally in coastal waters of the northern Atlantic and Pacific oceans) are direct food substances that are generally recognized as safe (GRAS) for human consumption for use as flavor enhancers and flavor adjuvants, when the maximum level in food does not exceed the current good manufacturing practice (GMP). [21CFR184.1120] "Kelp" (the dehydrated, ground product prepared from *Macrocystis pyrifera, Laminaria digitata, Laminaria saccharina*, and *Laminaria cloustoni*) is approved as a food additive for direct addition to food for human consumption as a source of iodine or as a dietary supplement. [21CFR172.365] In New Zealand, Japan and other Asian countries, dried sea kelp is a common food; the exact species of kelp used varies according to location.[16] The EFSA NDA Panel concluded that an alcohol extract of *Ecklonia cava* is safe for the use in food supplements at a maximum intake level of 163 mg/day for adolescents from 12 to 14 years of age, 230 mg/day for adolescents above 14 years of age, and 263 mg/day for adults.[9]

In animal drugs, feeds, and related products, brown algae (kelp; *Laminaria* spp. and *Nereocystis* spp.) are GRAS as natural substances [21CFR582.30] and as solvent-free natural extractives [21CFR582.40] used in conjunction with spices and other natural seasonings and flavorings.

In the US, "kelp" is present in OTC medications for weight loss. [21CFR310.545] However, there are inadequate data to establish a general recognition of the safety and effectiveness of this ingredient for that specified use. Several other sources refer to the use of *Fucus vesiculosus* for weight loss.[60,61]

Pastes of seaweed, made by cold grinding or freeze crushing, are used in thalassotherapy, in which the pastes are applied to the body and then warmed under infrared radiation.[16] This treatment, in conjunction with seawater hydrotherapy, is said to provide relief for rheumatism and osteoporosis. In folk medicine, preparations of *Fucus vesiculosus* are used to treat hypothyroidism, iodine deficiency, arteriosclerosis, digestive disorders, menstrual abnormalities, cellulite, and sprains.[60,62] In herbal folk medicine, *Laminaria hyperborean* is used for thyroid regulation, and *Macrocystis Pyrifera* is used to treat thyroid conditions, anemia in pregnancy, and hypertension, weight loss, and as an immunity booster.[60]

Brown algae have been used as fertilizers and soil conditioners (*Ascophyllum*, *Sargassum*, *Ecklonia*, and *Fucus* species), animal feed for sheep, cattle, horses, pigs, and chickens (*Alaria esculenta*, and *Ascophyllum* and *Laminaria* species), feed and feed binder for fish and abalone (*Macrocystis pyrifera*), and biomass fuel (*Macrocystis pyrifera*), and they have been used for waste water/effluent treatment and removal of heavy metals (*Sargassum*, *Laminaria*, and *Ecklonia* species).[16,37] Brown algae are used as biomonitors for heavy metal pollution in estuarine and coastal waters worldwide, and to evaluate the quality of their surrounding environment.[45]

TOXICOKINETIC STUDIES

Obtaining data on the toxicokinetics of uncharacterized, complex mixtures would be impractical, as is the case with many botanical ingredients. No toxicokinetics studies were discovered in the published literature, and no unpublished data were submitted.

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

No acute dermal or inhalation toxicity studies were discovered in the published literature, and no unpublished data were submitted. Acute oral toxicity studies summarized below are presented in Table 22**.**

Oral

Cystoseira Compressa Extract was not toxic to mice when given a single dose of up to 2000 mg/kg by gavage.[63] The oral LD_{50}s of two Fucus Vesiculosus Extracts were 1000 and 500 mg/kg for male mice and between 1000 and 2000 mg/kg and < 750 mg/kg for female mice.[23] In rats (sex not stated), the oral LD_{50}s of two Fucus Vesiculosus Extracts were between 1000 and 2000 mg/kg for one extract and > 2000 mg/kg for the second extract.[23] There were no signs of toxicity when rats were given a single dose of up to 4000 mg/kg Laminaria Japonica Extract via oral gavage.[64] Sargassum Fulvellum Extract and Sargassum Thunbergii Extract were not toxic to mice that were given a single dose of 5000 mg in 10 ml Tween-80 via gavage.[65]

Short-Term, Subchronic, and Chronic Toxicity Studies

No repeated dose dermal or inhalation toxicity studies were discovered in the published literature, and no unpublished data were submitted. Short-term, subchronic, and chronic oral toxicity studies summarized below are presented in Table 23.

Oral

Ascophyllum Nodosum was not toxic when it was fed to pigs via a 10% oral diet for 23 days, or rats fed a 15% diet for 4 weeks.[66,63] Ecklonia Cava Extract was not toxic to rats dosed with up to 3000 mg/kg via oral gavage once daily in rats, and twice daily in dogs, for 13 weeks.[9,21] An enzyme extract of Ecklonia Cava Extract (starting at doses of 2000 mg/kg) administered by gavage for 2 weeks caused reduced ovary and brain weights in female rats.[21] Hepatic effects in rats were observed when animals were dosed with 2000 mg/kg/day via gavage of an alcohol Ecklonia Cava Extract for 4 weeks. When rats were dosed with the same extract in doses of 1500 mg/kg/day for 13 weeks, there were also decreases in body weight gain and organ weights (the hepatic effects resolved after 4 weeks recovery).[9]

Increased liver weights were apparent when two ethanol Fucus Vesiculosus Extracts (starting at doses 200 mg/kg/day) were administered by gavage for 4 weeks in male rats.[23] While consuming high-fat diets, there were no adverse effects caused by alcohol Ecklonia Cava Extract when mice were given doses of up to 5 mg/day via gavage for 4 weeks.[67] An ethanol Laminaria Japonica Extract (up to 400 mg/kg) administered by gavage for 6 weeks caused decreased body weight gain, fat-pad weights, and serum and hepatic lipid levels in rats.[27] Vomiting was the only adverse effect when Ecklonia Cava Extract in capsules was orally administered (in increasing amounts up to 1000 mg/kg over 8 days) to dogs.[9] A *Ecklonia cava* powder (up to 0.15%; inference for Ecklonia Cava Extract and Ecklonia Cava Water) administered in feed for 28 days was not toxic to weanling pigs.[68] An *Undaria pinnatifida* extract (hydrolyzed in hydrochloric acid) administered orally for 28 days was not toxic to rats up to 1000 mg/kg/day, but alanine aminotransferase (ALT) and triglyceride levels in males and high-density lipoprotein (HDL) cholesterol in females increased at 2000 mg/kg/day.[31]

In rats, doses of 1200 to 4000 mg/kg Cladosiphon Okamuranus Extract given once a day for 3 months via gavage caused a dose-dependent increase in clotting time and decrease in alkaline phosphatase (ALP) that was not observed with lower doses.[19] There were no other adverse effects reported.

Laminaria Japonica Powder (up to 5%) was incorporated in the feed of mice from the age of 7 weeks until death. There were no dose-dependent effects on the lifespan of mice.[29] Undaria Pinnatifida Extract administered via drinking did not cause any toxic effects in rats when administered for 32 weeks.[69] Undaria Pinnatifida Extract (up to 5%) incorporated into feed of rats for 36 weeks did not cause any toxic effects.[29] The no observable adverse effect level (NOAEL) of a Laminaria Japonica Extract administered to rats by gavage for 6 months was 300 mg/kg/day.[64] In females, a decrease in aspartate aminotransferase (AST) was observed starting at 300 mg/kg/day and, at 2500 mg/kg/day, there was decreased serum glucose concentration. After a 1-month recovery period, these changes in glucose and AST returned to baseline.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY (DART) STUDIES

No DART studies were discovered in the published literature, and no unpublished data were submitted.

GENOTOXICITY STUDIES

The in vitro and in vivo genotoxicity studies summarized below are presented in Table 24.

In Vitro

Ascophyllum Nodosum Extract was not genotoxic in an Ames assay (up to 5000 µg/plate), a mammalian cell gene mutation test (up to 500 µg/ml), or in chromosomal aberration assays (up to 5 mg/ml); in a mammalian cell gene mutation test, Ascophyllum Nodosum Extract was genotoxic to Chinese hamster ovary (CHO) cells starting at 1500 µg/ml.[6] An Ames test was performed according to the Organisation for Economic Co-operation and Development (OECD) test guideline (TG) 471 on a trade name mixture containing 4.7% Ascophyllum Nodosum Extract in 94.5% water.[44] No mutagenic activity was reported. Ecklonia Cava Extract was not genotoxic in Ames assays (up to 5000 µg/plate) or chromosomal aberration assays (up to 350 µg/plate).[9,21] Aqueous Fucus Vesiculosus Extract was not genotoxic in a chromosomal aberration assay (up to 1 mg/ml) or a comet assay (up to 1 mg/ml).[70] Laminaria Japonica Extract (up to 5000 µg/plate) was not mutagenic in an Ames assay or a chromosomal aberration assay.[26] Undaria Pinnatifida Extract was not genotoxic in Ames assays (up to 5000 µg/plate)[31,71,72] or chromosomal aberration assays (up to 5000 µg/ml).[71,72]

In Vivo

Ecklonia Cava Extract was not genotoxic in micronucleus assays up to 3000 mg/kg.[9,21] Laminaria Japonica Extract and Undaria Pinnatifida Extract were not genotoxic in micronucleus assays at up to 2000 mg/kg.[26,49,71,72]

CARCINOGENICITY STUDIES

No carcinogenicity studies were discovered in the published literature, and no unpublished data were submitted.

Tumor Promotion

Tumor promotion studies summarized below are presented in Table 25. The brown algae-derived ingredients that

were tested were not tumor promoters; instead, decreases in the number, incidence, and size of tumors in rats and mice were observed.

Dermal

Mice were treated dermally with a single dose of 7,12-dimethylbenz[a]anthracene (DMBA; a carcinogen) followed by biweekly treatments for fifteen weeks with 12-*O*-tetradecanoylphorbol-13-acetate (TPA; a tumor promotor) or Undaria Pinnatifida Extract (1 mg).[73] The mice treated with Undaria Pinnatifida Extract had a delayed appearance of skin tumors (14 vs 8 weeks) and fewer tumors (average 0.2 vs 3.7) compared to the TPA-treated mice.

Oral

Rats injected with azoxymethane (AOM; a carcinogen) and then fed a diet containing Hizikia Fusiforme Extract (2% and 6%) had a reduced number of colorectal tumors (21 vs 58) compared to rats injected with AOM and fed a normal diet.[74] A *Saccharina angustata* powder (5%; inference for Saccharina Angustata Extract) in feed delayed the appearance and reduced the incidences of mammary tumors in rats orally administered DMBA.[75]

Rats administered *N*-methyl-*N'*-nitro-*N*-nitrosoguanidine (MNNG; a carcinogen) followed by Sargassum Pallidum Extract (0, 400, 600 and 800 mg/kg/day) in drinking water for 8 weeks had decreased inflammatory responses; serum IL-6, IL-1β, and TNF-α levels and concentration of serum and gastric mucosa malondialdehyde (MDA; an oxidant) were decreased in a dose-dependent manner.[76] In rats administered Undaria Pinnatifida Powder (0, 1.0% or 5.0% in feed) for 8 weeks after oral administration of DMBA, the mean combined weight of all mammary tumors of each rat in treatment groups was lower than that in the control group (approximately 7 vs 20 g).[77] Undaria Pinnatifida Extract (100% as drinking water) for 32 weeks reduced the incidence of mammary tumors (22% vs 100%) after female rats were orally administered DMBA.[69]

OTHER RELEVANT STUDIES

Estrogenic Effects and Progesterone Receptor Binding

In Vitro

Fucus vesiculosus extract

Human granulosa cells (obtained from 8 women) were treated with a water:ethanol (1:1) *Fucus vesiculosus* extract (25, 50, or 75 µmol/l) for 9 days.[78] Ethanol (50%) served as the vehicle control. At 50 and 75 µmol/l, the extract significantly reduced 17-β-estradiol levels in human granulosa cells and also competed with estradiol (E2) and progesterone for binding to their receptors.

Affinity of this extract for estrogen receptor-α (ERα), ERβ, and progesterone receptor (PR)-B was determined by radiometric competitive binding assays.[78] Dried extract (0.5, 5, or 50 µmol/l final concentration) was re-solubilized in dimethyl sulfoxide and combined with ERα or ERβ and 0.5 nmol/l estradiol. Non-specific binding was estimated in the presence of 1 µmol/l diethylstilbesterol. To test PR-B binding, the extract was incubated with PR-B and 1.4 nmol/l radiolabeled progesterone. Non-specific binding was estimated in the presence of 1 µmol/l progesterone. The extract competed for and bound to ERα (IC_{50} = 42.2 µmol/l), ERβ (IC_{50} = 31.8 µmol/l), and PR-B (IC_{50} = 31.8 µmol/l), with a slightly greater affinity for ERβ. The inhibition of progesterone production was less prominent, and there was no concentration-response relationship. In contrast, there was a concentration-dependent occupancy of the estrogen and progesterone receptors. Compounds found in *Fucus vesiculosus* could act as estradiol antagonists by decreasing the affinity of either ERα or ERβ for its ligand.

In competitive radio-ligand binding assays, aromatase activity was estimated by measuring the incorporation of tritium from androstenedione into water in the presence or absence of a *Fucus vesiculosus* extract (10, 50, or 100 µmol/L).[78] Aromatase activity following treatment of human luteinized granulosa cells (hLGCs) with this extract did not change.

A chemically activated luciferase reporter (CALUX®) assay was used to determine the effect of an aqueous *Fucus vesiculosus* extract on activation of the ER.[79] Aromatase enzymatic activity was measured to determine the potential effect of this extract on E2 biosynthesis. In co-treatments with E2, this extract (2%) reduced the activation of the luciferase reporter by up to 50%, exhibiting potent ER antagonistic effects. The effect of this extract (0 to 2%) on aromatase activity was measured using recombinant human CYP19 enzymatic hydrolysis of the fluorescent substrate, 7-methoxy-4-rifluoromethyl coumarin, in a 96-well plate. Ketoconazole was used as the positive marker of aromatase inhibition. This extract inhibited aromatase activity (IC_{50} 2.0%). ER-dependent and -independent cancer cell lines showed significantly decreased viability with increasing *Fucus vesiculosus* extract concentrations; altered morphological features suggested apoptosis and autophagy. The cell line-specific sensitivity suggests that *Fucus vesiculosus* extract was not toxic at up to 2%, but instead induces cell death through modulated pathways.

Animal

Fucus vesiculosus powder

Female Sprague-Dawley rats (n = 8), that had two confirmed normal estrous cycles, were administered a *Fucus vesiculosus* powder (0, 175, or 350 mg/kg/day) on an apple wedge daily for 4 weeks.[78] Vaginal smears were obtained and daily logs were maintained to monitor estrous cycling. No adverse effects were observed during the course of the experiment. Administration of this powder resulted in a statistically-significant, dose-dependent increase in the length of the estrous cycle in the treated rats. In the control group, the mean number of days of the estrous cycle was 4.3 ± 0.96 days compared to 5.4 ± 1.7 days in the low-dose group and 5.9 ± 1.9 days in the high-dose group. Treatment with this powder caused an overall 100% increase in the mean length of the diestrus phase of the estrous cycle. The mean number of days in diestrus was 0.97 ± 0.22 among the controls compared to 1.4 ± 0.54 in the low-dose group and 2.1 ± 0.88 days in the high-dose group. Treatment had no significant effect on the number of days in estrus, proestrus, or metestrus during the mean estrous cycle. After treatment was stopped, five rats stopped normal estrous cycling; one remained in estrus and four in diestrus.

Blood samples were collected from female Sprague-Dawley rats (n = 19) before treatment, and at 2 and 4 weeks of the oral administration of this powder (0 or 175 mg/kg/d) on apple wedges.[78] At 2 weeks, mean serum 17β-estradiol levels were reduced from 48.9 ± 4.5 to 40.2 ± 3.2 ng/l and, after 4 weeks, reduced the levels from baseline to 36.7 ± 2.2 ng/l (25% decrease), suggesting an effect of dosing over time. Serum progesterone levels between controls and the treatment groups did not differ.

Blood samples were collected from female Sprague-Dawley rats (n = 8), that had naturally high circulating estradiol levels (≥ 50 µg/l), before, and after 1 week of the oral administration of this powder (350 mg/kg/day) on apple wedges.[78] Median serum 17-β-estradiol levels decreased by 38%. The range in reduction of serum 17-β-estradiol levels in 6 of the rats was 25% to 58%, whereas 2 rats had levels similar to their baseline levels. Progesterone levels were not significantly affected following this treatment. This could be due to the fact that in the studies with rats the blood samples were collected in the morning, and in the morning the 17-β-estradiol levels were at their peak but the progesterone levels were not.

Photoprotection

Sargassum muticum

The effect of a *Sargassum muticum* extract against cell death induced by UVB radiation was studied.[80] Cells were seeded in a 96-well plate at a concentration of $1x10^{-5}$ cells/mL. Sixteen hours after plating, 100 µg/mL of *Sargassum muticum* extract were added to the cells and exposed to UVB radiation at a dose of 150 mJ/cm^2. Cell viability was 61% in UVB (150 mJ/cm^2) irradiated cells and 70% in UVB-irradiated cells treated with *Sargassum muticum* extract. Decreased numbers of apoptotic bodies as well as DNA fragmentation was apparent in cells exposed to *Sargassum muticum* extract and UVB versus UVB exposure alone.

Hydrolyzed Fucoidan

Unpublished data were submitted on a trade name mixture containing 7% hydrolyzed fucoidan extracted from *Laminaria digitata*.[81] Fucoidan is a primary constituent in many brown algae species. Although not being reviewed in this report, fucoidan [defined in the *Dictionary* as a sulfated polysaccharide extracted from brown algae] and hydrolyzed F-fucoidan [defined in the *Dictionary* as the hydrolysate of F-fucoidan derived by acid enzyme or other method of hydrolysis; F-fucoidan is derived from various species of algae and is comprised of sulfated esters of fucose] are both cosmetic ingredients.[1]

According to the submission, this trade name mixture was not mutagenic in an Ames test. Also, in vitro studies were performed examining several endpoints.[81] To predict dermal irriation potential using reconstituted human epidermis, the trade name mixture was classified as a non-irritant. In a study in which Balb/c 3T3 cells were exposed to the trade name mixture at concentrations of 0%, 6.90%, 20.55%, 61.80%, or 100%, no toxic effects were observed after irradiation indicating no phototoxic potential. Also, in a neutral red uptake assay performed using BALB/c 3T3 cells, the modified maximum average score (MMAS) was < 25, and the trade name mixture reported to be not/mildly irritating.

DERMAL IRRITATION AND SENSITIZATION STUDIES

Irritation

In Vitro

Ascophyllum Nodosum Extract

In a cutaneous irritation test performed according to OECD TG 439 (reconstructed human epidermis test), a trade name mixture containing 4.7% Ascophyllum Nodosum Extract in 94.5% water was considered to be a non-irritant. No additional details were provided.[44]

In Vivo

Animal

Ascophyllum Nodosum Extract

A dermal irritation assay of an *Ascophyllum nodosum* extract (0.5 g in water) was conducted in accordance with the OECD TG 404 (Acute Dermal Irritation/Corrosion) using New Zealand White rabbits (n = 3 males).[6] The test substance was administered in three patches on areas of 12-20 cm^2 to the shaved backs of the rabbits under semi-occlusion for 3 min (patch 1), 1 h (patch 2), and 4 h (patch 3). There were no signs of irritation after the removal of patch 1 from one rabbit; patch 2 was then applied to the same rabbit. There were no signs of irritation after patch 2 was removed; patch 3 was then applied to all three rabbits. The test site was examined at 1, 24, 48, and 72 h after the removal of the last patch. The primary irritation index was 0 out of 8 at each observation.

Human

Laminaria japonica extract

A patch test on a skin cream containing a 50/50 aqueous/propylene glycol extract of *Laminaria japonica* (10%; 20 mg) was conducted.[28] Patches were applied to the forearms of subjects (n = 25) using Finn chambers for up to 48 h and scored for irritation 6 h after patch removal. The test substance had a score of 0 and was considered to be non-irritating.

Sensitization

Human

Alaria Esculenta Extract

The sensitization potential of a night cream containing 0.05% Alaria Esculenta Extract was tested using a human repeated insult patch test (HRIPT) in 105 subjects.[82] Approximately 0.2 g of the test material was applied to the upper back under a semi-occlusive patch. During the induction phase, patches were applied 3 times per week for 3 weeks, for a total of 9 applications. If the test site caused a moderate reaction (2-level), the application was moved to an adjacent area. If 3-level or 4-level reactions were noted, applications were discontinued. Two weeks after the final induction application, a challenge patch was applied to a previously untested site adjacent to the original patch site. Patches were removed and sites were scored 24 and 72 hours after application. The test substance did not indicate a potential for dermal irritation or allergic contact sensitization.

Sargassum Muticum Extract

An HRIPT was performed using an eye cream containing 0.076% Sargassum Muticum Extract followingthe same protocol described above.[83] Approximately 0.2 g of the test material was applied to the 1" x 1" absorbent pad portion of a clear adhesive dressing, and placed on the upper back of 103 subjects. The test substance did not indicate a potential for dermal irritation or allergic contact sensitization. Another HRIPT following the same protocol was performed using a skin care product containing 0.076% Sargassum Muticum Extract in 104 subjects.[84] No potential for dermal irritation or allergic contact sensitization was noted.

Phototoxicity

In Vitro

Ascophyllum Nodosum Extract

A phototoxicity study was performed according to OECD TG 432 (3T3 NRU phototoxicity test) using a trade name mixture containing 4.7% Ascophyllum Nodosum Extract in 94.5% water.[44] No phototoxic activity was reported. No additional details were provided.

OCULAR IRRITATION STUDIES

In Vitro

Ascophyllum Nodosum Extract

In a specifications data sheet, a trade name mixture containing 4.7% Ascophyllum Nodosum extract in 94.5% water was practically non-irritating when used in a Het-Cam test.[44] No additional details were provided.

Animal

Ascophyllum Nodosum Extract

An ocular irritation test was conducted on an *Ascophyllum nodosum* extract (100 mg) in accordance with OECD TG 405 (Acute Eye Irritation/Corrosion) using New Zealand White rabbits (n = 3 males).[6] The test substance was instilled into one eye of each rabbit; the other eye served as the control. After 1 h, both eyes were washed with water. The eyes were examined at 1, 24, 48, and 72 h and 7 days after instillation. The maximum irritation score was 6.7 out of 8 at 1 h post-instillation; the score decreased to 0 by day 7, which indicated that the induced changes were reversible, and thus, the effects of the test substance were classified as 'irritation' and not as 'corrosion.' The test substance was rated as a mild ocular irritant.

CLINICAL STUDIES

Case Reports

Oral case reports regarding brown algae-derived supplements are presented in Table 25. Decreased platelet count and an increased amount of arsenic in the blood was noted in subjects taking kelp supplements. [85,86]

Clinical Trials

Oral

Clinical trials summarized below are presented in Table 26.

In an oral clinical trial in which an *Ascophyllum nodosum* powder (0.5g/d) was administered to healthy female subjects, median urinary iodine concentrations increased from 78 mg/l to 140 mg/l, and thyroid-stimulating hormone (TSH) concentrations increased slightly, but remained within the normal range.[87] There were no adverse events reported. Administration of an alcohol extract of *Ecklonia cava* (400 mg/day) to subjects with hypercholesterolaemia for 12 weeks did not have an effect on hematology, clinical chemistry, or urinalysis parameters; however, one instance (2.2%) each of nausea, dyspepsia, diarrhea, and alopecia were reported.[9,88] A phlorotannin-rich extract of *Ecklonia cava* (0, 72, or 144 mg/day) was administered for 12 weeks to overweight patients in a randomized, double-blind study. Hematological and clinical chemistry did not reveal any adverse effects; the 144 mg/day group showed decreases in serum glucose and systolic blood pressure (SBP).[9] Administration of capsules containing a desalinated *Undaria pinnatifida* powder (average intake estimated to be 3.3 g per day) to hypertensive subjects for 8 weeks resulted in a decrease in the average SBP, diastolic blood pressure (DBP), and total cholesterol; adverse effects included two cases of indigestion and one case of diarrhea, both of which resolved quickly without treatment.[42]

Three pre-menopausal women with irregular menstrual cycles were administered a *Fucus vesiculosus* powder.[89] Subject number 1 was 43 years old with hypermenorrhea, polymenorrhea, dysmenorrhea, luteal phase deficiency, and endometriosis. Subject number 2 was 42 years old with hypermenorrhea, polymenorrhea, and dysmenorrhea. Subject number 3 was 21 years old with hypermenorrhea, dysmenorrhea, and endometriosis. Menstrual cycles were tracked for three cycles and serum 17β-estradiol and progesterone levels were measured before treatment started. Then the women were administered this powder in capsules (700 mg/day) for two menstrual cycles. Serum 17-β-estradiol and progesterone levels were measured again. Subject 2 stopped treatment at this point and subjects 1 and 3 continued treatment with a greater dose of this powder (1400 mg/day) for two more cycles. This powder increased the menstrual cycle length and reduced the days of menstruation in a dose-dependent manner (Table 27). In subject 1, the plasma estradiol levels were decreased (before: 626 ± 91 pg/ml; low dose: 164 ± 30 pg/ml; high dose: 92.5 ± 3.5 pg/ml) and the progesterone levels were increased (before: 0.58 ± 0.14 ng/ml; low-dose: 8.4 ± 2.6 ng/ml; high-dose: 16.8 ±0.7 ng/ml).[89]

Use Studies

Fucus vesiculosus extract

A gel formulation containing 1% of an aqueous extract of *Fucus vesiculosus* (0.2 ml) was tested in a double-blind, placebo-controlled experiment.[24] Female subjects (n = 10) applied the gel to one cheek at least twice per day (morning and evening) for 5 weeks. The same gel, without the extract, was applied to the other cheek. The skin was examined before the experiment began, daily, and after the experiment ended. There were no signs of erythema or edema during the experiment.

Sargassum Muticum Extract

The ophthalmic irritation potential of an eye cream containing 0.076% Sargassum Muticum Extract was tested in 31 subjects, approximately 50% of which wore soft contact lenses.[90] Subjects were directed to apply the cream twice daily at the eye contour, excluding eyelids. A comprehensive ocular examination was performed after 4 weeks of test material usage. The test material did not indicate a potential for ophthalmologic irritation and was considered safe for use by both contact and non-contact lens wearers.

SUMMARY

This is a review of the safety of 83 brown algae-derived ingredients as used in cosmetics. The ingredients in this review are extracts, powders, juices, or waters derived from one or multiple species of brown algae and may be derived from the whole or a defined part of the seaweed. "Brown algae" is a common name for seaweeds of the class *Phaeophyceae*, which have an abundance of xanthophyll pigments and are a known source of alginate. The most frequently reported function of brown algae in cosmetics is as a skin-conditioning agent; other reported functions include absorbent, antioxidant, binder, hair conditioning agent, oxidizing agent, and viscosity increasing agent.

Extraction methods and solvents vary, depending on the desired composition of the final ingredient. Powders, however, are generally the dried algae pulverized by milling. Inorganic arsenic, usually in the form of arsenosugars, is a natural constituent of brown algae and the amount in the harvested algae can be reduced by several methods. In addition to arsenic, brown algae exhibit an affinity for heavy metals and uptake is strongly dependent on environmental parameters.

According to VCRP survey data received in 2018, Fucus Vesiculosus Extract is reported to be used in 287 formulations (201 in leave-on formulations, 75 in rinse-off formulations, and 11 diluted for the bath). Laminaria Digitata Extract is reported to be used in 235 formulations and Macrocystis Pyrifera (Kelp) Extract in 188 formulations. All other in-use ingredients are reported to be used in 132 formulations or fewer. The results of the concentration of use surveys conducted by the Council in 2015 and 2016 indicate Laminaria Digitata Powder has the highest reported maximum concentration of use; it is used at up to 40% in face and neck formulations. Macrocystis Pyrifera (Kelp) Extract is reported to be used at up to 36.4% in eye lotions. The rest of these ingredients are reported to be used at 6% or less.

According to the US FDA, brown algae (i.e., several species of seaweeds that are harvested principally in coastal waters of the northern Atlantic and Pacific oceans) are direct food substances that are generally recognized as safe (GRAS) for human consumption for use as flavor enhancers and flavor adjuvants, when the maximum level in food does not exceed the current good manufacturing practice (GMP). "Kelp" (the dehydrated, ground product prepared from Macrocystis pyrifera, Laminaria digitata, Laminaria saccharina, and Laminaria cloustoni) is approved as a food additive for direct addition to food for human consumption as a source of iodine or as a dietary supplement. In animal drugs, feeds, and related products, brown algae (kelp; *Laminaria* spp. and *Nereocystis* spp.) are GRAS as natural substances and as solvent-free natural extractives used in conjunction with spices and other natural seasonings and flavorings. Acute oral administration of brown algae extracts was not toxic to mice, rats, and dogs. Cystoseira Compressa Extract was not toxic to mice up to 2000 mg/kg by gavage. Ecklonia Cava Extract was not toxic to rats and dogs up to 3000 mg/kg by gavage. The oral LD_{50}s of two different Fucus Vesiculosus Extracts were 500 mg/kg and greater for mice and rats. There were no signs of toxicity at up to 4000 mg/kg Laminaria Japonica Extract orally administered to rats. Sargassum Fulvellum Extract and Sargassum Thunbergii Extract administered by gavage were not toxic to mice.

In oral short-term and subchronic studies, there were some adverse effects observed. In rats, Cladosiphon Okamuranus Extract (1200 to 4000 mg/kg by gavage) caused a dose-dependent increase in clotting time and decrease in ALP; there were no other adverse effects reported. An enzyme extract of Ecklonia Cava Extract (starting at 2000 mg/kg) administered by gavage for 2 weeks caused reduced ovary and brain weights in female rats. Hepatic effects in rats were observed in an alcohol Ecklonia Cava Extract at 2000 mg/kg/day for 4 weeks and at 1500 mg/kg/day when administered for 13 weeks (the hepatic effects resolved after 4 weeks of recovery). There were increased liver weights in male rats treated with two ethanol Fucus Vesiculosus Extracts (starting at 200 mg/kg/day) administered by gavage for 4 weeks. Vomiting was the only adverse effect when Ecklonia Cava Extract capsules (in increasing amounts up to 1000 mg/kg over 8 days) were orally administered to dogs.

In other oral short-term and subchronic studies, there no adverse effects observed. Ascophyllum Nodosum was not toxic to pigs for 23 days or to rats for 4 weeks administered in feed at up to 10% and 15%, respectively. While consuming high-fat diets, there were no adverse effects caused by alcohol Ecklonia Cava Extract (up to 5 mg/day) administered to mice by gavage daily for 4 weeks and an ethanol Laminaria Japonica Extract (up to 400 mg/kg) administered by gavage for 6 weeks caused decreased body weight gain, fat-pad weights, and serum and hepatic lipid levels in rats. A *Ecklonia cava* powder (up to 0.15%; inference for Ecklonia Cava Extract and Ecklonia Cava Water) administered in feed for 28 days was not toxic to weanling pigs. An orally administered *Undaria pinnatifida* extract for 28 days was not toxic to rats up to 1000 mg/kg/day, but ALT and triglyceride levels in males and HDL cholesterol in females increased at 2000 mg/kg/day.

In a chronic oral toxicity study, the NOAEL of a Laminaria Japonica Extract administered to rats by gavage for 6 months was 300 mg/kg/day. In females, a decrease in AST was observed starting at 300 mg/kg/day and, at 2500 mg/kg/day, there was decreased serum glucose concentration; all effects returned to baseline after a 1-month recovery. Laminaria Japonica Powder incorporated into feed did not affect the lifespan of mice at up to 5%. In rats, Undaria Pinnatifida Extract administered as drinking water at 100% for 32 weeks and incorporated into the feed (at up to 5%) for 36 weeks did not cause any toxic effects.

In genotoxicity assays of several of the brown algae-derived ingredients, all results were negative with the exception of an Ascophyllum Nodosum Extract in one mammalian cell gene mutation test in which the extract was genotoxic starting at 1500 µg/ml in CHO cells. Ascophyllum Nodosum Extract was not genotoxic in an Ames assay and a mammalian cell gene mutation test (up to 500 µg/ml), and in chromosome aberration assays (up to 5 mg/ml). Cystoseira Compressa Extract (up to 5 mg/plate) was not genotoxic in an Ames assay. Ecklonia Cava Extract was not genotoxic in Ames assays (up to 5000 µg/plate) and chromosome aberration assays (up to 350 µg/plate). Aqueous Fucus Vesiculosus Extract was not genotoxic in

a chromosome aberration assay and a comet assay (up to 1 mg/ml). Laminaria Japonica Extract (up to 5000 µg/plate) was not mutagenic in an Ames assay and a chromosome aberration assay. Undaria Pinnatifida Extract was not genotoxic in Ames assays and chromosome aberration assays (up to 5000 µg/ml). In micronucleus assays, Ecklonia Cava Extract (up to 3000 mg/kg), Laminaria Japonica Extract (up to 2000 mg/kg), and Undaria Pinnatifida Extract (up to 2000 mg/kg) were not genotoxic. An Ames test was performed according to OECD TG 471 using a trade name mixture containing 4.7% Ascophyllum Nodosum Extract in 94.5% water.[44] No mutagenic activity was reported.

None of the orally or dermally administered brown algae-derived ingredients tested (e.g., Hizikia Fusiforme Extract, Saccharina Angustata Extract (inference from *Saccharina angustata* powder), Undaria Pinnatifida Extract, and Undaria Pinnatifida Powder) were tumor (mammary and colorectal) promoters; instead, decreases in the number, incidence, and/or size of tumors in rats were reported. Rats administered MNNG followed by 8 weeks of Sargassum Pallidum Extract (400 to 800 mg/kg/day) in drinking water exhibited decreased inflammatory responses.

A *Fucus vesiculosus* extract exhibited estrogen effects in several in vitro studies. This extract (50 and 75 µmol/l) reduced 17-β-estradiol levels in human granulosa cells and also competed with estradiol and progesterone for binding to their receptors. In another study, a *Fucus vesiculosus* extract competed for, and bound to, ERα (IC_{50} = 42.2 µmol/l), ERβ (IC_{50} = 31.8 µmol/l), and PR-B (IC_{50} = 31.8 µmol/l), with a slightly higher affinity for ERβ. In co-treatments with E2 (12.5 pM; EC_{50}), a *Fucus vesiculosus* extract (2%) reduced the activation of the luciferase reporter by up to 50%, exhibiting potent ER antagonistic effects. ER-dependent and -independent cancer cell lines showed significantly decreased viability with increasing test material concentrations. The cell line-specific sensitivity suggests that *Fucus vesiculosus* extract was not toxic at up to 2%, but instead induces cell death through modulated pathways. In one study, aromatase activity following treatment of hLGCs with a *Fucus vesiculosus* extract (10 to 100 µmol/L) did not change.

In in vivo studies, a *Fucus vesiculosus* powder exhibited estrogenic effects. Daily oral administration (175 and 350 mg/kg/day) for 4 weeks resulted in a dose-dependent increase in the length of the estrous cycle and an overall 100% increase in the mean length of the diestrus phase of the estrous cycle in the treated rats. Mean serum 17-β-estradiol levels were reduced at 2 weeks and further reduced at 4 weeks. Female rats that had naturally high circulating estradiol had reduced serum 17-β-estradiol (25% to 58% in all but 2 rats) after 1 week oral administration of a *Fucus vesiculosus* powder (350 mg/kg/day). This powder (700 and 1400 mg/day) increased the menstrual cycle length and reduced the days of menstruation in a dose-dependent manner in three female human subjects with hypermenorrhea, dysmenorrhea, and other related ailments. In one subject, the plasma estradiol levels were decreased and the progesterone levels were increased in a dose-dependent manner.

In an in vivo dermal irritation assay of an *Ascophyllum nodosum* extract (0.5 g in water) conducted in accordance with the OECD TG 404, a trade name mixture containing 4.7% Ascophyllum Nodosum Extract in 94.5% water was not considered to be an irritant. An *Ascophyllum nodosum* extract (0.5 g in water) administered to the shaved backs of rabbits under semi-occlusion for 4 h was not irritating. A skin cream containing a *Laminaria japonica* extract (10%; 20 mg) was not irritating to human subjects.

HRIPTs were performed using a night cream containing 0.05% Alaria Esculenta Extract, an eye cream containing 0.076% Sargassum Muticum Extract, and a skin care formulation containing 0.076% Sargassum Muticum Extract. No potential for dermal irritation or allergic contact sensitization was noted for any of the formulations.

A phototoxicity study was performed according to OECD TG 432 using a trade name mixture containing 4.7% Ascophyllum Nodosum Extract in 94.5% water. No phototoxic activity was reported.

According to a specifications data sheet, a trade name mixture containing 4.7% Ascophyllum Nodosum Extract in 94.5% water was practically non-irritating when used in a Het-Cam test.

An *Ascophyllum nodosum* extract (100 mg) administered to the eyes of rabbits had a maximum irritation score was 6.7 out of 8 at 1 h post-instillation. The score decreased to 0 by day 7 and was rated as a mild ocular irritant. The ophthalmic irritation potential of an eye cream containing 0.076% Sargassum Muticum Extract was tested in 31 subjects The test material did not indicate a potential for ophthalmologic irritation and was considered safe for use by both contact and non-contact lens wearers.

In oral human clinical trials, adverse effects of an *Ascophyllum nodosum* powder (0.5g/d), an *Ecklonia cava* extract (up to 400 mg/day), and an *Undaria pinnatifida* powder (average intake 3.3 g per day) were mild and transient. The adverse effects included nausea, indigestion, dyspepsia, and diarrhea.

A gel with an aqueous *Fucus vesiculosus* extract (1%; 0.2 ml) was applied to one cheek of human subjects at least twice per day (morning and evening) for 5 weeks. There were no signs of erythema or edema during the experiment.

Different studies were performed testing the toxic potential of fucoidan, a primary constituent in many brown algae species. No evidence of mutagenicity was reported when an Ames test was performed using a trade name mixture containing 7% hydrolyzed fucoidan extracted from *Laminaria digitata*. A dermal irritation assay was performed using the same trade name mixture containing. The product was classified as a non-irritant.

No phototoxic potential was reported when Balb/c 3T3 cells were exposed to a mixture containing 7% hydrolyzed fucoidan extracted from *Laminaria digitata.*

A neutral red uptake assay was performed on BALB/c 3T3 cells using a trade name mixture containing 7% hydrolyzed fucoidan extracted from *Laminaria digitata*. The product was reported to be not/mildly irritating.

In an in vitro study examining the photo-protection potential involving a *Sargassum muticum* extract, the effect of this extract against cell death induced by UVB radiation was studied. Cell viability was 61% in UVB (150 mJ/cm^2) irradiated cells and 70% in UVB-irradiated cells treated with SME. Decreased numbers of apoptotic bodies as well as DNA fragmentation was apparent in cells exposed to SME and UVB versus UVB exposure alone.

DISCUSSION

To be developed.

CONCLUSION

To be determined.

TABLES

Table 1. Brown algae ingredients included in this assessment

Agarum Cribrosum Extract	Fucus Vesiculosus	Macrocystis Pyrifera (Kelp) Juice
Alaria Esculenta Extract	Fucus Vesiculosus Extract	Macrocystis Pyrifera (Kelp) Protein
Ascophyllum Nodosum	Fucus Vesiculosus Powder	Nereocystis Luetkeana Extract
Ascophyllum Nodosum Extract	Halidrys Siliquosa Extract	Pelvetia Canaliculata Extract
Ascophyllum Nodosum Powder	Halopteris Scoparia Extract	Pelvetia Siliquosa Extract
Cladosiphon Novae-Caledoniae Extract	Himanthalia Elongata Extract	Phyllacantha Fibrosa Extract
Cladosiphon Okamuranus Extract	Himanthalia Elongata Powder	Saccharina Angustata Extract
Cystoseira Amentacea/Caespitosa/ Branchycarpa Extract	Hizikia Fusiforme Extract	Saccharina Japonica Extract
	Hizikia Fusiformis Water	Saccharina Longicruris Extract
Cystoseira Baccata Extract	Hizikia Fusiformis Callus Culture Extract	Sargassum Filipendula Extract
Cystoseira Balearica Extract	Hydrolyzed Ecklonia Cava Extract	Sargassum Fulvellum Extract
Cystoseira Caespitosa Extract	Hydrolyzed Fucus Vesiculosus Extract	Sargassum Fusiforme Extract
Cystoseira Compressa Extract	Hydrolyzed Fucus Vesiculosus Protein	Sargassum Glaucescens Extract
Cystoseira Compressa Powder	Laminaria Cloustoni Extract	Sargassum Horneri Extract
Cystoseira Tamariscifolia Extract	Laminaria Diabolica Extract	Sargassum Muticum Extract
Dictyopteris Polypodioides Extract	Laminaria Digitata Extract	Sargassum Pallidum Extract
Dictyota Coriacea Extract	Laminaria Digitata Powder	Sargassum Siliquastrum Extract
Durvillaea Antarctica Extract	Laminaria Hyperborea Extract	Sargassum Thunbergii Extract
Ecklonia Cava Extract	Laminaria Japonica Extract	Sargassum Vulgare Extract
Ecklonia Cava Water	Laminaria Japonica Powder	Sphacelaria Scoparia Extract
Ecklonia Kurome Extract	Laminaria Longissima Extract	Undaria Peterseniana Extract
Ecklonia Kurome Powder	Laminaria Ochroleuca Extract	Undaria Pinnatifida Extract
Ecklonia/Laminaria Extract	Laminaria Saccharina Extract	Undaria Pinnatifida Cell Culture Extract
Ecklonia Maxima Extract	Lessonia Nigrescens Extract	Undaria Pinnatifida Leaf/Stem Extract
Ecklonia Maxima Powder	Lessonia Nigrescens Powder	Undaria Pinnatifida Powder
Ecklonia Radiata Extract	Macrocystis Pyrifera (Kelp)	Undaria Pinnatifida Root Powder
Eisenia Arborea Extract	Macrocystis Pyrifera (Kelp) Blade/Pneumatocyst/Stipe Juice Extract	
Fucus Serratus Extract		
Fucus Spiralis Extract	Macrocystis Pyrifera (Kelp) Extract	

Table 2. Current and revised INCI names, definitions, and functions of the *brown algae*-derived ingredients in this safety assessment.[1]

Ingredient	Definition	Function
Agarum Cribrosum Extract	Agarum Cribrosum Extract is the extract of the alga, *Agarum cribrosum.*	Skin-conditioning agent - miscellaneous
Alaria Esculenta Extract	Alaria Esculenta Extract is the extract of the alga, *Alaria esculenta*.	Hair conditioning agent; skin protectant
Ascophyllum Nodosum	Ascophyllum Nodosum is the alga, *Ascophyllum nodosum.*	Skin-conditioning agent - miscellaneous
Ascophyllum Nodosum Extract 84775-78-0	Ascophyllum Nodosum Extract is the extract of the alga, *Ascophyllum nodosum.*	Skin-conditioning agent - miscellaneous
Ascophyllum Nodosum Powder	Ascophyllum Nodosum Powder is the powder obtained from the dried, ground alga, *Ascophyllum nodosum.*	Skin-conditioning agent - miscellaneous
Cladosiphon Novae-Caledoniae Extract	Cladosiphon Novae-Caledoniae Extract is the extract of the alga, *Cladosiphon novae-caledoniae.*	Humectant; skin protectant
Cladosiphon Okamuranus Extract	Cladosiphon Okamuranus Extract is the extract of the alga, *Cladosiphon okamuranus.*	Skin-conditioning agent - miscellaneous
Cystoseira Amentacea/Caespitosa/ Branchycarpa Extract	Cystoseira Amentacea/Caespitosa/Branchycarpa Extract is the extract of the algae, *Cystoseira amentacea, Cystoseira caespitosa*, and *Cystoseira branchycarpa*.	Skin-conditioning agent - miscellaneous
Cystoseira Baccata Extract	Cystoseira Baccata Extract is the extract of the alga, *Cystoseira baccata*.	Skin-conditioning agent - miscellaneous
Cystoseira Balearica Extract	Cystoseira Balearica Extract is the extract of the alga, *Cystoseira balearica.* The accepted scientific name for *Cystoseira balearica* is *Cystoseira brachycarpa.*	Skin-conditioning agent - miscellaneous
Cystoseira Caespitosa Extract	Cystoseira Caespitosa Extract is the extract of the alga, *Cystoseira caespitosa.* The accepted scientific name for *Cystoseira caespitosa* is *Cystoseira brachycarpa*.	Skin protectant
Cystoseira Compressa Extract	Cystoseira Compressa Extract is the extract of the alga, *Cystoseira compressa.*	Skin-conditioning agent - miscellaneous
Cystoseira Compressa Powder	Cystoseira Compressa Powder is the dried, ground powder obtained from the alga, *Cystoseira compressa.*	Skin-conditioning agent - miscellaneous
Cystoseira Tamariscifolia Extract	Cystoseira Tamariscifolia Extract is the extract of the alga, *Cystoseira tamarisfolia*.	Skin-conditioning agent - miscellaneous

Table 2. Current and revised INCI names, definitions, and functions of the *brown algae*-derived ingredients in this safety assessment.[1]

Ingredient	Definition	Function
Dictyopteris Polypodioides Extract	Dictyopteris Polypodioides Extract is the extract of the alga, *Dictyopteris polypodioides.*	Skin-conditioning agent – emollient; skin-conditioning agent - miscellaneous
Dictyopteris Membranacea Extract (Retired)	Dictyopteris Membranacea Extract (Retired) is the extract of the alga, *Dictyopteris membranacea*. The INCI Name, Dictyopteris Membranacea Extract, originally published in 2007, was designated with a retired status in 2015. For an interim period of time, trade name assignments formerly published with the INCI Name Dictyopteris Membranacea Extract will be retained in the retired monograph, and also published with the new name assignment based on the current genus and species name, Dictyopteris Polypodioides Extract.	Antioxidant
Dictyota Coriacea Extract	Dictyota Coriacea Extract is the extract of the alga, *Dictyota coriacea.*	Oxidizing agent
Durvillaea Antarctica Extract	Durvillaea Antarctica Extract is the extract of the alga, *Durvillaea antarctica*.	Skin-conditioning agent - miscellaneous
Ecklonia Cava Extract	Ecklonia Cava Extract is the extract of the alga, *Ecklonia cava*.	Humectant; skin-conditioning agent - humectant
Ecklonia Cava Water	Ecklonia Cava Water is the aqueous solution of the steam distillates obtained from the whole ~~plant~~, *Ecklonia cava.*	Skin protectant
Ecklonia Kurome Extract	Ecklonia Kurome Extract is the extract of the alga, *Ecklonia kurome.*	Skin-conditioning agent – humectant; skin-conditioning agent - miscellaneous
Ecklonia Kurome Powder	Ecklonia Kurome Powder is the powder obtained from the dried, ground alga, *Ecklonia kurome*.	Skin-conditioning agent - humectant
Ecklonia/Laminaria Extract	Ecklonia/Laminaria Extract is the extract of a mixture of the algae, *Ecklonia* and *Laminaria*.	Skin-conditioning agent - miscellaneous
Ecklonia Maxima Extract	Ecklonia Maxima Extract is the extract of the alga, *Ecklonia maxima*.	Skin-conditioning agent - miscellaneous
Ecklonia Maxima Powder	Ecklonia Maxima Powder is the powder obtained from the dried, ground alga, *Ecklonia maxima.*	Skin-conditioning agent - miscellaneous
Ecklonia Radiata Extract	Ecklonia Radiata Extract is the extract of the alga, *Ecklonia radiata.*	Hair conditioning agent; skin-conditioning agent - miscellaneous
Eisenia Arborea Extract	Eisenia Arborea Extract is the extract of the alga, *Eisenia arborea.*	Skin-conditioning agent - miscellaneous
Fucus Serratus Extract 94167-02-9	Fucus Serratus Extract is the extract of the alga, *Fucus serratus.*	Skin-conditioning agent - miscellaneous
Fucus Spiralis Extract	Fucus Spiralis Extract is the extract of the alga, *Fucus spiralis.*	Skin-conditioning agent – emollient; skin-conditioning agent - miscellaneous
Fucus Vesiculosus	Fucus Vesiculosus is the alga, *Fucus vesiculosus.*	Skin-conditioning agent - miscellaneous
Fucus Vesiculosus Extract 283-633-7	Fucus Vesiculosus Extract is the extract of the alga, *Fucus vesiculosus.*	Fragrance ingredient; skin-conditioning agent - miscellaneous
Fucus Vesiculosus Powder	Fucus Vesiculosus Powder is the powder obtained from dried, ground *Fucus vesiculosus.*	Skin-conditioning agent - miscellaneous
Halidrys Siliquosa Extract	Halidrys Siliquosa Extract is the extract of the alga, *Halidrys siliquosa.*	Skin-conditioning agent - miscellaneous
Halopteris Scoparia Extract	Halopteris Scoparia Extract is the extract of the alga, *Halopteris scoparia.*	Skin-conditioning agent - miscellaneous
Himanthalia Elongata Extract	Himanthalia Elongata Extract is the extract of the thallus of the alga, *Himanthalia elongata*.	Skin-conditioning agent - miscellaneous
Himanthalia Elongata Powder	Himanthalia Elongata Powder is the powder obtained from the dried, ground alga, *Himanthalia elongata.*	Absorbent; binder; viscosity increasing agent -aqueous
Hizikia Fusiforme Extract	Hizikia Fusiforme Extract is the extract of the alga, *Hizikia fusiforme.* The accepted scientific name for *Hizikia fusiforme* is *Sargassum fusiforme*.	Skin protectant; skin-conditioning agent - miscellaneous
Hizikia Fusiformis Water	Hizikia Fusiformis Water is the aqueous solution of the steam distillates obtained from the alga, *Hizikia fusiformis.*	Skin protectant
Hizikia Fusiformis Callus Culture Extract	Hizikia Fusiformis Callus Culture Extract is the extract of a culture of the callus of *Hizikia fusiformis.* The accepted scientific name for *Hizikia fusiformis* is *Sargassum fusiforme.*	Antifungal agent; antioxidant; hair conditioning agent; skin-conditioning agent - miscellaneous
Hydrolyzed Ecklonia Cava Extract	Hydrolyzed Ecklonia Cava Extract is the hydrolysate of an extract of the alga, *Ecklonia cava* derived by acid, enzyme or other method of hydrolysis.	Skin-conditioning agent - miscellaneous
Hydrolyzed Fucus Vesiculosus Extract 84696-13-9	Fucus Vesiculosus Extract is the extract of the alga, *Fucus vesiculosus.*	Fragrance ingredient; skin-conditioning agent – miscellaneous
Hydrolyzed Fucus Vesiculosus Protein	Hydrolyzed Fucus Vesiculosus Extract is the extract of the hydrolysate of *Fucus vesiculosus* derived by acid, enzyme or other method of hydrolysis.	None reported
Laminaria Cloustoni Extract 90046-11-0 92128-82-0	Laminaria Cloustoni Extract is the extract of the alga, *Laminaria cloustoni.* The accepted scientific name for *Laminaria cloustoni* is *Laminaria hyperborea.*	Fragrance ingredient
Laminaria Diabolica Extract	Laminaria Diabolica Extract is the extract of the alga, *Laminaria diabolica*. The accepted scientific name for *Laminaria diabolica* is *Saccharina japonica.*	Skin-conditioning agent - humectant

Table 2. Current and revised INCI names, definitions, and functions of the *brown algae*-derived ingredients in this safety assessment.[1]

Ingredient	Definition	Function
Laminaria Digitata Extract 90046-12-1 92128-82-0	Laminaria Digitata Extract is the extract of the alga, *Laminaria digitata.*	Fragrance ingredient; skin protectant; skin-conditioning agent - miscellaneous
Laminaria Digitata Powder	Laminaria Digitata Powder is the powder obtained from the dried, ground thallus of the alga, *Laminaria digitata.*	Skin-conditioning agent - miscellaneous
Laminaria Hyperborea Extract 90046-13-2 92128-82-0	Laminaria Hyperborea Extract is the extract of the alga, *Laminaria hyperborea.*	Fragrance ingredient; skin protectant
Laminaria Japonica Extract 92128-82-0	Laminaria Japonica Extract is the extract of the alga, *Laminaria japonica.* The accepted scientific name for *Laminaria japonica* is *Saccharina japonica.*	Fragrance ingredient
Laminaria Japonica Powder	Laminaria Japonica Powder is the powder obtained from the dried, ground alga, *Laminaria japonica.* The accepted scientific name for *Laminaria japonica* is *Saccharina japonica.*	Skin-conditioning agent - miscellaneous
Laminaria Longissima Extract	Laminaria Longissima Extract is the extract of the alga, *Laminaria longissima*. The accepted scientific name for *Laminaria longissima* is *Saccharina longissima*	Skin-conditioning agent - humectant
Laminaria Ochroleuca Extract 92128-82-0	Laminaria Ochroleuca Extract is the extract of the alga, *Laminaria ochroleuca*. The accepted scientific name for *Laminaria ochroleuca* is *Saccharina japonica.*	Fragrance ingredient; skin-conditioning agent - miscellaneous
Laminaria Saccharina Extract 90046-14-3 92128-82-0	Laminaria Saccharina Extract is the extract of the thallus of the alga, *Laminaria saccharina.* The accepted scientific name for *Laminaria saccharina* is *Saccharina latissima.*	Fragrance ingredient; skin-conditioning agent - miscellaneous
Lessonia Nigrescens Extract	Lessonia Nigrescens Extract is the extract of the alga, *Lessonia nigrescens.*	Skin protectant
Lessonia Nigrescens Powder	Lessonia Nigrescens Powder is the powder obtained from the dried, ground alga, *Lessonia nigrescens.*	Binder
Macrocystis Pyrifera (Kelp)	Macrocystis Pyrifera (Kelp) is the alga, *Macrocystis pyriferae.*	Viscosity increasing agent - aqueous
Macrocystis Pyrifera (Kelp) Blade/Pneumatocyst/Stipe Juice Extract	Macrocystis Pyrifera (Kelp) Blade/Pneumatocyst/Stipe Juice Extract is the extract of the juice derived from the blade, pneumatocyst and stipe of the alga, *Macrocystis pyrifera.*	Skin-conditioning agent - miscellaneous
Macrocystis Pyrifera (Kelp) Extract 347174-92-9	Macrocystis Pyrifera (Kelp) Extract is the extract of the alga, *Macrocystis pyrifera.*	Skin-conditioning agent - miscellaneous
Macrocystis Pyrifera (Kelp) Juice	Macrocystis Pyrifera (Kelp) Juice is the juice expressed from the alga, *Macrocystis pyrifera.*	Skin-conditioning agent - miscellaneous
Macrocystis Pyrifera (Kelp) Protein	Macrocystis Pyrifera (Kelp) Protein is the protein derived from the alga, *Macrocystis pyrifera.*	Skin-conditioning agent - miscellaneous
Nereocystis Luetkeana Extract	Nereocystis Luetkeana Extract is the extract of the alga, *Nereocystis luetkeana.*	Hair conditioning agent; skin-conditioning agent - miscellaneous
Pelvetia Canaliculata Extract 223751-75-5	Pelvetia Canaliculata Extract is the extract of the alga, *Pelvetia canaliculata.*	Skin protectant; skin-conditioning agent - miscellaneous
Pelvetia Siliquosa Extract	Pelvetia Siliquosa Extract is the extract of the alga, *Pelvetia siliquosa.*	Antioxidant; skin protectant; skin-conditioning agent - humectant
Phyllacantha Fibrosa Extract	Phyllacantha Fibrosa Extract is the extract of the alga, *Phyllacantha fibrosa*. The accepted scientific name for *Phyllacantha fibrosa* is *Cystoseira baccata*.	Skin-conditioning agent - miscellaneous
Saccharina Angustata Extract	Saccharina Angustata Extract is the extract of the alga, *Saccharina angustata*.	Skin-conditioning agent - emollient; skin-conditioning agent - miscellaneous
Laminaria Angustata Extract (Retired)	Laminaria Angustata Extract (Retired) is the extract of the alga, *Laminaria angustata*. The INCI Name, Laminaria Angustata Extract, originally published in 2003, was designated with a retired status in 2015. For an interim period of time, trade name assignments formerly published with the INCI Name Laminaria Angustata Extract will be retained in the retired monograph, and also published with the new name assignment based on the current genus and species name, Saccharina Angustata Extract.	Skin-conditioning agent - miscellaneous
Saccharina Japonica Extract	Saccharina Japonica Extract is the extract of the alga, *Saccharina japonica.*	Skin-conditioning agent - miscellaneous
Laminaria Ochotensis Extract (Retired)	Laminaria Ochotensis Extract (Retired) is the extract of the alga, *Laminaria ochotensis.* The INCI Name, Laminaria Ochotensis Extract, originally published in 2008, was designated with a retired status in 2015. For an interim period of time, trade name assignments formerly published with the INCI Name Laminaria Ochotensis Extract will be retained in the retired monograph, and also published with the new name assignment based on the current genus and species name, Saccharina Japonica Extract.	Skin-conditioning agent - emollient
Saccharina Longicruris Extract	Saccharina Longicruris Extract is the extract of the alga, *Saccharina longicruris.*	Skin-conditioning agent - humectant
Sargassum Filipendula Extract	Sargassum Filipendula Extract is the extract of the brown alga, *Sargassum filipendula*.	Skin-conditioning agent - miscellaneous
Sargassum Fulvellum Extract	Sargassum Fulvellum Extract is the extract of the alga, *Sargassum fulvellum.*	Skin-conditioning agent - miscellaneous

Table 2. Current and revised INCI names, definitions, and functions of the *brown algae*-derived ingredients in this safety assessment.[1]

Ingredient	Definition	Function
Sargassum Fusiforme Extract	Sargassum Fusiforme Extract is the extract of the brown alga, *Sargassum fusiforme*.	Skin-conditioning agent - miscellaneous
Sargassum Glaucescens Extract	Sargassum Glaucescens Extract is the extract of the alga, *Sargassum glaucescens*.	Antioxidant
Sargassum Horneri Extract	Sargassum Horneri Extract is the extract of the alga, *Sargassum horneri*.	Skin-conditioning agent - miscellaneous
Sargassum Muticum Extract	Sargassum Muticum Extract is the extract of the alga *Sargassum muticum*.	Skin-conditioning agent - miscellaneous
Sargassum Pallidum Extract	Sargassum Pallidum Extract is the extract of the alga, *Sargassum pallidum*.	Antifungal agent; antioxidant
Sargassum Siliquastrum Extract	Sargassum Siliquastrum Extract is the extract of the alga, *Sargassum siliquastrum*.	Skin-conditioning agent - miscellaneous
Sargassum Thunbergii Extract	Sargassum Thunbergii Extract is the extract of the alga, *Sargassum thunbergii*.	Antimicrobial agent
Sargassum Vulgare Extract	Sargassum Vulgare Extract is the extract of the alga, *Sargassum vulgare*.	Skin-conditioning agent - miscellaneous
Sphacelaria Scoparia Extract	Sphacelaria Scoparia Extract is the extract of the alga, *Sphacelaria scoparia*. The accepted scientific name for *Sphacelaria scoparia* is *Halopteris scoparia*.	Corn/callus/wart remover
Undaria Peterseniana Extract	Undaria Peterseniana Extract is the extract of the alga *Undaria peterseniana*.	Skin-conditioning agent - miscellaneous
Undaria Pinnatifida Extract	Undaria Pinnatifida Extract is the extract of the alga, *Undaria pinnatifida*.	Skin protectant; skin-conditioning agent - miscellaneous
Undaria Pinnatifida Cell Culture Extract	Undaria Pinnatifida Cell Culture Extract is the extract of a cell culture suspension of *Undaria pinnatifida*.	Hair conditioning agent; skin-conditioning agent - miscellaneous
Undaria Pinnatifida Leaf/Stem Extract	Undaria Pinnatifida Leaf/Stem Extract is the extract of the leaves and stems of *Undaria pinnatifida*.	Skin-conditioning agent – emollient
Undaria Pinnatifida Powder	Undaria Pinnatifida Powder is the powder obtained from the dried, ground alga, *Undaria pinnatifida*.	Absorbent; binder; viscosity increasing agent - nonaqueous
Undaria Pinnatifida Root Powder	Undaria Pinnatifida Root Powder is the powder obtained from the dried, ground root-like structures of the alga, *Undaria pinnatifida*.	Humectant; skin-conditioning agent - humectant

Table 3. Descriptions of Major Algae Groups

Common Name	Kingdom	Class	Description	Reference
Brown Algae	Stramenopila	Phaeophyceae	-mostly large, leathery seaweeds -cellulose wall with alginic acid and fucoidan -derived alginic acid is used as a suspending, emulsifying, gel-forming and film-forming agent	12
Green Algae	Plantae	Chlorophyta	-usually green in color -cellulose cell walls -store starch -beta carotene -chlorophyll a & b	12
Diatoms	Stramenopila	Bacillariophyceae	-golden brown in color -silica cell walls -store oil as food reserve -carotenoids -chlorophyll a & c	12
Chrysophytes	Stramenopila	Chrysophyta	-consists of diatoms, golden-brown algae and yellow-green algae -cellulose cell walls with large amounts of silica -chlorophyll a &c	12,91
Blue Green Algae	Monera	Cyanophyta	-phycobilins present -store glycogen -prokaryotic -chlorophyll a -some are toxic	12
Red Algae	Plantae	Rhodophyta	-phycobilins present -store floridean starch -cellulose cell wall -chlorophyll a & d -source of agar -used as a stabilizer and thickener in many products	12
Dinoflagellates	Alveolata	Pyrrhophyta	-some produce toxins -mostly marine	12,92
Euglenoids	Euglenozoa	Euglenophyta	-common in freshwater -can be parasitic	12,93

Table 4. Taxonomy of Brown-Algae Derived Ingredients[94]

Subclass	Order	Family	Genus	Ingredient
Dictyotophycidae	Dictyotales	Dictyotacaea	Dictyopteris	Dictyopteris Polypodioides Extract
Dictyotophycidae	Dictyotales	Dictyotacaea	Dictyotaceae	Dictyota Coriacea Extract
Dictyotophycidae	Sphacelariales	Sphacelariaceae	Sphacelaria	Sphacelaria Scoparia Extract
Dictyotophycidae	Sphacelariales	Sphacelariaceae	Stypocaulaceae	Halopteris Scoparia Extract
Fucophycidae	Ectocarpales	Chordariaceae	Cladosiphon	Cladosiphon Novae-Caledoniae Extract
Fucophycidae	Ectocarpales	Chordariaceae	Cladosiphon	Cladosiphon Okamuranus Extract
Fucophycidae	Fucales	Durvillaeaceae	Durvillaea	Durvillaea Antarctica Extract
Fucophycidae	Fucales	Fucaceae	Ascophyllum	Ascophyllum Nodosum
Fucophycidae	Fucales	Fucaceae	Ascophyllum	Ascophyllum Nodosum Extract
Fucophycidae	Fucales	Fucaceae	Ascophyllum	Ascophyllum Nodosum Powder
Fucophycidae	Fucales	Fucaceae	Fucus	Fucus Serratus Extract
Fucophycidae	Fucales	Fucaceae	Fucus	Fucus Spiralis Extract
Fucophycidae	Fucales	Fucaceae	Fucus	Fucus Vesiculosus
Fucophycidae	Fucales	Fucaceae	Fucus	Fucus Vesiculosus Extract
Fucophycidae	Fucales	Fucaceae	Fucus	Fucus Vesiculosus Powder
Fucophycidae	Fucales	Fucaceae	Fucus	Hydrolyzed Fucus Vesiculosus Extract
Fucophycidae	Fucales	Fucaceae	Fucus	Hydrolyzed Fucus Vesiculosus Protein
Fucophycidae	Fucales	Fucaceae	Pelvitia	Pelvetia Canaliculata Extract
Fucophycidae	Fucales	Fucaceae	Pelvitia	Pelvetia Siliquosa Extract
Fucophycidae	Fucales	Himanthaliaceae	Himanthalia	Himanthalia Elongata Extract
Fucophycidae	Fucales	Himanthaliaceae	Himanthalia	Himanthalia Elongata Powder
Fucophycidae	Fucales	Sargassaceae	Cystoseira	Cystoseira Amentacea/Caespitosa/ Branchycarpa Extract
Fucophycidae	Fucales	Sargassaceae	Cystoseira	Cystoseira Baccata Extract
Fucophycidae	Fucales	Sargassaceae	Cystoseira	Cystoseira Balearica Extract
Fucophycidae	Fucales	Sargassaceae	Cystoseira	Cystoseira Caespitosa Extract
Fucophycidae	Fucales	Sargassaceae	Cystoseira	Cystoseira Compressa Extract
Fucophycidae	Fucales	Sargassaceae	Cystoseira	Cystoseira Compressa Powder
Fucophycidae	Fucales	Sargassaceae	Cystoseira	Cystoseira Tamariscifolia Extract
Fucophycidae	Fucales	Sargassaceae	Halidrys	Halidrys Siliquosa Extract
Fucophycidae	Fucales	Sargassaceae	Hizikia	Hizikia Fusiforme Extract
Fucophycidae	Fucales	Sargassaceae	Hizikia	Hizikia Fusiformis Water
Fucophycidae	Fucales	Sargassaceae	Hizikia	Hizikia Fusiformis Callus Culture Extract
Fucophycidae	Fucales	Sargassaceae	Phyllacantha	Phyllacantha Fibrosa Extract
Fucophycidae	Fucales	Sargassaceae	Sargassum	Sargassum Filipendula Extract
Fucophycidae	Fucales	Sargassaceae	Sargassum	Sargassum Fulvellum Extract
Fucophycidae	Fucales	Sargassaceae	Sargassum	Sargassum Fusiforme Extract
Fucophycidae	Fucales	Sargassaceae	Sargassum	Sargassum Glaucescens Extract
Fucophycidae	Fucales	Sargassaceae	Sargassum	Sargassum Horneri Extract
Fucophycidae	Fucales	Sargassaceae	Sargassum	Sargassum Muticum Extract
Fucophycidae	Fucales	Sargassaceae	Sargassum	Sargassum Pallidum Extract
Fucophycidae	Fucales	Sargassaceae	Sargassum	Sargassum Siliquastrum Extract
Fucophycidae	Fucales	Sargassaceae	Sargassum	Sargassum Thunbergii Extract
Fucophycidae	Fucales	Sargassaceae	Sargassum	Sargassum Vulgare Extract
Fucophycidae	Laminariales	Agaraceae	Agarum	Agarum Cribrosum Extract
Fucophycidae	Laminariales	Agaraceae	Alaria	Alaria Esculenta Extract
Fucophycidae	Laminariales	Alariaceae	Undaria	Undaria Peterseniana Extract
Fucophycidae	Laminariales	Alariaceae	Undaria	Undaria Pinnatifida Extract
Fucophycidae	Laminariales	Alariaceae	Undaria	Undaria Pinnatifida Cell Culture Extract
Fucophycidae	Laminariales	Alariaceae	Undaria	Undaria Pinnatifida Leaf/Stem Extract
Fucophycidae	Laminariales	Alariaceae	Undaria	Undaria Pinnatifida Powder
Fucophycidae	Laminariales	Alariaceae	Undaria	Undaria Pinnatifida Root Powder
Fucophycidae	Laminariales	Laminariaceae	Laminaria	Laminaria Cloustoni Extract
Fucophycidae	Laminariales	Laminariaceae	Laminaria	Laminaria Diabolica Extract
Fucophycidae	Laminariales	Laminariaceae	Laminaria	Laminaria Digitata Extract
Fucophycidae	Laminariales	Laminariaceae	Laminaria	Laminaria Digitata Powder
Fucophycidae	Laminariales	Laminariaceae	Laminaria	Laminaria Hyperborea Extract
Fucophycidae	Laminariales	Laminariaceae	Laminaria	Laminaria Japonica Extract
Fucophycidae	Laminariales	Laminariaceae	Laminaria	Laminaria Japonica Powder
Fucophycidae	Laminariales	Laminariaceae	Laminaria	Laminaria Longissima Extract
Fucophycidae	Laminariales	Laminariaceae	Laminaria	Laminaria Ochroleuca Extract
Fucophycidae	Laminariales	Laminariaceae	Laminaria	Laminaria Saccharina Extract

Table 4. Taxonomy of Brown-Algae Derived Ingredients[94]

Subclass	Order	Family	Genus	Ingredient
Fucophycidae	Laminariales	Laminariaceae	Macrocystis	Macrocystis Pyrifera (Kelp)
Fucophycidae	Laminariales	Laminariaceae	Macrocystis	Macrocystis Pyrifera (Kelp) Blade/Pneumatocyst/Stipe Juice Extract
Fucophycidae	Laminariales	Laminariaceae	Macrocystis	Macrocystis Pyrifera (Kelp) Extract
Fucophycidae	Laminariales	Laminariaceae	Macrocystis	Macrocystis Pyrifera (Kelp) Juice
Fucophycidae	Laminariales	Laminariaceae	Macrocystis	Macrocystis Pyrifera (Kelp) Protein
Fucophycidae	Laminariales	Laminariaceae	Nereocystis	Nereocystis Luetkeana Extract
Fucophycidae	Laminariales	Laminariaceae	Saccharina	Saccharina Angustata Extract
Fucophycidae	Laminariales	Laminariaceae	Saccharina	Saccharina Japonica Extract
Fucophycidae	Laminariales	Laminariaceae	Saccharina	Saccharina Longicruris Extract
Fucophycidae	Laminariales	Lessoniaceae	Ecklonia	Ecklonia Cava Extract
Fucophycidae	Laminariales	Lessoniaceae	Ecklonia	Ecklonia Cava Water
Fucophycidae	Laminariales	Lessoniaceae	Ecklonia	Ecklonia Kurome Extract
Fucophycidae	Laminariales	Lessoniaceae	Ecklonia	Ecklonia Kurome Powder
Fucophycidae	Laminariales	Lessoniaceae	Ecklonia	Ecklonia/Laminaria Extract
Fucophycidae	Laminariales	Lessoniaceae	Ecklonia	Ecklonia Maxima Extract
Fucophycidae	Laminariales	Lessoniaceae	Ecklonia	Ecklonia Maxima Powder
Fucophycidae	Laminariales	Lessoniaceae	Ecklonia	Ecklonia Radiata Extract
Fucophycidae	Laminariales	Lessoniaceae	Ecklonia	Hydrolyzed Ecklonia Cava Extract
Fucophycidae	Laminariales	Lessoniaceae	Eisenia	Eisenia Arborea Extract
Fucophycidae	Laminariales	Lessoniaceae	Lessonia	Lessonia Nigrescens Extract
Fucophycidae	Laminariales	Lessoniaceae	Lessonia	Lessonia Nigrescens Powder

Table 5.General characteristics and geographic distribution of brown algae species

Species (common name)	Description	Distribution/Habitat/Ecology	References
Agarum cribrosum	-	North Atlantic (Massachusetts to east Greenland) and North Pacific (Washington state to Japan and Russia) Forms thick beds at depths of 10-12 m	94
Alaria esculenta (dabberlocks, badderlocks, winged kelp)	Olive or yellow-brown fronds to 4 m long and 25 cm wide, more often about 1 m and 7.5 cm wide. Attached by a root-like holdfast at the base from which a narrow flexible stipe arises which continues into the leafy part of thealgae as a distinct mid-rib, generally with a yellow-brown color. The reproductive structures, apparent as dark-brown areas, are confined to unbranched leafy appendages borne on the stipe, usually in two rows.	North Atlantic Ocean Generally growing on rock in wave-exposed places, often forming a band at low water and in the shallow subtidal, but also occurring in tidal pools in the lower shore.	94,95
Ascophyllum nodosum (asco, sea whistle, bladderwrack, rockweed)	Closely related to *Fucus*. Up to 3 m in height and is yellow in areas exposed to sunlight and dark green or brown in its shaded parts. Single bladders are central in long, strap-like fronds. Fronds hang downwards. Multiple fronds grow from each basal holdfast;generally regenerates new fronds from base when one of the larger fronds is damaged. Reproduction takes place in spring in yellow receptacles, which develop in response to short days in autumn, mature during winter, and are at their most prolific in spring. Eggs and sperm are released into water, and eggs release a low molecular weight pheromone, finnavarene.	North Atlantic basin (Virginia to Spain) Has been observed in San Francisco Bay, but does not persist there. Sheltered intertidal rocks in shallow (usually where it is exposed at low or extreme low tides)	94-97
Cystoseira baccata (bushy berry wrack)	Thallus to 1 m long, usually solitary, attached by a thick, conical attachment disc. Axis simple or branched, and flattened; apex smooth and surrounded during periods of active growth by incurved young laterals. Lateral branch systems alternate, radially symmetrical, profusely branched in a repeatedly pinnate fashion and bearing sparse, filiform, occasionally bifurcated appendages on the branches; deciduous, leaving decurrent bases which give an irregular, zigzag outline to the axis. Air vesicles present in axes of branches of higher order, sometimes in chains; seasonal, particularly numerous in autumn. Receptacles 1-5 cm long, formed from axes of ultimate ramuli, irregularly nodose and bearing simple, filiform appendages.	S England, W Ireland north to W Scotland. Has been noted down to Morocco and in Mediterranean Sea. Lower intertidal in large sandy pools or lagoons, mostly in persistent stands.	94,95
Cystoseira tamariscifolia (bushy rainbow wrack)	Solitary thalli, up to 1 m long, bushy, with a pronounced greenish or bluish iridescence when submerged or wet; attached by a conical disc. Axis is cylindrical, up to 60 cm long, usually branched and with an inconspicuous apex. Lateral branch systems arising in spiral sequence, up to 60 cm long, profusely branched in a repeatedly pinnate fashion, showing radial symmetry with simple or bifid spine-like appendages: deciduous, leaving prominent scars or stumps. Cryptostomata present on branches and appendages. Ovoid air vesicles often present in axes of ultimate ramuli. Receptacles 1-2 cm long, formed from terminal regions of ultimate ramuli.	Western Mediterranean Sea/northern Africa to Ireland Large intertidal rock pools and lagoons and shallow subtidal shores	94,95
Dictyopteris polypodioides [*Dictyopteris membranacea* (Retired)]	Thallus flat and leaf-like, to 300 mm long and 20-30 mm broad; fronds olive to yellow-brown, translucent, and somewhat regularly dichotomously forked with a prominent midrib extending to the apices. Margins sometimes split to midrib. Has an unpleasant smell shortly after collection, which degenerates quickly.	Ireland (except for east coast), west Scotland, Wales, southwest England, to Portugal and West Africa Large pools at low water and shallow subtidal shores	94,95
Fucus serratus (serrated wrack, saw wrack, toothed wrack)	Dichotomously branched fronds arising from a small disc via a short stipe; distinct midrib.Algae grows to 300 mm with terminal, compressed receptacles with warty conceptacles. It is easily recognized by its saw-toothed frond, and a lack of swollen receptacles.	Widely distributed on all coasts of Britain and Ireland. Baltic Sea to Spain and Canary Islands. Introduced to Nova Scotia and has spread to New Brunswick and Maine. Zone forming on sheltered and semi-exposed shores.	94-96
Fucus spiralis (jelly bags, spiral wrack, flat wrack spiraled wrack)	Fronds lack bladders; elongated air bladders are on either side of the midrib. Fronds have twisted, dichotomous branches. This species is up to 20 cm long, attached to the substratum with a discoid holdfast. Color ranges from dark brown to olive-green.	North Atlantic and North Pacific; Baltic Sea to Morocco/Canary Islands and New York; Alaska to California. Introduced to Mediterranean Sea (France). Uppermost species of *Fucus* that occurs on shore.	96

Table 5.General characteristics and geographic distribution of brown algae species

Species (common name)	Description	Distribution/Habitat/Ecology	References
Fucus vesiculosus (paddy tang, red fucus, dyers fucus, swine tang, sea ware, bladder, rockweed, bladderwrack, popping wrack, wrack)	Paired bladders occur on either side of a prominent midrib. Frond is generally not strongly spiraled and receptacles do not have a sterile rim, and frond does not have a serrated margin. Attached by a small, strong disc which gives rise to a short stipe. This species is 15 to 90 cm long and 0.6 to 2.5 cm wide. Reproductive receptacles are swollen areas at tips of fronds that have many flask-shaped cavities called conceptacles, which house male and female reproductive structures known as antheridia (borne on antheridiophores) and oogonia (containing 8 eggs), respectively. Eggs and sperm are liberated onto surface of receptacles and a pheromone (sex-attracting substance) is released by eggs that attract sperm. Fertilization results in a zygote that forms a new *Fucus* adult.	North Atlantic (Canadian Arctic, Russia, White Sea, Baltic Sea) south to Canary Islands and West Indies Midshore zone A bladderless form occurs on more wave-exposed shores in the NE Atlantic. Grows in various conditions, from saline lagoons to exposed rocky shores, as well as on sheltered rocky shores. Forms dense canopies.	94-96,98
Halidrys siliquosa (podweed, sea oak)	Thallus 30-130 cm long, tawny to yellow-brown ochre, tough and leathery; attached by a large, discoid holdfast, giving rise to compressed, irregularly alternately branched fronds, with several orders of close branching in the same plane. Pod-shaped, segmented air bladders are produced replacing some lateral branches. Reproductive conceptacles forming in swollen conceptacles at apices of branches	Northeast Atlantic (Norway/Baltic Sea to Morocco) Large, mid-intertidal pools, often dominating in very large, sunny pools, but more often forming occasional stands. Occasionally forming extensive forests in shallow subtidal to about 10 m, generally in current-exposed locations. Widespread and common. Halidrys produces meroditerpenoids that seemingly act as antifouling agents preventing other organisms adhering to surface of the algae.	94,95
Halopteris scoparia (sea flax weed)	*Stypocaulon scoparium* may be synonymous	Northwest Atlantic (Baltic Sea to Canary Islands) and Mediterranean Sea	94
Himanthalia elongata (thongweed, buttonweed, sea spaghetti, sea thong, sea haricots)	Long thong-like fronds, basal mushroom-like buttons. Thallus consisting of a button-shaped vegetative thallus to 30 mm wide and 25 mm high, and a long, narrow, strap-like, sparingly branched, light yellow-brown reproductive receptacle to 2 m in length and up to 10 mm in width, on which conceptacles are borne. Buttons, initially club-shaped but later mushroom-like, develop from zygotes in late summer, mature in winter, and begin to form reproductive receptacles in January/February. Some 4-6 dichotomies are produced at this stage, and fronds then elongate and thicken, developing no further branches, and become reproductively mature in July-September.	Northwest Atlantic Ocean (Scandinavia to Spain) Gently sloping rocks, particularly on semi-wave-exposed shore, on which they may form a distinct zone at low water. Sparse populations sometimes develop in sheltered lagoons where thealgae are more yellow and less flattened.	94,95
Laminaria cloustoni [*Laminaria hyperborea*] (kelp, may weed, kelpie, liver weed, mirkle, pennant weed, strapwrack, cuvie, tangle, split whip wrack, sea rods, forest kelp, northern kelp)	Dark brown, to 2 m in length; with a claw-like, conical holdfast, a rough, rigid stipe which generally rises up out of the water, and is covered in epiphytes when older, and a laminate blade to 1.5 m long dividing into finger-like segments. Stipe is rugose (rough) when older, circular in cross-section, and snaps easily when bent; the holdfast is conical.	Northwest Atlantic Ocean (Scandinavia to Spain) Common at extreme low water in wave-exposed areas, and in the subtidal in optically clear water growing on rock to a depth of 32 m. Forms extensive closed communities at depths of 0-24 m. There are usually large quantities of ephytic red algae growing on the older stipes; the old fronds are cast off in spring and new ones grow below for a time.	94,95
Laminaria digitata (kelp)	Dark brown, to 2 m in length; with a claw-like holdfast, a smooth, flexible stipe, and a laminate blade to 1.5 m long split into finger-like segments. The stipe is oval in cross-section, and does not snap easily when bent. Underwater algae are more golden in color in sunlight.	North Atlantic (Arctic Canada/ Baltic Sea/Russia to Spain and New England) Very common in lower intertidal and shallow subtidal growing on rock. May form extensive meadows at low tide.	94,95

Table 5.General characteristics and geographic distribution of brown algae species

Species (common name)	Description	Distribution/Habitat/Ecology	References
Laminaria hyperborea (kelpie, liver weed, mirkle, pennant weed, strapwrack, cuvie, tangle, split whip wrack)	Dark brown, to 2 m in length; with a claw-like, conical holdfast, a rough, rigid stipe which generally sticks up out of the water, and is covered in epiphytes when older, and a laminate blade to 1.5 m long dividing into finger-like segments. Stipe is rugose (rough) when older, circular in cross-section, and snaps easily when bent; the holdfast is conical.	Northeast Atlantic (Scandinavia/Iceland to Spain and Canary Islands) Common at extreme low water in wave-exposed areas, and in subtidal in optically clear water growing on rock to a depth of 32 m. Forms extensive closed communities at depths of 0-24 m; there are usually large quantities of ephytic red algae growing on the older stipes; the old fronds are cast off in spring and new ones grow below for a time.	94,95,99
Laminaria saccharina [The accepted scientific name is *Saccharina latissima*] (sea belt, poor man's weather glass, sweet wrack, sugar wrack, sugar tang, oarweed, tangle, kelp, sugar sea belt, sweet tangle, sugarwrack, zuckertang)	Yellow brown, to 3 m in length; with a claw-like holdfast, a small, smooth, flexible stipe, and an undivided laminate blade to 3 m long with parallel, ruffled sides and a elongated, tongue-like appearance. Frond is characteristically dimpled with regular bullations (depressions). Stipe is relatively small, cylindrical in section and more flexible than those of *Laminaria digitata* and *Laminaria hyperborea*. It is only species in the NE Atlantic Ocean with an undivided frond, distinct bullations, and a frilly margin.	Circumboreal (Atlantic Ocean: Canada, Scandinavia, Greenland, Iceland to Galicia, Spain and Maine, but not known in the Bay of Biscay; Pacific Ocean: Alaska to California, Japan, Korea, Central Polynesia, India, New Zealand) Intertidal pools and occasional in shallow subtidal areas, becoming more abundant at low water in sheltered localities with fast-moving water, such as rapids systems. In subtidal, it is characteristic of intermittently disturbed areas.	94,95
Macrocystis pyrifera (giant kelp, sea ivy, giant pacific kelp)	This species reaches 45 meters long and grow in waters 6-20 (possibly up to 80) m deep, and grow at up to 30 cm per day. Now believed to be a monospecific genera ranging from intertidal to deep water with environments dictating morphology.	Eastern and southern Pacific Ocean in both hemispheres (Alaska to New Zealand and Australia) Dominant canopy-forming algae in southern and central California.	94,100,101
Pelvetia canaliculata (channeled wrack, cow tang)	This species is 80-120 mm long, yellow-brown in color, turning black when dry, and often so dry that fronds disintegrate when trodden upon; regularly dichotomously branched with a distinct channel on underside (side nearest rock), which holds moisture and apparently helps algae survive at very high levels on shore. Reproduction in conceptacles visible as dots on warty terminal receptacles. Usually infected by a fungus which may assist in allowing it to survive high in intertidal zone.	NE Atlantic from the Faroe Islands to Portugal Occurring very high on shore, generally above mean high water neap tides, on wave-exposed and sheltered shores, but absent from very exposed rocky shores.	94-96
Sargassum muticum	Thallus bushy, elongated, yellowish-tawny to dark brown, generally to 4 m long;tough, cylindrical, repeatedly alternately pinnately branched to the third or fourth order; whorls of distinctly flattened sculpted leaves at the base (resembling the leaves of Holly); with characteristic rounded-elliptical air bladders above and below, formed terminally. Reproductive receptacles below, formed in the axils of spiny leaves; spectacularly fecund. Basal holdfast penetrating and conical, persisting for several years. Reproductive plants detach easily, and continue to reproduce while drifting, and spreading the reproductive zygotes that develop on the surfaces of the receptacles. Terminal air bladders below; receptacles in the axils of spiny leaves.	Native to Japan; spread to China and Korea. Invasive in France, Spain and Portugal; western Mediterranean; Alaska south to Mexico. Throughout the intertidal in pools, but largest and commonest at low water.	94,95

Table 5.General characteristics and geographic distribution of brown algae species

Species (common name)	Description	Distribution/Habitat/Ecology	References
Undaria pinnatifida (sea mustard, precious sea grass, wakame)	Thallus laminate, yellowish to dark brown, usually 1-2 m, occasionally 3 m or more in length; holdfast spreading, dichotomously branched and claw-like, giving rise to a flattened oar-like stipe with a "fried-egg" like margin with small proliferations and basally with beautifully lobed sporophylls that coil around it when mature; stipe continuing into the fond as a flattened midrib that bears broadly lobed laciniate fronds with a roughly pyramidal shape. Frilly sporophylls coiling around the base of the flattened stipe at the base. A similar flattened midrib is not found in any other kelp in the Atlantic. *Alaria esculenta* has a midrib which is not flattened and the frond of *Alaria* is not lobed, although it may be similarly laciniate.	Native to Pacific Russia, Japan, China and Korea. NE Ireland, S England, NW France, NW Spain, Mediterranean Lower intertidal and very shallow subtidal (no more than a few m), particularly in sheltered locations, growing particularly on marinas, buoys, and similar floating structures in harbors. Often occurring on boat-hulls.	94

Table 5. Chemical and physical properties of brown algae-derived ingredients.

Property	Value	Reference
Ascophyllum Nodosum Extract		
Physical Form	Liquid	102,103
	Viscous liquid	104
	Solid flakes	6
Color	Black	6,102
	Dark brown	103
	Dark brown (aq. ext)	104
Odor	Marine-like/Fish-like	102,103
	Characteristic, seaweed (aq. ext)	104
	Odorless	6
Density/Specific Gravity	1.17	102
	1.1 (aq. ext.)	104
Bulk Density (g/ml)	0.58	6
Viscosity kg/(s m)	< 0.1	102
Melting Point °C	0 (aq. ext.)	104
	> 300	6
Boiling Point °C	100	102
	100 (aq. ext.)	104
	65 – 96	103
Water Solubility g/L @ 20 °C & pH 7.4 – 7.5	> 10,000	6
@ 20 °C	100%	102,103
	100%	104
Other Solubility g/L		
Acetone @ 22 °C	0.007	6
Ethyl acetate @ 22°C	0.009	6
Methanol @ 22 °C	0.251	6
log P_{ow}	-3.3 est.	5,6
Particle size	> 0.250 mm, 93.5%	6
	< 0.045 mm, none	
Ascophyllum Nodosum Powder		
Physical Form	Flakes or powder	105
	Powder	106
Color	Olive green	105
	Green	106
Odor	Marine-like	105
	Characteristic, fish-like	106
Water Solubility g/L	Insoluble	105
Ecklonia Cava Extract		
Physical Form	Powder (alcohol ext)	9
Color	Brown (alcohol ext)	9

aq. = aqueous; ext. = extract

Table 6. Methods of manufacture for brown algae-derived ingredients.

Ingredient (characterization)	Method of Manufacture	Reference
Ascophyllum Nodosum Extract	A trade name mixture containing 4.7% Ascophyllum Nodosum Extract in 94.5% water, reported a manufacturing process consisting of grinding the algae, extracting the water, fucoidan purification and ultrafiltration.	107
Ascophyllum Nodosum Extract	The species *Ascophyllum nodosum* is grinded, extracted by water, then undergoes fucoidan purification and ultrafiltration.	108
Cladosiphon Okamuranus Extract (high in fucoidan)	*Cladosiphon okamuranus* is hydrolyzed in 0.05 M or 0.5 M hydrochloric acid at 80°C for 30 min and then is neutralized with sodium hydroxide. Salt is removed by electrodialysis and then hydrolysate is lyophilized.	19
Dictyopteris Polypodioides Extract (high fractions of C_{11} hydrocarbons and sulfur compounds)	Air-dried algae material is extracted with diethyl ether. Solvent is removed vacuum distillation leaving a crude concrete extract. Crude extract is treated with hydrodistillation followed by liquid-liquid extraction with diethyl ether to obtain the essential oil.	20
Dictyopteris Polypodioides Extract (high fraction of sulfur compounds)	Air-dried algae material is extracted with diethyl ether. Solvent is removed by vacuum distillation leaving a crude concrete extract. Crude extract is then subjected to supercritical fluid (CO_2) extraction.	20
Dictyopteris Polypodioides Extract (high fractions of sesquiterpenes)	Air-dried algae material is extracted with diethyl ether. Solvent is removed vacuum distillation leaving a crude concrete extract. Crude extract is mixed with water and irradiated in a microwave oven (focused microwave-assisted hydrodistillation).	20
Ecklonia Cava Extract	Fresh, semidried *Ecklonia cava* seaweed is dried and crushed followed by alcohol (i.e., food-grade ethanol) extraction, purification, filtration, and concentration steps.	9
Ecklonia Cava Extract	Small pieces of *Ecklonia cava* fronds (~ 5 cm; 30 kg) are placed in 750 L of distilled water in the presence of enzymes (300 g pectinase and 300 g cellulase). Suspension is stirred for 24 h at 50°C, centrifuged at 3000 g for 20 min at 4°C, and vacuum filtered. Three volumes of 60% ethanol are then added for 18 h of extraction. Solution is filtered and concentrated using a rotary evaporator. Concentrated solution is made into powder using a spray dryer.	21
Ecklonia Cava Extract (high in polyphenols)	Dried *Ecklonia cava* powder is extracted with ethanol, concentrated, and freeze-dried.	22
Fucus Vesiculosus Extract (28.8% polyphenols)	Ethanol (30% - 35% aq.) extraction of *Fucus vesiculosus* (10% w/w) is performed at room temperature under mechanical stirring for 4 h. After filtration on a filter press, liquid phase undergoes an initial purification step to remove alginates by precipitation in presence of excess calcium chloride. Liquid phase undergoes a second purification step involving diafiltration to remove iodine and low molecular weight compounds. Extract is freeze-dried to obtain a powder extract.	23
Fucus Vesiculosus Extract (18% polyphenols plus 0.0012% fucoxanthin)	Ethanol (50% - 70% aq.) extraction of *Fucus vesiculosus* (10% w/w) is performed to solubilize a greater amount of carotenoids at room temperature under mechanical stirring for 2 h. After filtration on a filter press, liquid phase undergoes an initial purification step to remove alginates by precipitating them in presence of excess calcium chloride. After solid-liquid separation, a second extraction is performed under same conditions. Two liquid phases are then blended, submitted to diafiltration to remove iodine and low molecular weight compounds, and freeze-dried to obtain a powder extract.	23
Fucus Vesiculosus Extract	Driedalgae material is extracted with water for 24 h, with stirring at room temperature. Residue is then removed by filtration to give a slightly brown colored extract.	24
Laminaria Digitata Extract (high in oligosaccharides)	An aqueous extraction is conducted followed by enzymatic depolymerization that breaks the polysaccharide into oligosaccharides (e.g., smaller polymers with 3 to 10 sugar components). Final process involves chelating oligosaccharide with zinc sulfate (0.1% zinc-pyrrolidone).	25
Laminaria Japonica Extract (low-molecular weight fucoidan)	Enzyme hydrolysis	26
Laminaria Japonica Extract	Algae is rinsed with tap water to remove salt and dried in an air dryer at 60°C for 40 h. Dried material is ground with a hammer mill, and powder stored at −20°C until used. Dried powder (2.5 kg) is extracted 3 times with 96% (v/v) ethanol for 3 h at 70°C. Combined extracts are filtered and concentrated under reduced pressure to obtain ethanol extracts	27
Laminaria Japonica Extract	Freshly collected algae material is air dried with a fan for 24 h then ground into a fine powder. 5 g of powder is added to 100 mL of 1:1 water:propylene glycol at room temperature for 1 day. This procedure is repeated 2 times, and the combined extracts were stored at −20°C until use.	28
Laminaria Japonica Powder	Dried algaet is pulverized to desired size.	29
Sargassum Fusiforme Extract and Undaria Pinnatifida Extract (high in fucosterol and phytol)	Microwave-assisted extraction coupled with high-speed countercurrent chromatography.	30
Sargassum Fusiforme Extract and Undaria Pinnatifida Extract (high in lipids and antioxidant compounds)	Supercritical fluid extraction and subcritical water extraction.	30
Unidaria Pinnatifida Extract (high in fucoidan)	Algae material is hydrolyzed in 0.05 or 0.5 M hydrochloric acid at 80°C for 30 min then neutralized with 1 M sodium hydroxide. Resulting material is desalted by gel filtration and hydrolysate lyophilized.	31

Abbreviations: aq. = aqueous; HPLC = high-performance liquid chromatography

Table 7. Constituents in brown algae.

Constituent(s)	Description
Alkaloids	Tyramine (TYR, 4-hydroxyphenylethylamine) has been detected in *Laminaria saccharina*.[109] The alkaloids found in marine algae may be divided into three groups: phenylethylamine alkaloids, indole and halogenated indole alkaloids, and other alkaloids.
Amino acids	Brown algae contain all of the essential amino acids and are greater in threonine, valine, leucine, lysine, glycine, and alanine than are the green and blue algaes.[30] *Fucus spiralis* was reported to contain 63.5% essential amino acids per total protein, containing leucine (5.5 mg/g protein), isoleucine (15.3 mg/g protein), lysine (12.5 mg/g protein), glutamic acid (12.1 mg/g protein), arginine (11.7 mg/g protein), serine (11.5 mg/g protein), valine (11.1 mg/g protein), and threonine (10.9 mg/g protein).[110]
Betaines	Glycinebetaine, γ-aminobutyric acid betaine, and/or trigonelline have been found in Alaria esculenta, Ecklonia maxima, Ecklonia radiata, Eisenia arborea, Laminaria digitata Macrocystis pyrifera, Nereocystis luetkeana, Saccharina angustata, Saccharina japonica, and Undaria pinnatifida.[111]
Iodine	The concentration of iodine in *Alaria esculenta* was reported to have a range of approximately 200 mg/kg (dry wt) to approximately 700 mg/kg (dry wt) depending on year, season, location, and whether it was collected in the wild, a monoculture, or an integrated culture.[112] *Fucus vesiculosus* contains between 0.03% and 0.2% iodine in dried material.[113] The iodine content is highest in the spring in freshly cut young blades. In *Laminaria digitata*, iodine content is highest in late autumn and winter (0.75% to 1.20% dry wt) and lowest in summer (0.25% to 0.60% dry wt).[114] Iodine content for *Fucus spiralis* and *Laminaria ochroleuca* have been reported to be 232.7 and 883.5 mg/kg dry wt.[110]
Laminarins	Laminarins are basically a class of low molecular weight storage β-glucans. These are composed of (1,3)-β-D-glucan and can be up to 35% of the dry weight of brown algae.[115]
Lipids	Fucosterol and fucosterol derivatives are present in brown algae.[30] Fucoxanthine, tocopherols, and sterols are also found in brown algae.
Omega-3 fatty acids	Omega-3 fatty acids include stearidonic acid and hexadecatetraenoic acid.[116] These make up to 40% of the total fatty acid content in *Undaria pinnatifida*.
Phenolic compounds, polyphenols, and phlorotannins	Phlorotannins are found in brown algae.[30] Flavonoids are integral structural components of cell walls (e.g., eckol, phlorofucofuroeckol A, dieckol, catechin, and epigallocatechin).
Pheromones	The pheromones include lamoxirene 4 (e.g., Agarum cribrosum, Ecklonia radiata, Eisenia arborea, Laminaria digitata, Laminaria hyperborea, Laminaria japonica, Laminaria saccharina, Saccharina angustata, Undaria pinnatifida, Macrocystis pyrifera, and Nereocystis luetkeana), fucoserratene 6 (e.g., Fucus serratus, Fucus spiralis, and Fucus vesiculosus), hormonsirene 8 (e.g., Durvillaea antarctica), and finavarrene 12 (Ascophyllum nodosum). The major constituents of the essential oil of Dictyopteris polypodioides are C_{11} hydrocarbons sulfur products such as 3-hexyl-4,5-dithiacycloheptanone.[20]
Phytohormones	Auxins (plant hormones that cause the elongation of cells in shoots and are involved in regulating plant growth), such as indoleacetic acid are found in the genera *Macrocystis*, *Laminaria*, *Fucus*, *Ascophyllum*).[30,117] Cytokinins (genera *Fucus*, *Ascophyllum*, *Sargassum*, *Macrocystis*), gibberellins (genus *Fucus*), abscisic acid (genera *Ascophyllum*, *Laminaria*), and polyamines (genus *Dyctiota*) are also found.
Pigments	Carotenoids including fucoxanthin, β-carotene, zeaxanthin, violaxanthin, and antheraxanthin are found in brown algae.[30] These vary with season.
Protein	The protein content of algae varies according to species and season.[14,30] In general, the protein fraction of brown algae is low (1% to 24% dry wt.) compared with that of green or red algae (4% to 50% dry wt). Except for the species *Undaria pinnatifida*, which has a protein content between 11% and 24% (dry wt.), most commercial brown algae have a protein content lower than 15% (dry wt; e.g., *Ascophyllum nodosum*, 3% to 15%; *Fucus vesiculosus*, *Himanthalia elongate*, and *Laminaria digitata*, 8% to 15%). The protein content of *Fucus* sp. tend to range from 3% to 11% (e.g., *Fucus spiralis*, 9.71% dry weight).[110]
Sterols	Sterols found in brown algae include desmosterol, ergosterol, fucosterol, cholesterol, campesterol, stigmasterol, and β-sterol.[38,39]
Terpenoids	Terpenes, phenolic compounds, and meroterpenes make up the three major classes of secondary metabolites in brown seaweed.[30]

Table 8. Constituents in *Ascophyllum nodosum*, *Fucus vesiculosus*, and *Laminaria digitata*

	Ascophyllum nodosum (ppm) [118]	*Fucus vesiculosus* (ppm) [119]	*Fucus vesiculosus* (ppm) [118]	*Laminaria digitata* (ppm) [25]
Algin	NR	41300 – 500000	NR	
Alginic acid	NR	NR	NR	200000 – 450000
Aluminum	NR	75.0 - 631.0	NR	
Arsenic	NR	68.0	NR	
Ascorbic-acid	NR	30.0 - 258.0	NR	
Bromine	NR	150.0	NR	
Calcium	9847	3587 – 30400	11600	
Carbohydrates	NR	77290 – 655000	NR	10000 – 20000
β-carotene	NR	5.0 – 40.0	NR	
Chromium	NR	0.1 – 0.7	NR	
Cobalt	NR	0.2 – 1.6	NR	
Fat	NR	3540 – 30000	NR	10000 – 20000
Fiber	NR	98000	NR	
Fiber(crude)	NR	98000	NR	
Fiber(dietary)	NR	482000	NR	
Fucinicacid	NR	1000	NR	
Fucoidin	NR	600000	NR	20000 – 40000
Fucose	NR	240000	NR	
Iodine	NR	64.0 – 540.0	NR	3000 – 1100
Iron	133.4	2.0 – 16.0	189.9	
Kilocalories	NR	2490	NR	
Lead	NR	91.0	NR	
γ-Linolenic acid	NR	NR	NR	
Magnesium	8678	1023 – 8670	7320	5000 – 8000
Mannitol	NR	NR	NR	40000 – 160000
Manganese	19.6	0.9 – 7.6	82.8	
Mercury	NR	40.0	NR	
Niacin	NR	6.0 – 47.0	NR	
Phosphorus	NR	294.0 -2490	1935.7	
Potassium	37810	2490 – 21,100	37450	13000 – 38000
Selenium	NR	0.2 – 1.7	NR	
Silicon	NR	0.9 – 7.6	NR	
Sodium	45757	6620 – 56,100	21875	9000 – 22000
Sugars	NR	2360 – 20000	NR	
Tin	NR	3.0 – 24.0	NR	
Water	NR	882000	NR	730000 – 900000
Zinc	NR	0.1 – 0.6	NR	

NR = not reported

Table 9. Sterols in several brown algae

Species	Desmosterol (mg/kg)	Ergosterol (mg/kg)	Fucosterol (mg/kg)	Cholesterol (mg/kg)	Campesterol + Stigmasterol (mg/kg)	β-Sterol (mg/kg)	Brassicasterol (mg/kg)	Ssaringosterol (mg/kg)	24-ketocholesterol (mg/kg)	Total[a] (mg/kg)	Reference
Cystoseira tamariscifolia	44.1 ± 3.4	-	5260.2 ± 14.9	500.4 ± 2.6	680.9 ± 21.4	17.0 ± 0.3	NR	NR	NR	6502.6	[39]
Fucus spiralis	37.6 ± 3.8	-	3815.1 ± 329.5	325.1 ± 13.5	183.4 ± 0.3	-	NR	NR	NR	4361.0	[39]
Sargassum vulgare	47.2 ± 0.2	5.6 ± 0.4	4451.5 ± 16.7	406.3 ± 13.2	303.3 ± 18.9	15.2 ± 2.8	NR	NR	NR	5229.1	[39]

NR = not reported; - = not found

[a] Total may not be exact due to rounding.

Table 10. Constituents of ethanol extracts of *Fucus spiralis* and *Sargassum vulgare*.[41]

	Range (if provide; ppm)	
Constituent	***Fucus spiralis* extract**	***Sargassum vulgare* extract**
Arachidic Acid	ND	ND
Arachidonic Acid	465.6 ± 29.0	ND
Cholesterol	ND	127.4 ± 11.6
Eicosapentaenoic Acid	217.0 ± 11.4	ND
Fucosterol	317.6 ± 9.4	257.6 ± 43.6
γ-Linolenic Acid	ND	2413.6 ± 57.6
Mannitol (Total)	1273.8 ± 34.8	394.6 ± 15.2
Myristic Acid	69.8 ± 2.7	ND
Palmitic Acid	606.0 ± 20.6	340.4 ± 95.0
Phloroglucinol	< LOD	ND
Proline	396.8 ± 96.8	117.4 ± 11.0
β-Sitosterol	ND	ND
Stearic Acid	208.4 ± 21.4	204.0 ± 26.0
Vaccenic Acid	21,690.6 ± 1667.6	2848.6 ± 71.2

LOD = limit of detection; ND = not detected

Table 11. Composition of a 50/50 water/propylene glycol extract of *Laminaria japonica*[28]

Constituent	**Amount**
Constituent Groups (mg/g)	
Carbohydrate	6
Sugars	5
Proteins	2
Crude fat	2
Saturated fatty acid	1
Unsaturated fatty acid	None detected
Amino Acids (mg/L)	
Alanine	42.3
Ammonium chloride	16.2
Arginine	20.3
Aspartic acid	424.7
Glutamic acid	689.4
Glycine	1.7
Hydroxyproline	381.4
Phosphoserine	3.7
Serine	8.6
Threonine	4.2
Minerals (mg/g)	
Sodium	404
Calcium	300
Potassium	1022
Magnesium	35
Iron	0.5
Zinc	0.2

Table 12. Composition of enzyme hydrolysis extracts of *Laminaria japonica*[26]

Constituent	Concentration (% w/w)
	***Laminaria japonica* extract**[26]
Ash	4.1 ± 0.1
Fat	0.6 ± 0.1
Fucose	85.9
Moisture	3.9 ± 0.8
Monosaccharides (neutral)	NR
Protein	4.3 ± 0.3%
Sulfate	28.4 ± 2.1

NR = not reported

Table 13. Specifications of an alcohol extract of *Ecklonia cava* for use as a food supplement[9]

Parameter	Specification
Phlorotannin	90 ± 5.0%
Dieckol	6.6% – 9.9%
Moisture content	< 5%
Ash	< 5%
Insoluble substances	Negative
Substances not originating from *E. cava*	Negative
Viable cell count	< 3000 CFU/g
Staphylococcus aureus	Negative
Molds and yeasts	< 300 CFU/g
Salmonella spp.	Negative
Coliforms	Negative
Lead	< 3 mg/kg
Mercury	< 0.1 mg/kg
Cadmium	< 3 mg/kg
Arsenic	< 25 mg/kg
Iodine	150.0 – 650.0 mg/kg
Sieving size	> 60 (0.250 mm)

Table 14. Constituents of desalinated Undaria pinnatifida powder.[42]

Constituent	Amount (mg/g)
Ash	147
Calcium	13.6
Copper	0.00130
Dietary fiber	532
Iron	0.107
Lipid	14
Magnesium	13.4
Protein	209
Sodium	25.4
Zinc	0.02

Table 15. Amount of arsenic found in several brown algae species.[33]

Species	Arsenic Concentration (mg/kg wet wt.)	Arsenic Concentration (mg/kg dry wt.)
Ecklonia radiate	10[33]	-
Hizikia fusiforme	10[33]	-
Laminaria japonica	4[33]	-
Laminaria ochroleuca	-	56.8 ± 2.4[43]
Laminaria saccharina	-	52.4 ± 2.1[43]
Saccharina (spp)	-	< 0.3[120]
Sargassum fusiforme	-	67 - 96[120]
Sargassum thunbergii	4[33]	-
Unidaria pinnatifida	2.8 – 4.5[33]	< 0.3[120] 115 ± 9[43]

- = no data

Table 16. Arsenic -containing moieties found in various brown algae[43]

	Amount (mg/kg)			
Arsenic-Containing Moiety	***Laminaria ochroleuca***	***Laminaria saccharina***	***Sargassum fulvellum***	***Undaria pinnatifida***
Arsenic III	ND	ND	ND	ND
Arsenic V	ND	ND	69.9 ± 1.0	0.29 ± 0.03
Methylarsonate	ND	0.21 ± 0.03	ND	ND
Dimethylarsinate	0.26 ± 0.08	0.67 ± 0.02	2.1 ± 0.1	0.13 ± 0.03
Trimethylarsine oxide	ND	ND	ND	ND
Arsenobetaine	0.20 ± 0.02	0.09 ± 0.02	ND	ND
Phospate-sug po4	6.2 ± 0.1	6.9 ± 0.1	2.2 ± 0.1	0.30 ± 0.02
Sulfonate-sug so3	39.4 ± 1.6	30.7 ± 1.2	1.80 ± 0.10	ND
Sulfate-sug so4	ND	ND	9.0 ± 0.7	ND
Glycerol-sug gly	2.71 ± 0.04	2.9 ± 0.1	1.2 ± 0.2	0.87 ± 0.03
Arsenocholine	ND	ND	ND	ND
Inorganic arsenic	ND	ND	69.9	0.29

ND = not detected

Table 17. Arsenic species found in *Laminaria japonica* and an extract of *Laminaria japonica*[26]

	Amount (mg/kg)	
Arsenic Species	*Laminaria japonica*	*Laminaria japonica* extract[a]
Arsenic III	ND	ND
Arsenic V	ND	ND
Monomethylarsonic Acid	9.27 ± 0.96	1.35 ± 0.63
Dimethylarsinic Acid	9.23 ± 0.83	ND
Arsenobetaine	34.31 ±1.21	4.77 ± 0.88
Arsenocholine	6.19 ± 2.17	ND
Arsenic (sum)	59.00 ± 1.65	6.12 ± 2.005

ND = not detected

[a] Extracted by enzyme hydrolysis, high in low-molecular-weight fucoidan

Table 18. Heavy metals in brown algae species[45]

	Concentration of heavy metals (mg/kg dry weight)							Reference
Species	**Cadmium**	**Lead**	**Mercury**	**Copper**	**Zinc**	**Arsenic**	**Inorganic Arsenic**	
Alaria esculenta	0.22 – 7.9	0.2 – 1.9	< 0.005 - <0.071	0.39 - 4	7 - 45	<0.074 - 100	-	[121]
Fucus vesiculosus	1.7	11	-	12.7	89	13.5	-	[98]
Himanthalia elongate	0.310 – 0.326	0.203 – 0.259	0.008 – 0.016	1.14 – 1.25	48.5 – 48.7	32.9 – 36.7	0.166 – 0.245	[45]
Hizikia fusiforme	0.988 – 2.50	< 0.008[a] – 0.531	0.015 – 0.050	1.78 – 7.70	4.72 – 19.5	103 – 147	32.1 – 69.5	[45]
Laminaria spp.	0.085 – 1.83	< 0.008[a] – 0.460	0.001 – 0.005	0.91 – 2.50	10.3 – 23.2	51.7 – 68.3	0.052 – 0.443	[45]
Undaria pinnatifida	0.267 – 4.82	< 0.008[a] – 1.28	0.010 – 0.057	1.07 – 1.70	8.25 – 26.6	42.1 – 76.9	0.045 – 0.346	[45]

[a] Limit of detection.

spp. = multiple species

Table 19. Frequency of use according to duration and exposure of brown algae-derived ingredients.[49-51]

Use type	# Uses	Max. Conc. (%)	Uses	Max. Conc.(%)	Uses	Max. Conc.(%)	Uses	Max.Conc. (%)
	Agarum Cribrosum Extract		**Alaria Esculenta Extract**		**Ascophyllum Nodosum Extract**		**Ascophyllum Nodosum Powder**	
Total/range	**NR**	**0.012**	**37**	**0.0005-1**	**120**	**0.0000004-0.2**	**4**	**NR**
Duration of use[a]								
Leave-on	*NR*	*0.012*	*37*	*0.0005-1*	*91*	*0.0000004-0.2*	*3*	*NR*
Rinse-off	*NR*	*NR*	*NR*	*0.0015*	*29*	*0.00004-0.0032*	*NR*	*NR*
Diluted for (bath) use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*1*	*NR*
Exposure type								
Eye area	NR	NR	11	NR	16	0.025-0.2	NR	NR
Incidental Ingestion	NR	NR	3	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	NR	3[a]; 6[b]	0.0005[a]	23[a]; 44[b]	0.002[a]	2[a]	NR
Incidental Inhalation-Powder	NR	NR	6[b]	0.0015-0.05[c]	1; 44[b]	0.0000004-0.03[c]	NR	NR
Dermal Contact	NR	0.012	33	0.0005-1	104	0.0000004-0.2	4	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair-Non-Coloring	NR	NR	1	NR	13	0.00005-0.002	NR	NR
Hair- Coloring	NR	NR	NR	NR			NR	NR
Nail	NR	NR	NR	NR	3	0.000065-0.02	NR	NR
Mucous Membrane	NR	NR	3	NR	6	0.00004	1	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

	Cladosiphon Okamuranus Extract		**Dictyopteris Polypodioides Extract**[d]		**Durvillaea Antarctica Extract**		**Ecklonia Radiata Extract**	
Total/range	**9**	**0.005-0.05**	**1**	**0.01**	**NR**	**0.0001**	**NR**	**0.005-0.0051**
Duration of use								
Leave-on	*8*	*0.025-0.05*	*1*	*0.01*	*NR*	*0.0001*	*NR*	*0.0051*
Rinse-off	*1*	*0.005*	*NR*	*NR*	*NR*	*NR*	*NR*	*0.005*
Diluted for (bath) use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure type								
Eye area	1	0.025	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	0.01	NR	NR	NR	NR
Incidental Inhalation-Spray	3[a]; 3[b]	NR	1[b]	NR	NR	NR	NR	0.0051
Incidental Inhalation-Powder	3[b]	0.025[b]	1[b]	NR	NR	NR	NR	NR
Dermal Contact	9	0.005-0.05	1	NR	NR	NR	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair-Non-Coloring	NR	NR	NR	NR	NR	NR	NR	0.0051
Hair- Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	0.001	NR	NR
Mucous Membrane	NR	NR	NR	0.01	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

	Fucus Serratus Extract		**Fucus Vesiculosus**		**Fucus Vesiculosus Extract**		**Fucus Vesiculosus Powder**	
Total/range	**8**	**0.00001-0.05**	**NR**	**0.0003-0.0051**	**287**	**0.00002-6**	**3**	**NR**
Duration of use								
Leave-on	*8*	*0.05*	*NR*	*0.00098-0.0051*	*201*	*0.000032-6*	*1*	*NR*
Rinse-off	*NR*	*0.00001-0.05*	*NR*	*0.0003*	*75*	*0.00002-5*	*2*	*NR*
Diluted for (bath) use	*NR*	*NR*	*NR*	*NR*	*11*	*0.0001-5*	*NR*	*NR*
Exposure type								
Eye area	8	0.05	NR	NR	6	0.01-5	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	0.0005	NR	NR
Incidental Inhalation-Spray	3[a]; 4[b]	NR	NR	0.00098	1; 90[a]; 82[b]	0.00018-0.12; 0.0001-0.1[a]	1[b]	NR
Incidental Inhalation-Powder	4[b]	0.05[c]	NR	NR	82[b]	0.000032-6[c]	1[b]	NR
Dermal Contact	8	NR	NR	0.00098-0.0051	262	0.00002-6	3	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair- Non-Coloring	NR	0.000010	NR	0.0003	22	0.0001-5	NR	NR
Hair- Coloring	NR	NR	NR	NR	NR	0.0001-0.001	NR	NR
Nail	NR	NR	NR	NR	NR	0.02	NR	NR
Mucous Membrane	NR	NR	NR	NR	30	0.00002-5	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

Table 19. Frequency of use according to duration and exposure of brown algae-derived ingredients.[49-51]

Use type	# Uses	Max. Conc. (%)	Uses	Max. Conc.(%)	Uses	Max. Conc.(%)	Uses	Max.Conc. (%)
	Himanthalia Elongata Extract		**Laminaria Cloustoni Extract**		**Laminaria Digitata Extract**		**Laminaria Digitata Powder**	
Total/range	**9**	**NR**	**14**	**NR**	**235**	**0.00004-5**	**21**	**40**
Duration of use								
Leave-on	*7*	*NR*	*10*	*NR*	*162*	*0.0001-5*	*2*	*40*
Rinse-off	*2*	*NR*	*4*	*NR*	*66*	*0.00004-5*	*16*	*NR*
Diluted for (bath) use	*NR*	*NR*	*NR*	*NR*	*7*	*0.1-5*	*3*	*NR*
Exposure type								
Eye area	1	NR	1	NR	15	0.0035-0.5	NR	NR
Incidental Ingestion	NR	NR	NR	NR	2	NR	NR	NR
Incidental Inhalation-Spray	1[a]; 4[b]	NR	4[a]; 4[c]	NR	1; 44[a]; 67[c]	0.0007; 0.0035-5[a]	1[b]	NR
Incidental Inhalation-Powder	4[b]	NR	4[c]	NR	3; 67[c]	0.0001-0.1[c]	1[b]	40[b]
Dermal Contact	7	NR	14	NR	191	0.0001-5	15	40
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair- Non-Coloring	2	NR	NR	NR	36	0.0007-5	6	NR
Hair- Coloring	NR	NR	NR	NR	1	0.00004-0.0007	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	20	0.06-5	4	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

	Laminaria Hyperborea Extract		**Laminaria Japonica Extract**		**Laminaria Ochroleuca Extract**		**Laminaria Saccharina Extract**	
Total/range	**2**	**0.03**	**77**	**0.005-5**	**26**	**0.000024-0.63**	**132**	**0.00001-0.54**
Duration of use								
Leave-on	*2*	*0.03*	*62*	*0.0005-5*	*22*	*0.00017-0.63*	*85*	*0.000092-0.54*
Rinse-off	*NR*	*NR*	*15*	*0.0005-5*	*4*	*0.000024-0.017*	*47*	*0.00001-0.51*
Diluted for (bath) use	*NR*	*NR*	*NR*	*0.011-5*	*NR*	*NR*	*NR*	*NR*
Exposure type								
Eye area	NR	NR	3	0.0005-0.007	2	0.0034-0.63	NR	0.000092-0.019
Incidental ingestion	NR	NR	1	NR	1	NR	NR	NR
Incidental Inhalation-Spray	2[a]	NR	7[a]; 28[b]	0.3-5[a]	3[a]; 5[b]	0.017; 0.017[a]	40[a]; 19[c]	0.001-0.005
Incidental Inhalation-Powder	NR	0.03[c]	3; 1[c]; 28[b]	0.0035; 0.0055-5[c]	3; 5[b]	0.0005-0.17[c]	19[c]	0.0008; 0.000092-0.1[c]
Dermal Contact	2	0.03	72	0.0005-5	25	0.000024-0.63	120	0.000092-0.54
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	0.15[e]
Hair- Non-Coloring	NR	NR	1	0.0005-0.3	NR	0.017	12	0.00001-0.045
Hair- Coloring	NR	NR		NR	NR	0.017	NR	
Nail	NR	NR	2	NR	NR	NR	NR	0.001
Mucous Membrane	NR	NR	3	0.011-5	3	NR	4	0.51
Baby Products	NR	NR	1	NR	NR	NR	NR	NR

	Lessonia Nigrescens Extract		**Macrocystis Pyrifera (Kelp)**		**Macrocystis Pyrifera (Kelp) Extract**		**Macrocystis Pyrifera (Kelp) Protein**	
Total/range	**NR**	**0.032**	**2**	**NR**	**188**	**0.00005-36.4**	**3**	**NR**
Duration of use								
Leave-on	*NR*	*NR*	*1*	*NR*	*106*	*0.0002-36.4*	*1*	*NR*
Rinse-off	*NR*	*0.032*	*1*	*NR*	*78*	*0.00005-5*	*2*	*NR*
Diluted for (bath) use	*NR*	*NR*	*NR*	*NR*	*4*	*0.0051-1*	*NR*	*NR*
Exposure type								
Eye area	NR	NR	NR	NR	5	0.007-36.4	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	0.079	NR	NR
Incidental Inhalation-Spray	NR	NR	1[a]	NR	9; 38[a]; 26[b]	0.042-0.79; 0.0036-5[a]; 0.17[b]	NR	NR
Incidental Inhalation-Powder	NR	NR	NR	NR	2; 26[b]	0.0035; 0.001-33.3[c]; 0.17[b]	NR	NR
Dermal Contact	NR	0.032	2	NR	123	0.00005-36.4	3	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair- Non-Coloring	NR	NR	NR	NR	56	0.001-5	NR	NR
Hair- Coloring	NR	NR	NR	NR	4		NR	NR
Nail	NR	NR	NR	NR	5	0.0002-0.0011	NR	NR
Mucous Membrane	NR	NR	1	NR	34	0.0051-5	1	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

Table 19. Frequency of use according to duration and exposure of brown algae-derived ingredients.[49-51]

Use type	# Uses	Max. Conc. (%)	Uses	Max. Conc.(%)	Uses	Max. Conc.(%)	Uses	Max.Conc. (%)
	Pelvetia Canaliculata Extract		**Sargassum Filipendula Extract**		**Sargassum Fusiforme Extract**		**Sargassum Muticum Extract**	
Total/range	**47**	**0.00002-0.018**	**46**	**0.0001-1.2**	**7**	**NR**	**1**	**0.01-4**
Duration of use								
Leave-on	*34*	*0.00002-0.018*	*14*	*0.0001-1.2*	*4*	*NR*	*NR*	*2-4*
Rinse-off	*13*	*0.00004-0.0018*	*32*	*0.002-0.29*	*3*	*NR*	*1*	*0.01*
Diluted for (bath) use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure type[a]								
Eye area	6	0.00002-0.0007	2	NR	NR	NR	NR	2.5-4
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	1; 18[a]; 8[b]	0.00004-0.0007; 0.002-0.0035[a]	3; 5[a]; 1[b]	0.0001[a]	2[a]; 2[b]	NR	NR	NR
Incidental Inhalation-Powder	8[b]	0.002-0.018[c]	1[b]	0.8[c]	2[b]	NR	NR	NR
Dermal Contact	19	0.00002-0.018	16	0.002-1.2	7	NR	1	0.01-4
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair- Non-Coloring	24	0.00004-0.0025	7	0.0001-0.29	NR	NR	NR	NR
Hair- Coloring	1	0.0000-0.0007	23	0.011-0.29	NR	NR	NR	NR
Nail			NR	NR	NR	NR	NR	NR
Mucous Membrane	1	NR	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

	Sargassum Vulgare Extract		**Sphacelaria Scoparia Extract**		**Undaria Pinnatifida Extract**		**Undaria Pinnatifida Powder**	
Total/range	**NR**	**0.0075-0.016**	**8**	**0.016**	**74**	**0.00001-5**	**NR**	**0.1**
Duration of use								
Leave-on	*NR*	*0.009-0.016*	*6*	*0.016*	*64*	*0.00001-5*	*NR*	*NR*
Rinse-off	*NR*	*0.0075*	*2*	*NR*	*10*	*0.0001-5*	*NR*	*0.1*
Diluted for (bath) use	*NR*	*NR*	*NR*	*NR*	*NR*	*0.0001*	*NR*	*NR*
Exposure type								
Eye area	NR	0.011	NR	NR	4	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	0.009[a]	1[a]; 4[c]	NR	12[a]; 38[b]	0.002[a]	NR	NR
Incidental Inhalation-Powder	NR	0.011[c]	4[c]	NR	3; 38[b]	0.00001-5; 0.00001-5[c]	NR	NR
Dermal Contact	NR	0.011-0.016	8	0.016	68	0.00001-5	NR	0.1
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair- Non-Coloring	NR	0.0075-0.009	NR	NR	6	0.002-5	NR	NR
Hair- Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	2	NR	4	0.0001	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

	Kelp[f]		**Kelp Extract**[f]		**Laminaria Extract**[f]		
Total/range	**24**	**NS**	**15**	**NS**	**4**	**NS**	
Duration of use							
Leave-on	*9*	*NS*	*10*	*NS*	*2*	*NS*	
Rinse-off	*10*	*NS*	*4*	*NS*	*2*	*NS*	
Diluted for (bath) use	*5*	*NS*	*1*	*NS*	*NR*	*NS*	
Exposure type							
Eye area	NR	NS	1	NS	NR	NS	
Incidental Ingestion	1	NS	NR	NS	NR	NS	
Incidental Inhalation-Spray	3[a]; 3[b]	NS	5[a]; 1[b]	NS	1[b]	NS	
Incidental Inhalation-Powder	3[b]	NS	1[b]	NS	1[b]	NS	
Dermal Contact	19	NS	8	NS	2	NS	
Deodorant (underarm)	NR	NS	NR	NS	NR	NS	
Hair- Non-Coloring	4	NS	7	NS	2	NS	
Hair- Coloring	NR	NS	NR	NS	NR	NS	
Nail	NR	NS	NR	NS	NR	NS	
Mucous Membrane	11	NS	2	NS	NR	NS	
Baby Products	NR	NS	NR	NS	NR	NS	

NR = Not Reported; NS = Not Surveyed; Totals = Rinse-off + Leave-on + Diluted for Bath Product Uses.

Note: Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure type uses may not equal the sum total uses.

[a] It is possible these products may be sprays, but it is not specified whether the reported uses are sprays.

[b] Not specified whether a powder or a spray, so this information is captured for both categories of incidental inhalation.

[c] It is possible these products may be powders, but it is not specified whether the reported uses are powders.

[d] Frequency of use and concentration of use were reported under the INCI name Dictyopteris Membranacea Extract (Retired).

[e] Not spray.

[f] Reported in the VCRP under a non-INCI name and presented here for information purposes.

Table 20. Brown algae-derived ingredients with no reported uses in the VCRP or the Council survey.[49-51]

Ascophyllum Nodosum		Cladosiphon Novae-Caledoniae Extract
Cystoseira Amentacea/Caespitosa / Branchycarpa Extract	Cystoseira Baccata Extract	Cystoseira Balearica Extract
Cystoseira Caespitosa Extract	Cystoseira Compressa Extract	Cystoseira Compressa Powder
Cystoseira Tamariscifolia Extract	Dictyota Coriacea Extract	Ecklonia Cava Extract
Ecklonia Cava Water	Ecklonia Kurome Extract	Ecklonia Kurome Powder
Ecklonia/Laminaria Extract	Ecklonia Maxima Extract	Ecklonia Maxima Powder
Eisenia Arborea Extract	Fucus Spiralis Extract	Halidrys Siliquosa Extract
Halopteris Scoparia Extract	Himanthalia Elongata Extract	Himanthalia Elongata Powder
Hizikia Fusiforme Extract	Hizikia Fusiformis Water	Hizikia Fusiformis Callus Culture Extract
Hydrolyzed Ecklonia Cava Extract	Hydrolyzed Fucus Vesiculosus Extract	Hydrolyzed Fucus Vesiculosus Protein
Laminaria Diabolica Extract	Laminaria Japonica Powder	Laminaria Longissima Extract
Lessonia Nigrescens Powder	Macrocystis Pyrifera (Kelp) Blade/ Pneumatocyst/Stipe Juice Extract	Macrocystis Pyrifera (Kelp) Juice
Nereocystis Luetkeana Extract	Pelvetia Siliquosa Extract	Phyllacantha Fibrosa Extract
	Saccharina Angustata Extract [Laminaria Angustata Extract (Retired)]	Saccharina Japonica Extract [Laminaria Ochotensis Extract (Retired)]
Saccharina Longicruris Extract	Sargassum Fulvellum Extract	Sargassum Glaucescens Extract
Sargassum Horneri Extract	Sargassum Pallidum Extract	Sargassum Siliquastrum Extract
Sargassum Thunbergii Extract		Undaria Peterseniana Extract
Undaria Pinnatifida Cell Culture Extract	Undaria Pinnatifida Leaf/Stem Extract	Undaria Pinnatifida Root Powder

Table 21. Acute oral toxicity studies

Ingredient	Animals	No./Group	Vehicle	Concentration/Dose/Protocol	LD_{50}/Results	Reference
				ORAL		
Cystoseira Compressa Extract (methanol, hexane, and chloroform extracts)	Albino mice	2	Not specified	Up to 2000 mg/kg by gavage. Observed for 24 h.	There were no mortalities or clinical signs for any of the extracts.	40
Ecklonia Cava Extract (alcohol extract)	Sprague-Dawley (Crl:DC(DS)) rats	10/sex	Not specified	2000 mg/kg by gavage. Observed for 2 weeks.	There were no mortalities. Clinical signs were soft stools, diarrhea, mucus stools, compound-colored feces, and soiled perineal region from the day of administration until day 2.	9
Ecklonia Cava Extract (enzyme extract)	SD rats	5/sex	Distilled water	0 or 3000 mg/kg by oral gavage. Rats were observed for 14 days.	No abnormal changes in body weights, clinical signs, or mortalities were observed. Necropsy results showed no macroscopic lesions in any organs of treatment group.	21
Ecklonia Cava Extract (enzyme extract)	Beagle dogs	2/sex	Distilled water	3000 mg/kg by oral gavage in two equally divided doses approximately 6 h apart. Dogs were observed for 14 days.	No abnormal changes in body weights, clinical signs, or mortalities were observed. Necropsy results showed no macroscopic lesions in any organs of treatment group.	21
Fucus Vesiculosus Extract (28.8% polyphenols)	Swiss mice	7/sex	1% carboxymethyl-cellulose	1000 - 2000 mg/kg OECD GL 425 Administered by gavage. An Irwin test (determines the general effects of a test substance on the central nervous system and physiological functions) was performed at 1 and 5 h after administration of the extracts to detect motor, respiratory, temperature, circulatory, behavior, or other alterations. Mice were observed for 7 days.	LD_{50}: Males = 1000 mg/kg; females = between 1000 and 2000 mg/kg	23
Fucus Vesiculosus Extract (18% polyphenols plus 0.0012% fucoxanthin)	Swiss mice	7/sex	1% carboxymethyl-cellulose	1000 - 2000 mg/kg OECD GL 425 Administered by gavage. Irwin test was performed at 1 and 5 h after administration of the extracts to detect motor, respiratory, temperature, circulatory, behavior, or other alterations. Mice were observed for 7 days.	LD_{50}: Males = 500 mg/kg; females = < 750 mg/kg	23
Fucus Vesiculosus Extract (28.8% polyphenols)	Sprague-Dawley rats	7/sex	1% carboxymethyl-cellulose	1000 - 2000 mg/kg OECD GL 425 Administered by gavage. Irwin test was performed at 1 and 5 h after administration of the extracts to detect motor, respiratory, temperature, circulatory, behavior, or other alterations. Rats were observed for 7 days.	LD_{50}: Males and females = between 1000 and 2000 mg/kg	23

Table 21. Acute oral toxicity studies

Ingredient	Animals	No./Group	Vehicle	Concentration/Dose/Protocol	LD_{50}/Results	Reference
Fucus Vesiculosus Extract (18% polyphenols plus 0.0012% fucoxanthin)	Sprague-Dawley rats	7/sex	1% carboxymethyl-cellulose	1000 - 2000 mg/kg OECD GL 425 Administered by gavage. Irwin test was performed at 1 and 5 h after administration of the extracts to detect motor, respiratory, temperature, circulatory, behavior, or other alterations. Rats were observed for 7 days.	LD_{50}: Males and females = > 2000 mg/kg	23
Sargassum Fulvellum Extract (dichloromethane, ethanol, and water extracts)	BALB/c mice	5	Tween-80 (5%)	5000 mg in 10 ml vehicle by gavage. Observed for 2 weeks.	There were no mortalities. Most of the mice reacted immediately by perpetual gagging, jumping, sleeping, scaling, and writhing for 5–10 min.	65
Sargassum Thunbergii Extract	BALB/c mice	5	Tween-80 (5%)	5000 mg in 10 ml vehicle by gavage. Observed for 2 weeks.	There were no mortalities. Most of the mice reacted immediately by perpetual gagging, jumping, sleeping, scaling, and writhing for 5–10 min.	65

OECD GL = Organisation for Economic Co-operation and Development Guidelines

Table 22. Oral repeated dose studies

Test Article	Extraction Solvent/Method or Composition	Animals (n)	Study Duration	Vehicle	Dose/ Concentration	Results	Reference
				Short-Term			
Ascophyllum nodosum	Dried	Topigs Hybrid X Piétrain weanling pigs (20)	23 days	Feed	0, 2.5, 5.0, or 10.0 g/kg feed (0.25%, 0.5%, or 1.0%)	There were no adverse effects from treated feed. There were no effects on weight gain, feed consumption. Digestion characteristics were similar to controls (pH, fresh matter weight, and dry matter content), except for pH of part of the intestine was increased in the high-dose group (6.28 vs.5.96).	63
Ascophyllum nodosum	Freeze-dried and powdered	Male Sprague-Dawley rats (6)	4 weeks	Feed	0, 5%, 10%, or 15% in feed	Food intake, weight gain, and serum enzyme (alanine transaminase and aspartate transaminase) levels indicated that seaweed diets were well tolerated.	66
Cladosiphon Okamuranus Extract	hydrolyzing in HCl	Wistar Rats (12/group)	3 months	Water	300, 600, 1299, 2400, 4000 mg/kg bw/d	A dose-dependent increase in clotting time and decrease in alkaline phosphatase (ALP) was noted in high doses. No significant differences compares to control. No treatment-related changes in organ weights reported. No abnormalities is morphology of brain, thymus, lungs, heart, spleen, liver, adrenal glands, kidneys, testes, thyroids, prostate gland, uterus or ovaries.	19
Ecklonia Cava Extract	Alcohol extract	Male ICR mice (10)	4 weeks	None	0, 1.25, 2.5 or 5 mg/day Mice were fed high fat diet (20% fat) or normal diet (5% to 10% fat). After 1 week, mice in high fat diets were administered Ecklonia Cava Extract by gavage while continuing on the high fat diet.	There were no mortalities. There was a dose-dependent lower body weight of ~ 12% - ~ 16% in the mice administered the extract compared to control group. Triglycerides, total cholesterol and LDL cholesterol were decreased in all treated groups. Liver enzymes (GPT and GOT), BUN, and creatinine values in serum were similar to controls. No data on feed consumption provided.	67

Table 22. Oral repeated dose studies

Test Article	Extraction Solvent/Method or Composition	Animals (n)	Study Duration	Vehicle	Dose/ Concentration	Results	Reference
Ecklonia Cava Extract	Enzyme extract	SD rats (5/sex)	14 days	Water	0, 1000, 2000, or 5000 mg/kg by gavage	- There were no mortalities. No dose-related clinical abnormalities or body weight changes. - Macroscopic examination did not reveal any treatment-related abnormal lesions in males or females at necropsy; although redness in thymus, red spot in lung, and congestion and red spot in cervical lymph node were sporadically observed without a dose-dependent relationship. - Females in the 2000 and 5000 mg/kg groups had decreases in absolute and relative left ovary weights relative to control group and decreases in absolute brain weights were observed in females in 5000 mg/kg group.	21
Ecklonia Cava Extract	Alcohol extract	Sprague-Dawley (Crl:CD(SD)) rats (5/sex)	4 weeks	None	0, 500, 1000, or 2000 mg/kg/day by gavage.	- Compound-colored stools were observed in all rats in all dosing groups starting from day 1 of dosing. Salivation after dosing was observed sporadically in 1 female in the 1000 mg/kg/day group and in 2 males and 2 females in the 2000 mg/kg/day group on days 5 to 17 of dosing. - In clinical chemical investigations in 2000 mg/kg/day group, increases in ALT, and decreases in total protein, triglycerides and glucose were observed in males. Absolute and relative liver weights and absolute kidney weights were increased in males in 2000 mg/kg/day group. In females, relative heart weights were decreased in 1000 and 2000 mg/kg/day groups. There were no differences between study groups concerning body weight. Histopathologically, atrophy of periportal hepatocytes in livers was detected in male rats in 2000 mg/kg/day group.	9
Ecklonia Cava Extract	Alcohol extract	Beagle dogs (2/sex)	8 days 2-week observation period	Capsule	Day 1, 100 mg/kg; Day 4, 300 mg/kg; and day 8, 1000 mg/kg	There were no mortalities. Compound-colored stools were observed in all dogs in 300 and 1000 mg/kg groups. Vomiting was observed in 1 male and 1 female dog when treated at 1000 mg/kg.	9
Ecklonia cava powder (inference for Ecklonia Cava Extract and Ecklonia Cava Water)	Freshly collected fronds were dried and powdered	Landrace x Yorkshire x Duroc weanling pigs (50)	28 days	In feed (growing-finishing diet)	0%, 0.05%, 0.1%, or 0.15% in feed	No mortalities. Weight gain was similar to controls. No significant effect on serum level of IgG, IgA, and IgM.	68
Fucus Vesiculosus Extract (28.8% polyphenols)	Ethanol (30% - 35% aq)	Sprague-Dawley rats (7/sex)	4 weeks	1% CMC	0, 200, or 750 mg/kg/day by gavage	- There were no mortalities. -Males: body and most organ weights were similar to controls. Livers had an increase weight (21%) at necropsy. - Females: body and organ weights were similar to controls.	23
Fucus Vesiculosus Extract (18% polyphenols plus 0.0012% fucoxanthin)	Ethanol (50% - 70% aq.)	Sprague-Dawley rats (7/sex)	4 weeks	1% CMC	0, 200, or 750 mg/kg/day by gavage	- There were no mortalities. - Males: body and most organ weights were similar to controls. Livers had an increase weight (25%) at necropsy. - Females: body and organ weights were similar to controls.	23
Laminaria Japonica Extract	Ethanol extract	Sprague-Dawley rats (6)	6 weeks	Not clear (probably daily gavage)	0, 100, 200, or 400 mg/kg starting after 6 weeks of a 12-week high-fat diet	- There were no mortalities. - Treatment groups had decreased the body weight gain, fat-pad weights, and serum and hepatic lipid levels in high-fat-induced obese rats. Histological analysis showed that treated groups had decreased number of lipid droplets and size of adipocytes compared to untreated high-fat diet group.	27

Table 22. Oral repeated dose studies

Test Article	Extraction Solvent/Method or Composition	Animals (n)	Study Duration	Vehicle	Dose/ Concentration	Results	Reference
					Subchronic Oral		
Ecklonia Cava Extract	Alcohol extract	Sprague–Dawley (Crl:CD(SD)) rats (10/sex;5 additional in control and high-dose groups)	13 weeks 4-week recovery period for 5 rats in control and high-dose group	Water	0, 375, 750, or 1500 mg/kg/day	- Compound-colored stools in all dose levels; not considered to be of toxicological significance. -At 750 and 1500 mg/kg/day, BUN was decreased in males, glucose was decreased in females, and neutrophil counts were increased in females, compared to controls. Sporadic salivation occurred in females. - At 1500 mg/kg/day, incidence of salivation in females increased and occurred in male rats. Salivation was mainly observed after gavage, but to some degree also before. It was considered by authors to be a temporary sign caused by the test substance, since it was no longer evident later in the day. Number of rats with salivation increased with study duration. -At 1500 mg/kg/day, males and females had a lower body weight (11.7% and 8.7%, respectively) at end of study compared to controls (not statistically significant). This effect was dose related, appearing to a minor degree also at lower dose levels. Body weight effects were more pronounced in recovery group in both sexes. Feed consumption was not decreased. Blood chemistry analyses showed increases of phosphorus and ALT concentrations and a decrease of triglycerides in males, and a decrease of glucose in females, compared to controls. Prothrombin time was increased in males compared to controls. These changes were not evident after recovery period. There were no compound related findings in histopathological investigations including liver.	[9]
Ecklonia Cava Extract	Enzyme extract	SD rats (5/sex)	13 weeks	Water	0, 500, 1000, 2000, or 3000 mg/kg by gavage	- There were no mortalities. None of groups had any dose-related clinical abnormalities or body weight changes. - Urinalysis and hematological analysis showed no treatment-related adverse effects. - Serum biochemistry and organ weights showed sporadic changes. However, sporadic changes might not have any relationship with treatment because these changes were very minimal within physiologically acceptable ranges without consistency between male and female rats. - Gross visual and macroscopic changes were not observed in organs of treated rats. Histopathological examination of sampled organs revealed a few spontaneous lesions which might be unrelated to treatment because there was no difference in incidence between control and treatment groups.	[21]
					Chronic Oral		
Laminaria Japonica Powder	Dried and powdered	Male CDF1 mice (6)	Life time	Feed	0, 2%, 5%	Mean lifespans were similar in all groups: 907 ± 135, 746 ± 183, and 851 ± 225 days for 0, 2%, and 5%, respectively.	[29]
Undaria Pinnatifida Extract	Filtered aqueous extract of powdered stems and thick leaves	Female Sprague-Dawley (SD) rats (12)	32 weeks	Drinking water	1.5 g in 1000 mL water	There were no mortalities. Body weight changes were similar between groups.	[69]
Undaria Pinnatifida Powder	Dried and ground	Female SD rats (5)	36 weeks	Feed	0, 1.0%, or 5.0%	There were no mortalities. Body weight changes, thyroid weights, and T4 levels were similar between groups.	[77]

Table 22. **Oral repeated dose studies**

Test Article	Extraction Solvent/Method or Composition	Animals (n)	Study Duration	Vehicle	Dose/ Concentration	Results	Reference

ALP = alkaline phosphatase; ALT = alanine aminotransferase; AMP = adenosine monophosphate; AST = aspartate aminotransferase; BUN = blood urea nitrogen; CMC = carboxymethylcellulose; GOT = glutamic oxaloacetic transaminase; GPT = glutamic pyruvic transaminase; HDL = high-density lipoprotein; IgA = immunoglobulin A; IgG = immunoglobulin G; IgM = immunoglobulin M; LDL = low-density lipoprotein; MCHC = mean corpuscular hemoglobin concentration; T4 = thyroxin

Table 23. **Genotoxicity studies**

Ingredient/Test Article	Extraction Solvent/ Method	Concentration/ Vehicle	Procedure	Test System	Results	Reference
			In Vitro			
Ascophyllum Nodosum Extract	Not specified	50, 150, 500, 1500, or 5000 µg/plate; in water	Ames assay, with and without metabolic activation in accordance with OECD GL 471 (bacterial reverse mutation test). Negative control: histidine; positive control: 4-nitroquinoline-N-oxide, 3-methylmethane sulphonate, 2-aminoanthracene, and sodium azide. There was no solvent control.	*S. typhimurium* (strains TA97, TA98, TA100, TA102, and TA1535)	Not genotoxic in all strains	[6]
Ascophyllum Nodosum Extract	Not specified	150, 500, 1500, or 5000 µg/ml; in water	Mammalian cell gene mutation test accordance with OECD GL 476 (in vitro mammalian cell gene mutation test) with and without metabolic activation. Positive control without metabolic activation: ethylmethanesulphonate, with metabolic activation: BaP	CHO; K1 sub clone CHO K1	Increased mutant frequencies at 1500 and 5000 µg/ml without metabolic activation; no increase in mutation frequencies at lower concentrations. No increase in mutation frequencies at any concentration with metabolic activation.	[6]
Ascophyllum Nodosum Extract	Not specified	With metabolic activation: 0.63, 1.25, 2.5, or 5 mg/ml; without metabolic activation: 1.25, 2.5, or 5 mg/ml	Chromosome aberration assay in accordance with OECD GL 487 (in vitro mammalian chromosome aberration test) with and without metabolic activation. Negative control: medium (serum free cell culture medium); positive controls: CPA, MMC, and colchicine	Human lymphocytes	Not genotoxic	[6]
Ascophyllum Nodosum Extract	Not specified	Experiment I: With metabolic activation: 1.25, 2.5, or 5 mg/ml; without metabolic activation: 1.25, 2.5, or 5 mg/ml Experiment II: without metabolic activation: 0.63, 1.25, 2.5, or 5 mg/ml Serum free cell culture medium	Chromosome aberration assay in accordance with OECD 487 with and without metabolic activation. Negative control: solvent (serum free cell culture medium); Positive control: CPA, MMC, colchicine	Human peripheral lymphocytes	Not genotoxic or cytotoxic	[6]

Table 23. Genotoxicity studies

Ingredient/Test Article	Extraction Solvent/ Method	Concentration/ Vehicle	Procedure	Test System	Results	Reference
Ascophyllum Nodosum Extract	Not specified	4.7% Ascophyllum Nodosum Extract	An Ames test was performed using a trade name mixture containing 4.7% Ascophyllum nodosum extract in 94.5% water. The procedure was done in accordance to OECD 471.	Not specified	Not mutagenic or pro-mutagenic activity	44
Cystoseira Compressa Extract	n-Hexane, chloroform, and methanol	1, 2.5, or 5 mg/plate	Ames Assay with and without metabolic activation. Negative control: DMSO. Positive controls: BaP, 2-nitrofluorene, and sodium azide.	*S. typhimurium* (strains TA98 and TA100)	Not mutagenic	40
Ecklonia Cava Extract	Enzymatic extraction	911 - 3500 µg/plate; distilled water	Ames assay, with and without metabolic activation. OECD GL 471	*S. typhimurium* (strains TA98, TA100, TA1535, and TA1537) and *E. coli* (WP2uvrA)	Not genotoxic	21
Ecklonia Cava Extract	Alcohol	Up to 5000 µg/plate; vehicle not specified	Ames assay, with and without metabolic activation	*S. typhimurium* (strains TA98, TA100, TA1535, and TA1537) and *E. coli* (WP2uvrA(pKM101))	Not genotoxic or cytotoxic	9
Laminaria digitata	Not specified	Not specified	Ames assay, with and without metabolic activation	S. typhimurium	No evidence of mutagenicity	81
Ecklonia Cava Extract	Alcohol	Up to 290 µg/mL	Chromosome aberration test, with and without metabolic activation	CHL cells	Not genotoxic	9
Ecklonia Cava Extract	Enzymatic extraction	87.5 – 350 µg/plate; distilled water	Chromosome aberration test, with and without metabolic activation. OECD GL 473	CHL cells	Not genotoxic	21
Fucus Vesiculosus Extract	Aqueous	0, 0.25, 0.5, or 1 mg/ml; cell medium	Chromosome aberration assay OECD GL 487	Human peripheral lymphocytes	Frequency of chromosome aberrations, mitotic index and extent of DNA damage in cells treated with extract were similar to controls at all concentrations.	70
Fucus Vesiculosus Extract	Aqueous	0, 0.25, 0.5, or 1 mg/ml; cell medium	Comet assay	Human peripheral lymphocytes	Extent of DNA damage in cells treated with extract was similar to controls at all concentrations.	70
			In Vivo			
Ecklonia Cava Extract	Alcohol	0 or 2000 mg/kg	Micronucleus assay. Test substance administered via oral gavage. Bone marrow (2,000 erythrocytes) was checked for frequency of micronuclei, after 24, 48, and 72 h.	Male Crlj:CD1(ICR) mice (n = 3)	There was no increase in frequency of micronuclei in any of the time points.	9
Ecklonia Cava Extract	Alcohol	0, 500, 1000, or 2000 mg/kg	Micronucleus assay. Test substance administered via oral gavage. Bone marrow (2,000 erythrocytes) was checked for the frequency of micronuclei, after 24 h.	Male Crlj:CD1(ICR) mice (n = 5)	There was no increase in frequency of micronuclei polychromatic erythrocytes (PCE)/(PCE + normochromatic erythrocytes (NCE)) ratio was not significantly different between treatment groups and control groups. No evidence of genotoxicity.	9

Table 23. Genotoxicity studies

Ingredient/Test Article	Extraction Solvent/ Method	Concentration/ Vehicle	Procedure	Test System	Results	Reference
Ecklonia Cava Extract	Enzymatic extraction	1000, 2000, or 3000 mg/kg; distilled water	Mouse micronucleus assay. The number of mice used in the study was not provided. Administered by gavage. Saline and MMC were the controls. OECD GL 474	Male ICR mice	There were no mortalities or abnormal clinical signs in any group. There were no increases in structural or numerical chromosomal aberrations at any dose compared to the negative control.	[21]

BaP = benzo(a)pyrene; CHL = Chinese hamster lung; CHO = Chinese hamster ovary; CPA = cyclophosphamide; HCl = hydrochloric acid; MMC = mitomycin C; MNPCE = micronucleated polychromatic erythrocyte; NCE = normochromatic erythrocyte; PBS = phosphate-buffered saline; PCE = polychromatic erythrocytes

Table 24. Tumor promotion studies

Test Article	Extraction/solvent/ method	Dose/Exposure Route	Species (n)	Tumor Type	Carcinogenicity Model	Results	Reference
				Dermal			
Undaria Pinnatifida Extract	Dichloromethane extract	1 mg	Female ICR mice (n not specified)	Skin	- Initiation: a single dermal dose of DMBA (50 µg) - 1 week later, mice were dermally treated twice per week with TPA (1 µg) or Undaria Pinnatifida Extract (1 mg) 1 h prior to treatment with TPA for 15 weeks	TPA: tumors > 1 mm were observed after week 8; average number of tumors was 3.7. Undaria Pinnatifida Extract and TPA: mice did not show 1-mm tumors until week 14 (< 5%); average number of tumors was 0.2.	[73]
				Oral			
Hizikia Fusiforme Extract	95% Ethanol aq.	0, 2%, or 6% in feed	Male F344 rats (10, control, 8)	Colorectal	- Group 1 – standard diet - Group 2 – injected with AOM (15 mg/1 ml/kg once a week for 2 weeks) and standard diet - Group 3 – Injected with AOM and diet with 2% Hizikia Fusiforme Extract - Group 4 – Injected with AOM and diet with 6% Hizikia Fusiforme Extract - After 8 weeks, the rats were killed and necropsied.	- Body weights were similar among groups at 11 weeks. - No tumors were found in the negative control group and 58 tumors were found in the positive control group. Treatment groups had reduced number of tumors (21 each). - Immuno-histochemistry analysis of PCNA expression, a marker of tumor cell proliferation and apoptosis, was lower in treatment groups than in treated control group.	[74]

Table 24. Tumor promotion studies

Test Article	Extraction/solvent/ method	Dose/Exposure Route	Species (n)	Tumor Type	Carcinogenicity Model	Results	Reference
Saccharina Angustata Extract (inference from *Saccharina angustata* powder)	Dried and milled	0 or 5% in feed	Female Sprague-Dawley rats (54)	Mammary	- After 50 days on respective diets, 4 rats in each group were killed and examined for abnormalities. None were found. - At 55 days treatment groups were administered DMBA by gavage after fasting. - Rats were palpated weekly for tumors. - The rats were killed at 181 - 188 days after DMBA administration and necropsied.	- Weight gains were similar among groups. - First tumors in the control group appeared at 11.0 weeks and 19.8 in the treatment group. - 41 of 54 rats (76%) in control group and 34 of 54 rats (63%) in the treatment group had 1 or more adenocarcinomas at necropsy. - During treatment, 13 rats (8 control and 5 experimental) were euthanized between 74 and 170 days post- DMBA. 10 of these rats had developed large (~ 4 cm in diameter) mammary tumors, 2 developed malignant lymphomas, and 1 developed a large necrotic ear gland tumor (Zymbal's gland carcinoma). There were no other deaths. - 12 tumor-free rats (6 from each group) were found to have small nonpalpable mammary masses; 11 of these were found to be adenocarcinomas and 1 to be an adenoma. 93% of all tumors found in the mammary gland region at autopsy were adenocarcinomas; 5 tumors, which were mostly fibroadenoma but which had focal proliferations of malignant epithelial cells. Other tumors consisted of 7 fibroadenomas, 5 adenomas, 3 epidermal inclusion cysts, and 1 adenocarcinoma of sebaceous glands.	[75]
Sargassum Pallidum Extract	Aqueous. Boiled under reflux and filtered.	400, 600 or 800 mg/kg/day	Male Wistar rats (10)	Gastric	- Group 1 – distilled water - Group 2 – 800 mg/kg/day Sargassum Pallidum Extract - Group 3 - 6 – MNNG (25 mg/ml) in drinking for 25 weeks; then 0, 400, 600, or 800 mg/kg Sargassum Pallidum Extract for 8 weeks - All rats were killed at 33 weeks, blood analyzed, and stomachs examined.	- There were no mortalities. - Compared to group 1 (control), Sargassum Pallidum Extract increased serum IL-2, IL-4, and IL-10 levels in group 2; serum IL-2, IL-4, and IL-10 levels in group 3 were decreased. - Compared to group 1, Sargassum Pallidum Extract decreased serum IL-6, IL-1β, and TNF-α levels in group 2; serum IL-6, IL-1β, and TNF-α levels in group 3 were increased. - Compared with group 3, Sargassum Pallidum Extract dose-dependently decreased serum IL-6, IL-1β, and TNF-α levels in groups 4, 5, and 6. - Concentration of serum and gastric mucosa MDA decreased in a dose-dependent manner in groups 4, 5, and 6. - Concentration of serum and gastric mucosa GSH and antioxidant enzyme activities increased in a dose-dependent manner in groups 4, 5, and 6. - Sargassum Pallidum Extract could decrease inflammatory response and improve immunity function partly through stimulating inflammatory cytokines (IL-2, IL-4, IL-10) production and inhibiting pro-inflammatory cytokines production.	[76]

Table 24. Tumor promotion studies

Test Article	Extraction/solvent/ method	Dose/Exposure Route	Species (n)	Tumor Type	Carcinogenicity Model	Results	Reference
Undaria Pinnatifida Powder	Not specified	0, 1.0% or 5.0% in feed	Female Sprague-Dawley (SD) rats (11)	Mammary	- Initiation: a single dose of DMBA (20 mg) by gastric intubation - Once tumors reached 1 cm, rats were dived between 3 treatment groups for 8 weeks - Rats were then killed and all mammary tumors were histologically examined and thyroid glands, ovaries, and adrenal glands were weighed. Blood samples collected for measurement of serum total iodine concentration and serum T4 levels.	No differences in body weight gains between groups. Tumors in control group increased by more than 450%; tumor growth was suppressed in the 1% group and there was almost no change in tumor size in the 5% group. Mean combined weight of all mammary tumors of each rat in treatment groups was lower than that in the control group (~ 7 vs 20 g) at end of experiment. Weights of thyroid glands, ovaries, and adrenal glands did not differ among groups. Concentration of serum iodine was greater in treatment groups compared to controls. Serum iodine concentration had a positive relationship with concentration of Undaria Pinnatifida Powder in diet. Serum T4 levels showed no differences among groups. Test substance did not promote mammary tumors and suppressed tumor growth after a single dose of DMBA.	[77]
Undaria Pinnatifida Extract	Filtered aqueous extract of powdered stems and thick leaves	1.5 g in 1000 mL water	Female Sprague-Dawley (SD) rats (12)	Mammary	- Initiation: a single dose of DMBA (20 mg) by gastric intubation - 1 week later, treatment began for 32 weeks - Mammary tumors were removed and measured	- Body weight gains were similar in both groups - Incidence of tumors at end of experiment was 22% vs 100% (controls) - The number of tumors was an average of < 1 vs. ~ 7 (controls) - Total tumor diameters was < 250 vs > 5000 mm - Histologically, mammary tumors were cystic adenocarcinoma, and tumors in treatment group had a decreased density of epithelial cells and fibrosis.	[69]

AOM = azoxymethane; DMBA = 7,12-dimethylbenz(*a*)anthracene; GSH = glutathione; MDA = malondialdehyde; MNNG = *N*-methyl-*N*′-nitro-N-nitrosoguanidine; PCNA = proliferating cell nuclear antigen; T4 = thyroxin; TPA = 12-*O*-tetradecanoylphorbol-13-acetate

Table 25. Case Reports of brown algae

Ingredient/substance (dose, if known)	Details	Reference
Fucus vesiculosus supplement (1200 mg 3 times per day)	18-year-old female presented with polyuria, polydipsia, extreme faintness, and a general poor condition. She had been on a hypocaloric diet for 3 months and taking *Fucus vesiculosus* supplements. Renal biopsy showed widespread tubular degeneration, and diffuse lymphomonocytic infiltrate; the glomeruli displayed scarce and focal mesangial proliferation, but the basal membrane appeared intact. The supplement was tested for heavy metals: arsenic, 21.3 mg/kg; cadmium, 0.3 ppm; mercury, 0.06 ppm; and chrome, 4 ppm. The patient recovered within 1 year.	[122]
Kelp tablets	54-year-old female developed thrombocytopenia with mucocutaneous bleeding after ingesting kelp tablets (that contained 1.3 µg/g arsenic) twice daily for 6 weeks. Marrow aspirate demonstrated normal megakaryocytes and dyserythropoiesis. After discontinuation of the supplements and treatment with steroids and azathioprine, her platelet count recovered after 3 months.	[85]
Kelp supplements	A 54-year-old woman presented with a 2-year history of worsening alopecia and memory loss. She also had a rash, increasing fatigue, nausea, and vomiting to the point of disablement. She took daily kelp supplements. A urine sample showed an arsenic level of 83.6 µg/g creatinine (normal < 50 µg/g creatinine). A sample from her kelp supplements contained 8.5 mg/kg arsenic. Within weeks of discontinuing the supplements, her symptoms resolved and arsenic blood and urine levels were undetectable.	[86]

Table 26. Oral clinical trials

Test Article	Extraction/ Solvent Method or Characterization	Study group	Study Details	Results	Reference
Ascophyllum Nodosum Powder (0.5 g/day)	Powdered plant	Healthy female subjects (n = 42)	After a 4-day period of keeping a food diary, subjects were administered capsules containing extract or potassium iodide daily for 14 days, then repeated 4-day food diary. All-day urine sample was collected on fourth day of run-in period and last day of treatment period (day 19) and fasted blood samples were collected on fourth day of run-in period and on day after treatment period (day 20).	There was an increase in urinary iodine concentrations (median 140 mg/l vs78 mg/l) in the treatment group. TSH increased slightly but within normal range 2 subjects. Increase in TSH concentrations may be associated with iodine-induced hypothyroidism, especially in those subjects with low iodine stores, although no change in the concentrations of thyroid hormones was observed. There were no adverse events reported during this experiment.	87
Ecklonia Cava Extract (400 mg/day)	Alcohol	Subjects with hyper-cholesterolaemia (n = 52)	Uncontrolled, open-label, single-arm study for 12 weeks	Hematological, clinical chemistry, and urinalysis did not reveal any adverse effects. There was one instance (2.2%) each of nausea, dyspepsia, diarrhea, and alopecia reported.	9,88
Ecklonia Cava Extract (0, 72, or 144 mg/day)	Phlorotannin-rich	Overweight subjects (n = 32 or 33)	Randomized, double-blind, three-arm, parallel trial for 12 weeks	Hematological and clinical chemistry did not reveal any adverse effects. Only high-dose group showed significant decreases in serum glucose and systolic blood pressure. No adverse signs were observed during the trial.	9
Ecklonia Cava Extract (0 or 400 mg/day)	Alcohol	Overweight subjects (n = 40)	Randomized, double-blind, and placebo-controlled trial for 12 weeks. Administered as 200 mg twice per day in capsules	There were no adverse events reported that were related to the test substance.	22
Undaria Pinnatifida Powder (desalinated; 5040 mg/day)	Powdered	Hypertensive subjects (n = 18)	Subjects were gender and age matched to control group. Capsules (420 mg/capsule; 4 capsules/dose) 3 times/day with meals. Examined for body weight, BP, and blood chemistry parameters prior to experiment, at 4 weeks, and at 8 weeks. 1 subject in treatment group left study for personal reasons, so final number of paired subjects was 18, (some of her data (e.g., adverse effects) were used).	Compliance was not consistent; 6 subjects followed protocol; 1 ingested 9 capsules/day, 2 ingested 8 capsules/day, 6 ingested 6 capsules/day, and 3 ingested 3capsules/day. Average intake was estimated to be 7.9 capsules or 3.3 g/day. Average SBP in treatment group decreased by 13 mmHg from the baseline after 4 weeks, and was reduced by 8 mmHg below baseline after 8 weeks. Average DBP decreased by 9 mmHg from baseline after 4 weeks and by 8 mmHg after 8 weeks. There were no significant changes in either SBP or DBP in control group. However, the differences in reductions in SBP and DBP were significant between the treatment group and control group. Hypercholesterolemia subjects in treatment group had decreased total cholesterol by 8% after 4 weeks; no changes were observed in subjects with normal cholesterol levels. Adverse effects included 2 cases of indigestion and 1 case of diarrhea, all of which resolved quickly without treatment.	42

BP = blood pressure; DBP = diastolic blood pressure; SBP = systolic blood pressure; TSH = thyroid-stimulating hormone

Table 27. Change in menstrual cycle with the oral administration of Fucus Vesiculosus Powder[89]

	Menstrual cycle length			Days of Menstruation		
Subject	Baseline	Low-Dose	High-Dose	Baseline	Low-Dose	High-Dose
1	16.3 ± 0.6 days	26.0 ± 1.4 days	31.2 ± 1.1 days	9.3 ± 0.6 days	6.3 ± 1.8 days	4.5 ± 0.7 days
2	23.0 ± 1.7 days	28.5 ± 0.7 days	-	8.0 ± 1.0 days	5.3 ± 2.5 days	-
3	27.3 ± 0.6 days	31.5 ± 0.7 days	36.0 ± 2.8 days	6.3 ± 1.5 days	5.8 ± 0.4 days	3.5 ± 0.7 days

- = no data

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2018 VCRP Data for Brown Algae-Derived Ingredients

03C - Eye Shadow	ALARIA ESCULENTA EXTRACT	8
03D - Eye Lotion	ALARIA ESCULENTA EXTRACT	2
03G - Other Eye Makeup Preparations	ALARIA ESCULENTA EXTRACT	1
05I - Other Hair Preparations	ALARIA ESCULENTA EXTRACT	1
07A - Blushers (all types)	ALARIA ESCULENTA EXTRACT	6
07B - Face Powders	ALARIA ESCULENTA EXTRACT	5
07C - Foundations	ALARIA ESCULENTA EXTRACT	1
07E - Lipstick	ALARIA ESCULENTA EXTRACT	3
07I - Other Makeup Preparations	ALARIA ESCULENTA EXTRACT	1
12C - Face and Neck (exc shave)	ALARIA ESCULENTA EXTRACT	4
12D - Body and Hand (exc shave)	ALARIA ESCULENTA EXTRACT	2
12F - Moisturizing	ALARIA ESCULENTA EXTRACT	3
		37

03D - Eye Lotion	ASCOPHYLLUM NODOSUM (SEAWEED) EXTRACT (84775780)	8
03G - Other Eye Makeup Preparations	ASCOPHYLLUM NODOSUM (SEAWEED) EXTRACT	8
05A - Hair Conditioner	ASCOPHYLLUM NODOSUM (SEAWEED) EXTRACT	6
05F - Shampoos (non-coloring)	ASCOPHYLLUM NODOSUM (SEAWEED) EXTRACT	3
05G - Tonics, Dressings, and Other Hair Grooming Aids	ASCOPHYLLUM NODOSUM (SEAWEED) EXTRACT	4
07B - Face Powders	ASCOPHYLLUM NODOSUM (SEAWEED) EXTRACT	1
07F - Makeup Bases	ASCOPHYLLUM NODOSUM (SEAWEED) EXTRACT	2
08B - Cuticle Softeners	ASCOPHYLLUM NODOSUM (SEAWEED) EXTRACT	1
08G - Other Manicuring Preparations	ASCOPHYLLUM NODOSUM (SEAWEED) EXTRACT	2
10A - Bath Soaps and Detergents	ASCOPHYLLUM NODOSUM (SEAWEED) EXTRACT	6
11A - Aftershave Lotion	ASCOPHYLLUM NODOSUM (SEAWEED) EXTRACT	1
11E - Shaving Cream	ASCOPHYLLUM NODOSUM (SEAWEED) EXTRACT	1
12A - Cleansing	ASCOPHYLLUM NODOSUM (SEAWEED) EXTRACT	5
12C - Face and Neck (exc shave)	ASCOPHYLLUM NODOSUM (SEAWEED) EXTRACT	40
12D - Body and Hand (exc shave)	ASCOPHYLLUM NODOSUM (SEAWEED) EXTRACT	4
12F - Moisturizing	ASCOPHYLLUM NODOSUM (SEAWEED)	16

	EXTRACT	
12G - Night	ASCOPHYLLUM NODOSUM (SEAWEED) EXTRACT	2
12H - Paste Masks (mud packs)	ASCOPHYLLUM NODOSUM (SEAWEED) EXTRACT	8
12I - Skin Fresheners	ASCOPHYLLUM NODOSUM (SEAWEED) EXTRACT	1
12J - Other Skin Care Preps	ASCOPHYLLUM NODOSUM (SEAWEED) EXTRACT	1
		120

02A - Bath Oils, Tablets, and Salts	ASCOPHYLLUM NODOSUM POWDER	1
12F - Moisturizing	ASCOPHYLLUM NODOSUM POWDER	2
12J - Other Skin Care Preps	ASCOPHYLLUM NODOSUM POWDER	1
		4

03G - Other Eye Makeup Preparations	CLADOSIPHON OKAMURANUS EXTRACT	1
07C - Foundations	CLADOSIPHON OKAMURANUS EXTRACT	1
12A - Cleansing	CLADOSIPHON OKAMURANUS EXTRACT	1
12C - Face and Neck (exc shave)	CLADOSIPHON OKAMURANUS EXTRACT	3
12F - Moisturizing	CLADOSIPHON OKAMURANUS EXTRACT	1
12G - Night	CLADOSIPHON OKAMURANUS EXTRACT	2
		9

12C - Face and Neck (exc shave)	DICTYOPTERIS MEMBRANACEA EXTRACT (RETIRED)	1

03D - Eye Lotion	FUCUS SERRATUS EXTRACT	1
12C - Face and Neck (exc shave)	FUCUS SERRATUS EXTRACT	4
12F - Moisturizing	FUCUS SERRATUS EXTRACT	2
12G - Night	FUCUS SERRATUS EXTRACT	1
		8

02A - Bath Oils, Tablets, and Salts	FUCUS VESICULOSUS (BLADDERWRACK) EXTRACT	3
02B - Bubble Baths	FUCUS VESICULOSUS (BLADDERWRACK) EXTRACT	2
02D - Other Bath Preparations	FUCUS VESICULOSUS (BLADDERWRACK) EXTRACT	6
03D - Eye Lotion	FUCUS VESICULOSUS (BLADDERWRACK) EXTRACT	2
03F - Mascara	FUCUS VESICULOSUS (BLADDERWRACK) EXTRACT	3
03G - Other Eye Makeup Preparations	FUCUS VESICULOSUS (BLADDERWRACK) EXTRACT	1
04E - Other Fragrance Preparation	FUCUS VESICULOSUS (BLADDERWRACK) EXTRACT	1
05A - Hair Conditioner	FUCUS VESICULOSUS (BLADDERWRACK) EXTRACT	7
05C - Hair Straighteners	FUCUS VESICULOSUS (BLADDERWRACK) EXTRACT	1
05F - Shampoos (non-coloring)	FUCUS VESICULOSUS (BLADDERWRACK) EXTRACT	7
05G - Tonics, Dressings, and Other Hair Grooming Aids	FUCUS VESICULOSUS (BLADDERWRACK) EXTRACT	6
05I - Other Hair Preparations	FUCUS VESICULOSUS (BLADDERWRACK) EXTRACT	1
07F - Makeup Bases	FUCUS VESICULOSUS (BLADDERWRACK) EXTRACT	1
07I - Other Makeup Preparations	FUCUS VESICULOSUS (BLADDERWRACK) EXTRACT	1
10A - Bath Soaps and Detergents	FUCUS VESICULOSUS (BLADDERWRACK) EXTRACT	14
10E - Other Personal Cleanliness Products	FUCUS VESICULOSUS (BLADDERWRACK) EXTRACT	5
11A - Aftershave Lotion	FUCUS VESICULOSUS (BLADDERWRACK) EXTRACT	1
11E - Shaving Cream	FUCUS VESICULOSUS (BLADDERWRACK) EXTRACT	1
11F - Shaving Soap	FUCUS VESICULOSUS (BLADDERWRACK) EXTRACT	1
11G - Other Shaving Preparation Products	FUCUS VESICULOSUS (BLADDERWRACK) EXTRACT	1
12A - Cleansing	FUCUS VESICULOSUS	12

	(BLADDERWRACK) EXTRACT	
12B - Depilatories	FUCUS VESICULOSUS (BLADDERWRACK) EXTRACT	1
12C - Face and Neck (exc shave)	FUCUS VESICULOSUS (BLADDERWRACK) EXTRACT	48
12D - Body and Hand (exc shave)	FUCUS VESICULOSUS (BLADDERWRACK) EXTRACT	33
12E - Foot Powders and Sprays	FUCUS VESICULOSUS (BLADDERWRACK) EXTRACT	1
12F - Moisturizing	FUCUS VESICULOSUS (BLADDERWRACK) EXTRACT	36
12G - Night	FUCUS VESICULOSUS (BLADDERWRACK) EXTRACT	1
12H - Paste Masks (mud packs)	FUCUS VESICULOSUS (BLADDERWRACK) EXTRACT	25
12I - Skin Fresheners	FUCUS VESICULOSUS (BLADDERWRACK) EXTRACT	4
12J - Other Skin Care Preps	FUCUS VESICULOSUS (BLADDERWRACK) EXTRACT	18
13B - Indoor Tanning Preparations	FUCUS VESICULOSUS (BLADDERWRACK) EXTRACT	42
13C - Other Suntan Preparations	FUCUS VESICULOSUS (BLADDERWRACK) EXTRACT	1
		287

12C - Face and Neck (exc shave)	FUCUS VESICULOSUS POWDER	1
12H - Paste Masks (mud packs)	FUCUS VESICULOSUS POWDER	2
		3

03G - Other Eye Makeup Preparations	HIMANTHALIA ELONGATA EXTRACT	1
05A - Hair Conditioner	HIMANTHALIA ELONGATA EXTRACT	1
05I - Other Hair Preparations	HIMANTHALIA ELONGATA EXTRACT	1
12C - Face and Neck (exc shave)	HIMANTHALIA ELONGATA EXTRACT	1
12D - Body and Hand (exc shave)	HIMANTHALIA ELONGATA EXTRACT	3
12F - Moisturizing	HIMANTHALIA ELONGATA EXTRACT	1
12H - Paste Masks (mud packs)	HIMANTHALIA ELONGATA EXTRACT	1
		9

07F - Makeup Bases	KAPPAPHYCUS ALVAREZII EXTRACT	1
10E - Other Personal Cleanliness Products	KAPPAPHYCUS ALVAREZII EXTRACT	2
12C - Face and Neck (exc shave)	KAPPAPHYCUS ALVAREZII EXTRACT	2
		5

03D - Eye Lotion	LAMINARIA CLOUSTONI EXTRACT	1
07F - Makeup Bases	LAMINARIA CLOUSTONI EXTRACT	1
12A - Cleansing	LAMINARIA CLOUSTONI EXTRACT	3
12C - Face and Neck (exc shave)	LAMINARIA CLOUSTONI EXTRACT	4
12F - Moisturizing	LAMINARIA CLOUSTONI EXTRACT	2
12G - Night	LAMINARIA CLOUSTONI EXTRACT	1
12H - Paste Masks (mud packs)	LAMINARIA CLOUSTONI EXTRACT	1
12I - Skin Fresheners	LAMINARIA CLOUSTONI EXTRACT	1
		14

02A - Bath Oils, Tablets, and Salts	LAMINARIA DIGITATA EXTRACT	2
02B - Bubble Baths	LAMINARIA DIGITATA EXTRACT	3
02D - Other Bath Preparations	LAMINARIA DIGITATA EXTRACT	2
03D - Eye Lotion	LAMINARIA DIGITATA EXTRACT	3
03E - Eye Makeup Remover	LAMINARIA DIGITATA EXTRACT	2
03F - Mascara	LAMINARIA DIGITATA EXTRACT	4
03G - Other Eye Makeup Preparations	LAMINARIA DIGITATA EXTRACT	6
05A - Hair Conditioner	LAMINARIA DIGITATA EXTRACT	4
05B - Hair Spray (aerosol fixatives)	LAMINARIA DIGITATA EXTRACT	1
05F - Shampoos (non-coloring)	LAMINARIA DIGITATA EXTRACT	12
05G - Tonics, Dressings, and Other Hair Grooming Aids	LAMINARIA DIGITATA EXTRACT	18
05I - Other Hair Preparations	LAMINARIA DIGITATA EXTRACT	1
06H - Other Hair Coloring Preparation	LAMINARIA DIGITATA EXTRACT	1
07B - Face Powders	LAMINARIA DIGITATA EXTRACT	3
07C - Foundations	LAMINARIA DIGITATA EXTRACT	3
07E - Lipstick	LAMINARIA DIGITATA EXTRACT	1
07F - Makeup Bases	LAMINARIA DIGITATA EXTRACT	1
07I - Other Makeup Preparations	LAMINARIA DIGITATA EXTRACT	2
09A - Dentifrices	LAMINARIA DIGITATA EXTRACT	1
10A - Bath Soaps and Detergents	LAMINARIA DIGITATA EXTRACT	6

10C - Douches	LAMINARIA DIGITATA EXTRACT	1
10E - Other Personal Cleanliness Products	LAMINARIA DIGITATA EXTRACT	4
11A - Aftershave Lotion	LAMINARIA DIGITATA EXTRACT	4
12A - Cleansing	LAMINARIA DIGITATA EXTRACT	18
12C - Face and Neck (exc shave)	LAMINARIA DIGITATA EXTRACT	36
12D - Body and Hand (exc shave)	LAMINARIA DIGITATA EXTRACT	31
12F - Moisturizing	LAMINARIA DIGITATA EXTRACT	20
12G - Night	LAMINARIA DIGITATA EXTRACT	3
12H - Paste Masks (mud packs)	LAMINARIA DIGITATA EXTRACT	17
12I - Skin Fresheners	LAMINARIA DIGITATA EXTRACT	3
12J - Other Skin Care Preps	LAMINARIA DIGITATA EXTRACT	22
		235

02A - Bath Oils, Tablets, and Salts	LAMINARIA DIGITATA POWDER	1
02D - Other Bath Preparations	LAMINARIA DIGITATA POWDER	2
05A - Hair Conditioner	LAMINARIA DIGITATA POWDER	2
05F - Shampoos (non-coloring)	LAMINARIA DIGITATA POWDER	4
10E - Other Personal Cleanliness Products	LAMINARIA DIGITATA POWDER	1
12C - Face and Neck (exc shave)	LAMINARIA DIGITATA POWDER	1
12H - Paste Masks (mud packs)	LAMINARIA DIGITATA POWDER	9
12J - Other Skin Care Preps	LAMINARIA DIGITATA POWDER	1
		21

12F - Moisturizing	LAMINARIA HYPERBOREA EXTRACT	2

01B - Baby Lotions, Oils, Powders, and Creams	LAMINARIA JAPONICA EXTRACT	1
03D - Eye Lotion	LAMINARIA JAPONICA EXTRACT	2
03F - Mascara	LAMINARIA JAPONICA EXTRACT	1
05F - Shampoos (non-coloring)	LAMINARIA JAPONICA EXTRACT	1
07A - Blushers (all types)	LAMINARIA JAPONICA EXTRACT	2

07B - Face Powders	LAMINARIA JAPONICA EXTRACT	3
07C - Foundations	LAMINARIA JAPONICA EXTRACT	10
07E - Lipstick	LAMINARIA JAPONICA EXTRACT	1
07F - Makeup Bases	LAMINARIA JAPONICA EXTRACT	2
08G - Other Manicuring Preparations	LAMINARIA JAPONICA EXTRACT	2
10A - Bath Soaps and Detergents	LAMINARIA JAPONICA EXTRACT	1
10E - Other Personal Cleanliness Products	LAMINARIA JAPONICA EXTRACT	1
12A - Cleansing	LAMINARIA JAPONICA EXTRACT	3
12C - Face and Neck (exc shave)	LAMINARIA JAPONICA EXTRACT	26
12D - Body and Hand (exc shave)	LAMINARIA JAPONICA EXTRACT	2
12F - Moisturizing	LAMINARIA JAPONICA EXTRACT	5
12G - Night	LAMINARIA JAPONICA EXTRACT	2
12H - Paste Masks (mud packs)	LAMINARIA JAPONICA EXTRACT	9
12J - Other Skin Care Preps	LAMINARIA JAPONICA EXTRACT	3
		77

03C - Eye Shadow	LAMINARIA OCHROLEUCA EXTRACT	2
07B - Face Powders	LAMINARIA OCHROLEUCA EXTRACT	3
07C - Foundations	LAMINARIA OCHROLEUCA EXTRACT	2
07E - Lipstick	LAMINARIA OCHROLEUCA EXTRACT	1
07I - Other Makeup Preparations	LAMINARIA OCHROLEUCA EXTRACT	2
10E - Other Personal Cleanliness Products	LAMINARIA OCHROLEUCA EXTRACT	2
12A - Cleansing	LAMINARIA OCHROLEUCA EXTRACT	1
12C - Face and Neck (exc shave)	LAMINARIA OCHROLEUCA EXTRACT	3
12D - Body and Hand (exc shave)	LAMINARIA OCHROLEUCA EXTRACT	2
12F - Moisturizing	LAMINARIA OCHROLEUCA EXTRACT	2
12H - Paste Masks (mud packs)	LAMINARIA OCHROLEUCA EXTRACT	1
12J - Other Skin Care Preps	LAMINARIA OCHROLEUCA EXTRACT	4
13B - Indoor Tanning Preparations	LAMINARIA OCHROLEUCA EXTRACT	1
		26

05A - Hair Conditioner	LAMINARIA SACCHARINA EXTRACT reported as SACCHARINA LATISSIMA (KELP) EXTRACT*	4
05F - Shampoos (non-coloring)	SACCHARINA LATISSIMA (KELP) EXTRACT	4
05G - Tonics, Dressings, and Other Hair Grooming Aids	SACCHARINA LATISSIMA (KELP) EXTRACT	4
07C - Foundations	SACCHARINA LATISSIMA (KELP) EXTRACT	9
07I - Other Makeup Preparations	SACCHARINA LATISSIMA (KELP) EXTRACT	2
10A - Bath Soaps and Detergents	SACCHARINA LATISSIMA (KELP) EXTRACT	2
10E - Other Personal Cleanliness Products	SACCHARINA LATISSIMA (KELP) EXTRACT	2
11A - Aftershave Lotion	SACCHARINA LATISSIMA (KELP) EXTRACT	4
11D - Preshave Lotions (all types)	SACCHARINA LATISSIMA (KELP) EXTRACT	1
11E - Shaving Cream	SACCHARINA LATISSIMA (KELP) EXTRACT	1
12A - Cleansing	SACCHARINA LATISSIMA (KELP) EXTRACT	27
12C - Face and Neck (exc shave)	SACCHARINA LATISSIMA (KELP) EXTRACT	19
12F - Moisturizing	SACCHARINA LATISSIMA (KELP) EXTRACT	33
12G - Night	SACCHARINA LATISSIMA (KELP) EXTRACT	1
12H - Paste Masks (mud packs)	SACCHARINA LATISSIMA (KELP) EXTRACT	6
12I - Skin Fresheners	SACCHARINA LATISSIMA (KELP) EXTRACT	2
12J - Other Skin Care Preps	SACCHARINA LATISSIMA (KELP) EXTRACT	11
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* The accepted scientific name for *Laminaria saccharina* is *Saccharina latissima.*

10A - Bath Soaps and Detergents	MACROCYSTIS PYRIFERA (KELP)	1
12F - Moisturizing	MACROCYSTIS PYRIFERA (KELP)	1
		2

02A - Bath Oils, Tablets, and Salts	MACROCYSTIS PYRIFERA (KELP) EXTRACT	3
02B - Bubble Baths	MACROCYSTIS PYRIFERA (KELP) EXTRACT	1
03D - Eye Lotion	MACROCYSTIS PYRIFERA (KELP) EXTRACT	1
03E - Eye Makeup Remover	MACROCYSTIS PYRIFERA (KELP) EXTRACT	1
03G - Other Eye Makeup Preparations	MACROCYSTIS PYRIFERA (KELP) EXTRACT	3
04E - Other Fragrance Preparation	MACROCYSTIS PYRIFERA (KELP) EXTRACT	6
05A - Hair Conditioner	MACROCYSTIS PYRIFERA (KELP) EXTRACT	10
05B - Hair Spray (aerosol fixatives)	MACROCYSTIS PYRIFERA (KELP) EXTRACT	3
05F - Shampoos (non-coloring)	MACROCYSTIS PYRIFERA (KELP) EXTRACT	12
05G - Tonics, Dressings, and Other Hair Grooming Aids	MACROCYSTIS PYRIFERA (KELP) EXTRACT	20

05H - Wave Sets	MACROCYSTIS PYRIFERA (KELP) EXTRACT	1
05I - Other Hair Preparations	MACROCYSTIS PYRIFERA (KELP) EXTRACT	10
06H - Other Hair Coloring Preparation	MACROCYSTIS PYRIFERA (KELP) EXTRACT	4
07A - Blushers (all types)	MACROCYSTIS PYRIFERA (KELP) EXTRACT	2
07B - Face Powders	MACROCYSTIS PYRIFERA (KELP) EXTRACT	2
07C - Foundations	MACROCYSTIS PYRIFERA (KELP) EXTRACT	3
08A - Basecoats and Undercoats	MACROCYSTIS PYRIFERA (KELP) EXTRACT	2
08E - Nail Polish and Enamel	MACROCYSTIS PYRIFERA (KELP) EXTRACT	2
08G - Other Manicuring Preparations	MACROCYSTIS PYRIFERA (KELP) EXTRACT	1
10A - Bath Soaps and Detergents	MACROCYSTIS PYRIFERA (KELP) EXTRACT	16
10E - Other Personal Cleanliness Products	MACROCYSTIS PYRIFERA (KELP) EXTRACT	14
11A - Aftershave Lotion	MACROCYSTIS PYRIFERA (KELP) EXTRACT	2
11E - Shaving Cream	MACROCYSTIS PYRIFERA (KELP) EXTRACT	1
12A - Cleansing	MACROCYSTIS PYRIFERA (KELP) EXTRACT	6
12B - Depilatories	MACROCYSTIS PYRIFERA (KELP) EXTRACT	8
12C - Face and Neck (exc shave)	MACROCYSTIS PYRIFERA (KELP) EXTRACT	13
12D - Body and Hand (exc shave)	MACROCYSTIS PYRIFERA (KELP) EXTRACT	13
12F - Moisturizing	MACROCYSTIS PYRIFERA (KELP) EXTRACT	14
12G - Night	MACROCYSTIS PYRIFERA (KELP) EXTRACT	1
12H - Paste Masks (mud packs)	MACROCYSTIS PYRIFERA (KELP) EXTRACT	5
12I - Skin Fresheners	MACROCYSTIS PYRIFERA (KELP) EXTRACT	3
12J - Other Skin Care Preps	MACROCYSTIS PYRIFERA (KELP) EXTRACT	5
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10A - Bath Soaps and Detergents	MACROCYSTIS PYRIFERA (KELP) PROTEIN	1
12H - Paste Masks (mud packs)	MACROCYSTIS PYRIFERA (KELP) PROTEIN	1
12J - Other Skin Care Preps	MACROCYSTIS PYRIFERA (KELP) PROTEIN	1
		3

03D - Eye Lotion	PELVETIA CANALICULATA EXTRACT	1
03F - Mascara	PELVETIA CANALICULATA EXTRACT	3
03G - Other Eye Makeup Preparations	PELVETIA CANALICULATA EXTRACT	2
05A - Hair Conditioner	PELVETIA CANALICULATA EXTRACT	4
05B - Hair Spray (aerosol fixatives)	PELVETIA CANALICULATA EXTRACT	1
05F - Shampoos (non-coloring)	PELVETIA CANALICULATA EXTRACT	6
05G - Tonics, Dressings, and Other Hair Grooming Aids	PELVETIA CANALICULATA EXTRACT	12

05I - Other Hair Preparations	PELVETIA CANALICULATA EXTRACT	1
06H - Other Hair Coloring Preparation	PELVETIA CANALICULATA EXTRACT	1
10E - Other Personal Cleanliness Products	PELVETIA CANALICULATA EXTRACT	1
12A - Cleansing	PELVETIA CANALICULATA EXTRACT	1
12C - Face and Neck (exc shave)	PELVETIA CANALICULATA EXTRACT	8
12F - Moisturizing	PELVETIA CANALICULATA EXTRACT	4
12G - Night	PELVETIA CANALICULATA EXTRACT	2
		47

03D - Eye Lotion	SARGASSUM FILIPENDULA EXTRACT	2
05A - Hair Conditioner	SARGASSUM FILIPENDULA EXTRACT	1
05B - Hair Spray (aerosol fixatives)	SARGASSUM FILIPENDULA EXTRACT	3
05F - Shampoos (non-coloring)	SARGASSUM FILIPENDULA EXTRACT	2
05G - Tonics, Dressings, and Other Hair Grooming Aids	SARGASSUM FILIPENDULA EXTRACT	1
06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	SARGASSUM FILIPENDULA EXTRACT	23
07I - Other Makeup Preparations	SARGASSUM FILIPENDULA EXTRACT	1
11F - Shaving Soap	SARGASSUM FILIPENDULA EXTRACT	1
12A - Cleansing	SARGASSUM FILIPENDULA EXTRACT	2
12C - Face and Neck (exc shave)	SARGASSUM FILIPENDULA EXTRACT	1
12F - Moisturizing	SARGASSUM FILIPENDULA EXTRACT	4
12H - Paste Masks (mud packs)	SARGASSUM FILIPENDULA EXTRACT	3
12J - Other Skin Care Preps	SARGASSUM FILIPENDULA EXTRACT	2
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12C - Face and Neck (exc shave)	SARGASSUM FUSIFORME EXTRACT	2
12F - Moisturizing	SARGASSUM FUSIFORME EXTRACT	2
12H - Paste Masks (mud packs)	SARGASSUM FUSIFORME EXTRACT	3
		7

12H - Paste Masks (mud packs)	SARGASSUM MUTICUM EXTRACT	1

10A - Bath Soaps and Detergents	SPHACELARIA SCOPARIA EXTRACT	2
12D - Body and Hand (exc shave)	SPHACELARIA SCOPARIA EXTRACT	4
12F - Moisturizing	SPHACELARIA SCOPARIA EXTRACT	1
12J - Other Skin Care Preps	SPHACELARIA SCOPARIA EXTRACT	1
		8

03D - Eye Lotion	UNDARIA PINNATIFIDA EXTRACT	4
05A - Hair Conditioner	UNDARIA PINNATIFIDA EXTRACT	1
05F - Shampoos (non-coloring)	UNDARIA PINNATIFIDA EXTRACT	3
05I - Other Hair Preparations	UNDARIA PINNATIFIDA EXTRACT	2
07B - Face Powders	UNDARIA PINNATIFIDA EXTRACT	3
07C - Foundations	UNDARIA PINNATIFIDA EXTRACT	3
07I - Other Makeup Preparations	UNDARIA PINNATIFIDA EXTRACT	2
10A - Bath Soaps and Detergents	UNDARIA PINNATIFIDA EXTRACT	1
10E - Other Personal Cleanliness Products	UNDARIA PINNATIFIDA EXTRACT	3
12A - Cleansing	UNDARIA PINNATIFIDA EXTRACT	1
12C - Face and Neck (exc shave)	UNDARIA PINNATIFIDA EXTRACT	26
12D - Body and Hand (exc shave)	UNDARIA PINNATIFIDA EXTRACT	12
12F - Moisturizing	UNDARIA PINNATIFIDA EXTRACT	8
12G - Night	UNDARIA PINNATIFIDA EXTRACT	4
12H - Paste Masks (mud packs)	UNDARIA PINNATIFIDA EXTRACT	1
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There were no reported uses in the 2018 VCRP:

Agarum Cribrosum Extract
Ascophyllum Nodosum
Asterionellopsis Glacialis Extract
Cladosiphon Novae-Caledoniae Extract
Cystoseira Amentacea/Caespitosa/Branchycarpa Extract
Cystoseira Baccata Extract
Cystoseira Balearica Extract
Cystoseira Caespitosa Extract
Cystoseira Compressa Extract
Cystoseira Compressa Powder
Cystoseira Tamariscifolia Extract
Dictyopteris Polypodioides Extract
Dictyota Coriacea Extract
Durvillaea Antarctica Extract

Ecklonia Cava Extract
Ecklonia Cava Water
Ecklonia Kurome Extract
Ecklonia Kurome Powder
Ecklonia/Laminaria Extract
Ecklonia Maxima Extract
Ecklonia Maxima Powder
Ecklonia Radiata Extract
Eisenia Arborea Extract
Fucus Spiralis Extract
Fucus Vesiculosus
Halidrys Siliquosa Extract
Halopteris Scoparia Extract
Himanthalia Elongata Powder
Hizikia Fusiforme Extract
Hizikia Fusiformis Water
Hizikia Fusiformis Callus Culture Extract
Hydrolyzed Ecklonia Cava Extract
Hydrolyzed Fucus Vesiculosus Extract
Hydrolyzed Fucus Vesiculosus Protein
Laminaria Diabolica Extract
Laminaria Japonica Powder
Laminaria Longissima Extract
Lessonia Nigrescens Extract
Lessonia Nigrescens Powder
Macrocystis Pyrifera (Kelp) Blade/Pneumatocyst/Stipe Juice Extract
Macrocystis Pyrifera (Kelp) Juice
Nereocystis Luetkeana Extract
Pelvetia Siliquosa Extract
Phyllacantha Fibrosa Extract
Rissoella Verruculosa Extract
Saccharina Angustata Extract
Laminaria Angustata Extract (Retired)
Saccharina Japonica Extract
Laminaria Ochotensis Extract (Retired)
Saccharina Longicruris Extract
Sargassum Fulvellum Extract
Sargassum Glaucescens Extract
Sargassum Horneri Extract
Sargassum Pallidum Extract
Sargassum Siliquastrum Extract
Sargassum Thunbergii Extract
Sargassum Vulgare Extract
Sahel Scenedesmus Extract
Undaria Peterseniana Extract
Undaria Pinnatifida Cell Culture Extract
Undaria Pinnatifida Leaf/Stem Extract
Undaria Pinnatifida Powder
Undaria Pinnatifida Root Powder

02A - Bath Oils, Tablets, and Salts	KELP	1
02D - Other Bath Preparations	KELP	4
05E - Rinses (non-coloring)	KELP	1
05F - Shampoos (non-coloring)	KELP	1
05G - Tonics, Dressings, and Other Hair Grooming Aids	KELP	2
09C - Other Oral Hygiene Products	KELP	1
10A - Bath Soaps and Detergents	KELP	2
10E - Other Personal Cleanliness Products	KELP	3
12C - Face and Neck (exc shave)	KELP	3
12F - Moisturizing	KELP	1
12H - Paste Masks (mud packs)	KELP	2
12J - Other Skin Care Preps	KELP	3
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02D - Other Bath Preparations	KELP EXTRACT	1
03D - Eye Lotion	KELP EXTRACT	1
05F - Shampoos (non-coloring)	KELP EXTRACT	1
05G - Tonics, Dressings, and Other Hair Grooming Aids	KELP EXTRACT	1
05H - Wave Sets	KELP EXTRACT	2
05I - Other Hair Preparations	KELP EXTRACT	3
10E - Other Personal Cleanliness Products	KELP EXTRACT	1
12C - Face and Neck (exc shave)	KELP EXTRACT	1
12F - Moisturizing	KELP EXTRACT	1
12G - Night	KELP EXTRACT	3
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05C - Hair Straighteners	LAMINARIA EXTRACT	1
05F - Shampoos (non-coloring)	LAMINARIA EXTRACT	1
12D - Body and Hand (exc shave)	LAMINARIA EXTRACT	1
12J - Other Skin Care Preps	LAMINARIA EXTRACT	1
		4

05A - Hair Conditioner	PHAEOPHYCEAE (BROWN ALGAE)	4

02D - Other Bath Preparations	SEAWEED EXTRACT	1
03D - Eye Lotion	SEAWEED EXTRACT	3
03G - Other Eye Makeup Preparations	SEAWEED EXTRACT	1
05A - Hair Conditioner	SEAWEED EXTRACT	1
05F - Shampoos (non-coloring)	SEAWEED EXTRACT	7
05G - Tonics, Dressings, and Other Hair Grooming Aids	SEAWEED EXTRACT	1
05I - Other Hair Preparations	SEAWEED EXTRACT	4
07B - Face Powders	SEAWEED EXTRACT	1
07E - Lipstick	SEAWEED EXTRACT	1
07F - Makeup Bases	SEAWEED EXTRACT	2
07I - Other Makeup Preparations	SEAWEED EXTRACT	1
10A - Bath Soaps and Detergents	SEAWEED EXTRACT	3
12A - Cleansing	SEAWEED EXTRACT	7
12C - Face and Neck (exc shave)	SEAWEED EXTRACT	18
12D - Body and Hand (exc shave)	SEAWEED EXTRACT	2
12F - Moisturizing	SEAWEED EXTRACT	9
12G - Night	SEAWEED EXTRACT	4
12H - Paste Masks (mud packs)	SEAWEED EXTRACT	4
12I - Skin Fresheners	SEAWEED EXTRACT	1
12J - Other Skin Care Preps	SEAWEED EXTRACT	11
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Concentration of Use by FDA Product Category – Brown Algae-Derived Ingredients*

Agarum Cribrosum Extract
Alaria Esculenta Extract
Ascophyllum Nodosum Extract
Ascophyllum Nodosum Powder
Cladosiphon Novae-Caledoniae Extract
Cladosiphon Okamuranus Extract
Cystoseira Amentacea/Caespitosa/Branchycarpa Extract
Cystoseira Baccata Extract
Cystoseira Balearica Extract
Cystoseira Caespitosa Extract
Cystoseira Compressa Extract
Cystoseira Compressa Powder
Cystoseira Tamariscifolia Extract
Dictyopteris Membranacea Extract (Retired)
Dictyopteris Polypodioides Extract
Dictyota Coriacea Extract
Durvillea Antarctica Extract
Ecklonia Cava Extract
Ecklonia Cava Water
Ecklonia Kurome Extract
Ecklonia Kurome Powder
Ecklonia/Laminaria Extract
Ecklonia Maxima Extract
Ecklonia Maxima Powder
Ecklonia Radiata Extract
Eisenia Arborea Extract
Fucus Serratus Extract
Fucus Spiralis Extract
Fucus Vesiculosus Extract
Fucus Vesiculosus Powder
Halidrys Siliquosa Extract
Halopteris Scoparia Extract
Himanthalia Elongata Extract
Himanthalia Elongata Powder
Hizikia Fusiforme Extract
Hizikia Fusiformis Water
Hizikia Fusiformis Callus Culture Extract
Hydrolyzed Ecklonia Cava Extract
Hydrolyzed Fucus Vesiculosus Extract
Hydrolyzed Fucus Vesiculosus Protein
Laminaria Angustata Extract (Retired)
Laminaria Cloustoni Extract
Laminaria Diabolica Extract
Laminaria Digitata Extract
Laminaria Digitata Powder
Laminaria Hyperborea Extract
Laminaria Japonica Extract
Laminaria Japonica Powder
Laminaria Longissima Extract
Laminaria Ochotensis Extract (Retired)
Laminaria Ochroleuca Extract
Laminaria Saccharina Extract
Lessonia Nigrescens Extract
Lessonia Nigrescens Powder
Macrocystis Pyrifera (Kelp)
Macrocystis Pyrifera (Kelp) Blade/Pneumatocyst/Stipe Juice Extract
Macrocystis Pyrifera (Kelp) Extract
Macrocystis Pyrifera (Kelp) Juice
Macrocystis Pyrifera (Kelp) Protein
Nereocystis Luetkeana Extract
Pelvetia Canaliculata Extract
Pelvetia Siliquosa Extract
Phyllacantha Fibrosa Extract
Saccharina Angustata Extract
Saccharina Japonica Extract
Saccharina Longicruris Extract
Sargassum Filipendula Extract
Sargassum Fulvellum Extract
Sargassum Fusiforme Extract
Sargassum Horneri Extract
Sargassum Muticum Extract
Sargassum Pallidum Extract
Sargassum Siliquastrum Extract
Sargassum Vulgare Extract
Sphacelaria Scoparia Extract
Undaria Peterseniana Extract
Undaria Pinnatifida Extract
Undaria Pinnatifida Cell Culture Extract

Undaria Pinnatifida Leaf/Stem Extract Undaria Pinnatifida Root Powder
Undaria Pinnatifida Powder

Ingredient	Product Category	Maximum Concentration of Use
Agarum Cribrosum Extract	Other skin care preparations	0.012%
Alaria Esculenta Extract	Foundations	0.03%
Alaria Esculenta Extract	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.0015%
Alaria Esculenta Extract	Face and neck products Not spray	 0.0015-0.05%
Alaria Esculenta Extract	Night products Not spray	 1%
Alaria Esculenta Extract	Indoor tanning preparations	0.0005%
Ascophyllum Nodosum Extract	Eye lotion	0.025-0.2%
Ascophyllum Nodosum Extract	Hair conditioners	0.00005-0.0002%
Ascophyllum Nodosum Extract	Shampoos (noncoloring)	0.00005-0.002%
Ascophyllum Nodosum Extract	Tonics, dressings and other hair grooming aids	0.002%
Ascophyllum Nodosum Extract	Nail polish and enamel	0.000065%
Ascophyllum Nodosum Extract	Other manicuring preparations	0.02%
Ascophyllum Nodosum Extract	Other personal cleanliness products	0.00004%
Ascophyllum Nodosum Extract	Face and neck products Not spray	 0.0032-0.03%
Ascophyllum Nodosum Extract	Body and hand products Not spray	 0.0000004-0.02%
Ascophyllum Nodosum Extract	Moisturizing products Not spray	 0.03%
Ascophyllum Nodosum Extract	Paste masks and mud packs	0.0032%
Ascophyllum Nodosum Extract	Other skin care preparations	0.045%
Cladosiphon Okamuranus Extract	Eye lotion	0.025%
Cladosiphon Okamuranus Extract	Foundation	0.05%
Cladosiphon Okamuranus Extract	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.005%
Cladosiphon Okamuranus Extract	Face and neck products Not spray	 0.025%
Dictyopteris Membranacea Extract	Lipstick	0.01%
Durvillea Antartica Extract	Basecoats and undercoats (manicuring preparations)	0.0001%
Ecklonia Radiata Extract	Hair conditioners	0.005%
Ecklonia Radiata Extract	Hair sprays Aerosol Pump spray	 0.0051% 0.0051%
Ecklonia Radiata Extract	Shampoos (noncoloring)	0.0051%
Ecklonia Radiata Extract	Other hair preparations (noncoloring)	

	Spray	0.0051%
Fucus Serratus Extract	Eye lotions	0.05%
Fucus Serratus Extract	Hair conditioners	0.00001%
Fucus Serratus Extract	Shampoos (noncoloring)	0.00001%
Fucus Serratus Extract	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.05%
Fucus Serratus Extract	Face and neck products Not spray	 0.05%
Fucus Vesiculosis Extract	Bath oils, tablets and salts	0.0001-0.01%
Fucus Vesiculosis Extract	Bubble baths	5%
Fucus Vesiculosis Extract	Other bath preparations	0.0051%
Fucus Vesiculosis Extract	Eyebrow pencil	0.02%
Fucus Vesiculosis Extract	Eye shadow	0.01%
Fucus Vesiculosis Extract	Eye lotion	0.017%
Fucus Vesiculosis Extract	Mascara	0.02-5%
Fucus Vesiculosis Extract	Perfume	0.01%
Fucus Vesiculosis Extract	Hair conditioners	0.0006-0.17%
Fucus Vesiculosis Extract	Hair sprays Aerosol Pump spray	 0.001% 0.00018-0.0006%
Fucus Vesiculosis Extract	Rinses (noncoloring)	0.00012-0.01%
Fucus Vesiculosis Extract	Shampoos (noncoloring)	0.0001-5%
Fucus Vesiculosis Extract	Tonics, dressings and other hair grooming aids	0.0001-0.01%
Fucus Vesiculosis Extract	Other hair preparations (noncoloring)	0.0015%
Fucus Vesiculosis Extract	Hair lighteners with color	0.0001%
Fucus Vesiculosis Extract	Lipstick	0.0005%
Fucus Vesiculosis Extract	Other makeup preparations	0.005%
Fucus Vesiculosis Extract	Other manicuring preparations	0.02%
Fucus Vesiculosis Extract	Bath soaps and detergents	0.00076-3.1%
Fucus Vesiculosis Extract	Other personal cleanliness products	0.00002%
Fucus Vesiculosis Extract	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.00011-0.17%
Fucus Vesiculosis Extract	Face and neck products Not spray	 0.005-0.05%
Fucus Vesiculosis Extract	Body and hand products Not spray	 0.000032-6%
Fucus Vesiculosis Extract	Foot products Not spray or powder Spray	 0.08% 0.12%
Fucus Vesiculosis Extract	Moisturizing products Not spray	 0.0051-5%
Fucus Vesiculosis Extract	Night products Not spray	 0.016-0.05%
Fucus Vesiculosis Extract	Paste masks and mud packs	0.0025-0.05%
Fucus Vesiculosis Extract	Other skin care preparations	0.03%

Fucus Vesiculosis Extract	Suntan products Not spray	0.00098%
Laminaria Digitata Extract	Bath oils, tablets and salts	0.1%
Laminaria Digitata Extract	Bubble baths	5%
Laminaria Digitata Extract	Eye lotion	0.095-0.5%
Laminaria Digitata Extract	Mascara	0.0035%
Laminaria Digitata Extract	Hair conditioners	0.0007-5%
Laminaria Digitata Extract	Hair sprays Aerosol	0.0007%
Laminaria Digitata Extract	Shampoos (noncoloring)	0.0007-0.0039%
Laminaria Digitata Extract	Tonics, dressings and other hair grooming aids	0.0035%
Laminaria Digitata Extract	Other hair preparations (noncoloring)	0.0007%
Laminaria Digitata Extract	Hair rinses (coloring)	0.0007%
Laminaria Digitata Extract	Hair shampoos (coloring)	0.0007%
Laminaria Digitata Extract	Hair bleaches	0.00004%
Laminaria Digitata Extract	Foundations	0.013%
Laminaria Digitata Extract	Bath soaps and detergents	0.06%
Laminaria Digitata Extract	Skin cleansing products (cold creams, cleansing lotions, liquids and pads)	0.6%
Laminaria Digitata Extract	Face and neck products Not spray	0.0001-0.1%
Laminaria Digitata Extract	Body and hand products Not spray	0.005-0.08%
Laminaria Digitata Extract	Moisturizing products Not spray	0.01%
Laminaria Digitata Extract	Skin fresheners	5%
Laminaria Digitata Extract	Other skin care preparations	0.1-0.5%
Laminaria Digitata Powder	Face and neck products Not spray	40%
Laminaria Hyperborea Extract	Body and hand products Not spray	0.03%
Laminaria Japonica Extract	Bath oils, tablets and salts	0.011-5%
Laminaria Japonica Extract	Other eye makeup preparations	0.0005-0.007%
Laminaria Japonica Extract	Hair conditioners	0.0005-0.0006%
Laminaria Japonica Extract	Rinses (noncoloring)	0.0012%
Laminaria Japonica Extract	Shampoos (noncoloring)	0.0006%
Laminaria Japonica Extract	Tonics, dressings and other hair grooming aids	0.3%
Laminaria Japonica Extract	Blushers	0.0035%
Laminaria Japonica Extract	Face powders	0.0035%
Laminaria Japonica Extract	Foundations	0.018%
Laminaria Japonica Extract	Rouges	0.019%
Laminaria Japonica Extract	Other makeup preparations	0.018%
Laminaria Japonica Extract	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.0055%

Laminaria Japonica Extract	Face and neck products Not spray	 0.011-5%
Laminaria Japonica Extract	Body and hand products Not spray	 0.0055%
Laminaria Japonica Extract	Paste masks and mud packs	0.0005-5%
Laminaria Japonica Extract	Skin fresheners	5%
Laminaria Japonica Extract	Other skin care preparations	0.0005%
Laminaria Ochroleuca Extract	Eyeliner	0.63%
Laminaria Ochroleuca Extract	Eye shadow	0.017%
Laminaria Ochroleuca Extract	Eye lotion	0.0034-0.02%
Laminaria Ochroleuca Extract	Hair conditioners	0.017%
Laminaria Ochroleuca Extract	Shampoos (noncoloring)	0.017%
Laminaria Ochroleuca Extract	Tonics, dressings and other hair grooming aids	0.017%
Laminaria Ochroleuca Extract	Hair dyes and colors	0.017%
Laminaria Ochroleuca Extract	Foundations	0.00017-0.02%
Laminaria Ochroleuca Extract	Rouges	0.017%
Laminaria Ochroleuca Extract	Aftershave lotions	0.00024%
Laminaria Ochroleuca Extract	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.000024-0.017%
Laminaria Ochroleuca Extract	Face and neck products Not spray Spray	 0.0026-0.17% 0.017%
Laminaria Ochroleuca Extract	Body and hand products Not spray	 0.0005-0.017%
Laminaria Ochroleuca Extract	Moisturizing products Not spray	 0.0034-0.017%
Laminaria Ochroleuca Extract	Night products Not spray	 0.0034-0.017%
Laminaria Ochroleuca Extract	Suntan products Not spray	 0.0034-0.05%
Laminaria Saccharina Extract	Eye lotion	0.002-0.019%
Laminaria Saccharina Extract	Eye makeup remover	0.000092%
Laminaria Saccharina Extract	Shampoos (noncoloring)	0.00001-0.045%
Laminaria Saccharina Extract	Tonics, dressings and other hair grooming aids	0.001-0.002%
Laminaria Saccharina Extract	Face powders	0.0008%
Laminaria Saccharina Extract	Foundations	0.01%
Laminaria Saccharina Extract	Nail polish and enamel	0.001%
Laminaria Saccharina Extract	Bath soaps and detergents	0.51%
Laminaria Saccharina Extract	Deodorants Not spray	 0.015%
Laminaria Saccharina Extract	Aftershave lotions	0.005-0.023%
Laminaria Saccharina Extract	Preshave lotions	0.23%
Laminaria Saccharina Extract	Shaving cream	0.023%
Laminaria Saccharina Extract	Skin cleansing (cold creams, cleansing	0.000092-0.01%

	lotions, liquids and pads)	
Laminaria Saccharina Extract	Face and neck products Not spray	 0.0031-0.1%
Laminaria Saccharina Extract	Body and hand products Not spray Not spray, not powder	 0.000092-0.0031% 0.54%
Laminaria Saccharina Extract	Moisturizing products Not spray	 0.023%
Laminaria Saccharina Extract	Night products Not spray	 0.019%
Laminaria Saccharina Extract	Paste masks and mud packs	0.0078%
Laminaria Saccharina Extract	Other skin care preparations	0.0008-0.005%
Laminaria Saccharina Extract	Indoor tanning preparations	0.005%
Lessonia Nigrescens Extract	Paste masks and mud packs	0.032%
Macrocystis Pyrifera (Kelp) Extract	Bath oils, tablets and salts	0.028-1%
Macrocystis Pyrifera (Kelp) Extract	Bubble baths	0.21%
Macrocystis Pyrifera (Kelp) Extract	Other bath preparations	0.0051-0.41%
Macrocystis Pyrifera (Kelp) Extract	Eye lotion	0.2-36.4%
Macrocystis Pyrifera (Kelp) Extract	Eye makeup remover	0.0098%
Macrocystis Pyrifera (Kelp) Extract	Other eye makeup preparations	0.007%
Macrocystis Pyrifera (Kelp) Extract	Colognes and toilet waters	0.084%
Macrocystis Pyrifera (Kelp) Extract	Other fragrance preparations	0.042%
Macrocystis Pyrifera (Kelp) Extract	Hair conditioners	0.001-0.17%
Macrocystis Pyrifera (Kelp) Extract	Shampoos (noncoloring)	0.001-5%
Macrocystis Pyrifera (Kelp) Extract	Tonics, dressings and other hair grooming aids	0.0036-5%
Macrocystis Pyrifera (Kelp) Extract	Blushers	0.0035%
Macrocystis Pyrifera (Kelp) Extract	Face powders	0.0035%
Macrocystis Pyrifera (Kelp) Extract	Foundations	0.018-0.98%
Macrocystis Pyrifera (Kelp) Extract	Lipstick	0.079%
Macrocystis Pyrifera (Kelp) Extract	Rouges	0.019%
Macrocystis Pyrifera (Kelp) Extract	Other makeup preparations	0.018%
Macrocystis Pyrifera (Kelp) Extract	Nail creams and lotions	0.0002%
Macrocystis Pyrifera (Kelp) Extract	Nail extenders	0.00044%
Macrocystis Pyrifera (Kelp) Extract	Nail polish and enamel	0.0011%
Macrocystis Pyrifera (Kelp) Extract	Bath soaps and detergents	0.01-5%
Macrocystis Pyrifera (Kelp) Extract	Aftershave lotions	0.007-0.042%
Macrocystis Pyrifera (Kelp) Extract	Shaving cream (aerosol, brushless and lather)	0.05%
Macrocystis Pyrifera (Kelp) Extract	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.00005-1.5%
Macrocystis Pyrifera (Kelp) Extract	Depilatories	0.0002%
Macrocystis Pyrifera (Kelp) Extract	Face and neck products Not spray Spray	 0.001-33.3% 0.79%
Macrocystis Pyrifera (Kelp) Extract	Body and hand products	

	Not spray	0.42-0.98%
Macrocystis Pyrifera (Kelp) Extract	Foot products Not spray, not powder	0.17% 0.2%
Macrocystis Pyrifera (Kelp) Extract	Moisturizing products Not spray	 0.42%
Macrocystis Pyrifera (Kelp) Extract	Paste masks and mud packs	0.5-0.6%
Macrocystis Pyrifera (Kelp) Extract	Skin fresheners	5%
Macrocystis Pyrifera (Kelp) Extract	Other skin care preparations	0.41-0.98%
Macrocystis Pyrifera (Kelp) Extract	Suntan products Not spray	 0.0098%
Macrocystis Pyrifera (Kelp) Extract	Indoor tanning preparations	0.0098%
Pelvetia Canaliculata Extract	Eye lotion	0.00002%
Pelvetia Canaliculata Extract	Mascara	0.0007%
Pelvetia Canaliculata Extract	Hair conditioners	0.0007%
Pelvetia Canaliculata Extract	Hair sprays Aerosol Pump spray	 0.0007% 0.00004%
Pelvetia Canaliculata Extract	Shampoos (noncoloring)	0.0007%
Pelvetia Canaliculata Extract	Tonics, dressings and other hair grooming aids	0.0035%
Pelvetia Canaliculata Extract	Other hair preparations (noncoloring)	0.0007%
Pelvetia Canaliculata Extract	Hair rinses (coloring)	0.0007%
Pelvetia Canaliculata Extract	Hair shampoos (coloring)	0.0007%
Pelvetia Canaliculata Extract	Hair bleaches	0.00004%
Pelvetia Canaliculata Extract	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.0004-0.0018%
Pelvetia Canaliculata Extract	Face and neck products Not spray	 0.002-0.018%
Pelvetia Canaliculata Extract	Skin fresheners	0.002%
Pelvetia Canaliculata Extract	Suntan products Not spray	 0.0044%
Sargassum Filipendula Extract	Hair conditioners	0.0048-0.29%
Sargassum Filipendula Extract	Shampoos (noncoloring)	0.15%
Sargassum Filipendula Extract	Tonics, dressings and other hair grooming aids	0.0001%
Sargassum Filipendula Extract	Hair dyes and colors	0.011-0.29%
Sargassum Filipendula Extract	Skin cleansing (cold creams, cleansing lotion, liquids and pads)	0.002%
Sargassum Filipendula Extract	Face and neck products Not spray	 0.8%
Sargassum Filipendula Extract	Moisturizing products Not spray	 1.2%
Sargassum Filipendula Extract	Paste masks and mud packs	0.15%
Sargassum Muticum Extract	Eye lotion	4%
Sargassum Muticum Extract	Other eye makeup preparations	2.5%
Sargassum Muticum Extract	Skin cleansing (cold creams, cleansing	0.01%

	lotions, liquids and pads)	
Sargassum Muticum Extract	Other skin care preparations	2-4%
Sargassum Vulgare Extract	Eye lotion	0.011%
Sargassum Vulgare Extract	Shampoos (noncoloring)	0.0075%
Sargassum Vulgare Extract	Tonics, dressings and other hair grooming aids	0.009%
Sargassum Vulgare Extract	Face and neck products Not spray	0.011%
Sargassum Vulgare Extract	Other skin care preparations	0.016%
Sphacelaria Scoparia Extract	Body and hand products Not spray, not powder	0.016%
Undaria Pinnatifida Extract	Other bath preparations	0.0001%
Undaria Pinnatifida Extract	Shampoos (noncoloring)	5%
Undaria Pinnatifida Extract	Tonics, dressings and other hair grooming aids	0.002%
Undaria Pinnatifida Extract	Other hair preparations (noncoloring)	0.0031%
Undaria Pinnatifida Extract	Face powders	0.00001%
Undaria Pinnatifida Extract	Foundations	0.00001%
Undaria Pinnatifida Extract	Makeup bases	0.00001%
Undaria Pinnatifida Extract	Bath soaps and detergents	0.0001%
Undaria Pinnatifida Extract	Face and neck products Not spray	0.00001-0.001%
Undaria Pinnatifida Extract	Body and hand products Not spray	5%
Undaria Pinnatifida Powder	Shaving soap	0.1%

*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 2015
Table prepared: July 3, 2015

Concentration of Use by FDA Product Category – Additional Algae Ingredients for the Brown Algae Report*

Asterionellopsis Glacialis Extract
Kappaphycus Alvarezii Extract
Rissoella Verruculosa Extract
Sahel Scenedesmus Extract

Ingredient	Product Category	Maximum Concentration of Use
Kappaphycus Alvarezii Extract	Other personal cleanliness products	0.024%

*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 2015
Table prepared July 7, 2015

Concentration of Use by FDA Product Category – Brown Algae Additions*

Ascophyllum Nodosum
Fucus Vesiculosus
Sargassum Glaucescens Extract
Sargassum Thunbergii Extract

Ingredient	Product Category	Maximum Concentration of Use
Fucus Vesiculosis	Shampoos (noncoloring)	0.0003%
Fucus Vesiculosis	Moisturizing products Not spray	 0.0051%
Fucus Vesiculosis	Suntan products Not spray Aerosol	 0.00098% 0.00098%

*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 2015-2016
Table prepared February 12, 2016

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 8, 2018

SUBJECT: Hydrolyzed fucoidan extracted from *Laminaria digitata*

Lessonia. 2015. Safety certificate: Fucoreverse PF (contains 7% hydrolyzed fucoidan).

More information about Fucoreverse can be found on the internet at :
http://www.lessonia.com/vars/fichiers/Fiches-anglais/cosmetic-ingredients/marine-actives/fucoreverse-plaquette-2018-LD.pdf

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LESSONIA cosmetics + ingredients	SAFETY CERTIFICATE	Code : EN LAB REG 11 T Révision : 1 Date d'application : 17/02/2015 Page 1/6

Rédacteur(s) : C. BALCON	Approbateur(s) : C. WINCKLER

Je soussigné, Christophe WINCKLER, Président de Lessonia, certifie que le produit suivant :
I hereby, Christophe WINCKLER, President of Lessonia, certify that the following product:

FUCOREVERSE PF (F325) contains 7% hydrolyzed fucoidan extracted from Laminaria digitata

a fait l'objet de tests toxicologiques décrits ci-dessous.
was subject to toxicological tests described hereafter.

IRRITATION CUTANÉE / CUTANEOUS IRRITATION

Étude	ÉVALUATION DE LA TOLÉRANCE CUTANÉE D'UNE MATIERE PREMIERE COSMÉTIQUE SELON LE TEST 42 BIS : METHODE DE PREDICTION DE L'IRRITATION CUTANEE AIGÜE
Référence de l'étude	TV.01.C_2015/1883
Période d'essai	29/07/2015 – 31/07/2015
Méthode	Test 42 Bis : 42 minutes d'application + 42 heures après incubation
Quantité de produit testé	240 mg +/- 2 mg
Résumé de l'étude	L'étude est réalisé sur de l'épiderme humain reconstitué (Sterlab epidermis). Le produit est appliqué sur la surface de l'épiderme pendant 42 minutes. L'épiderme est incubé pendant 42 heures. L'évaluation de la viabilité cellulaire est réalisée selon la méthode MTT après 42 heures d'incubation. Le test est validé par un contrôle négatif et positif (SDS à 5%)
Résultat	% de viabilité cellulaire = 96.11%
Conclusion	Conformément aux observations enregistrées pendant l'étude et le résultat de la viabilité cellulaire obtenue après incubation (96.11%), le produit est classé **non irritant.**

Study	BIOLOGICAL EVALUATION OF A COSMETIC RAW MATERIAL TEST 42 BIS : TEST METHOD FOR THE PREDICTION OF ACUTE SKIN IRRITATION
Study reference	TV.01.C_2015/1883
Study period	29/07/2015 – 31/07/2015
Test method	42 Bis : 42 minutes application + 42 hours post-incubation
Applied product quantity	240 mg +/- 2 mg
Methodology abstract	Study is performed on reconstituted human epidermis (Sterlab epidermis). Product is deposed to the surface of epidermis for 42 minutes. Epidermis is post-incubation for 42 hours. The assessment of cell viability by MTT method is realized after 42 hours incubation. Test method is validated by negative and positive controls (SDS, 5%)

Result	% of cell viability = 96.11%
Conclusion	In accordance with observations performed during this study and the results of cell viability obtained after incubation (96.11%), the product is classified as **non irritant.**

IRRITATION OCULAIRE / OCULAR IRRITATION

Étude	ÉVALUATION IN VITRO DU POTENTIEL D'IRRITATION OCULAIRE – METHODE D'ABSORPTION AU ROUGE NEUTRE
Référence de l'étude	BPL/2015/1884
Période d'essai	14/07/2015 – 17/07/2015
Méthode	Méthode d'absorption au rouge neutre
Résumé de l'étude	Les cellules BALB/c 3T3 sont ensemencées et exposées à différentes concentration du produit testé. Après 24 heures d'incubation, l'absorption du rouge neutre est mesurée sur les lysosomes/endosomes et dans les vacuoles de cellules viables et est utilisée comme indicateur de viabilité cellulaire. Jour 1 : les cellules BALB/c 3T3, clone 31 (ATCC CCL-163) sont ensemencées dans une plaque 96 puits à raison de 1x104 cellules/puit et maintenues pendant 24 heures (37°C, 95% HR, 5% CO2). Jour 2 : Après 24 heures d'incubation, le milieu est remplacé par un nouveau milieu contenant le produit testé ou le contrôle positif. Les plaques sont incubées pendant 24 heures (37°C, 95% HR, 5% CO2). Les cellules traitées avec le milieu de culture sont utilisées comme contrôle négatif. Jour 3 : les cellules sont observées visuellement au microscope. Puis le milieu, les échantillons, les contrôles positifs et négatifs sont retirés. Les cellules sont lavées avec du PBS et un nouveau milieu contenant du rouge neutre (RN) est ajouté aux puits. Les cellules sont incubées pendant 3 heures (37°C, 95% HR, 5% CO2). Après incubation, le milieu au RN est retiré et les cellules sont lavées avec du PBS et une solution ETOH/acide acétique/eau déionisée est ajoutée aux puits. Les plaques sont agitées pendant 10 minutes et sont lues à 540 nm. 2 essais sont répétés pour le produit et les contrôles.
Résultat	RN50 > 1000 µg/ml MMAS (Score moyen maximum modifié) < 25
Conclusion	Conformément aux résultats obtenus, le produit est classé **non/faiblement irritant.**

Study	IN VITRO EVALUATION OF THE OCULAR IRRITATION POTENCY – NEUTRAL RED UPTAKE ASSAY
Study reference	BPL/2015/1884
Study period	14/07/2015 – 17/07/2015
Test method	Neutral red uptake assay
Methodology	BALB/c 3T3 cells were seeded and exposed to tested product in a concentration

abstract	range. After 24h incubation, Neutral Red Uptake in the lysosomes/endosomes and in vacuoles of living cells was measured and used as quantitative indicator of cell number and viability. 1st DAY: BALB/c 3T3, clone 31 (ATCC CCL-163) was seeded in 96-well plate at 1 x 104 cells/well and maintained for 24h (37°C, 95% RH, 5% CO2). 2nd DAY: after 24 h incubation, medium was removed and new medium containing tested product, positive controls was added to the wells. Plates were incubated for 24h (37°C, 95% RH, 5% CO2). Cells treated with culture medium were used as negative control. 3rd DAY: cells were observed at microscope for a visual evaluation, then, medium, sample, positive and negative control were removed. Cells were washed with PBS and new medium containing Neutral Red (NR) was added to the wells. Cells were incubated for 3h (37°C, 95% RH, 5% CO2). After incubation, NR-medium was removed and cells washed with PBS and solubilising solution (ETOH/acetic acid/deionized water) was added to the wells. Plate was shaked for 10 minutes and then red at 540 nm. Two replicates were used for test sample and controls.
Result	NR50 > 1000 µg/ml MMAS (Modified Maximum Average Score)< 25
Conclusion	According to obtained results, the product is **not/mild irritant**.

POTENTIEL PHOTOTOXIQUE / PHOTOTOXIC POTENTIAL

Étude	ETUDE IN VITRO 3T3 NRU PT – EVALUATION DU POTENTIEL PHOTOTOXIQUES D'UNE MATIERE PREMIERE COSMETIQUE
Référence de l'étude	TV.01.C_2015/1848
Période d'essai	29/07/2015
Méthode	Méthode du test 3T3 NRU PT
Quantité de produit testé	Quatre mécanismes, par lesquels une absorption de lumière par un chromophore (substance chimique) peut induire une réponse phototoxique, ont été identifiés. Tous induisent des dommages cellulaires. Par conséquent, the test de phototoxicité in vitro 3T3 NRU est basé sur la comparaison de la cytotoxicité d'une substance chimique quand elle est soumise à une exposition ou non d'une dose non cytotoxique de lumière UVA visible. La cytotoxicité est exprimée par une réduction de l'absorption du rouge neutre, 24 heures après traitement par la substance chimique et irradiation, dépendante de la concentration testée. Les cellules Balb/c 3T3 sont maintenues en culture pendant 24 heures pour la formation de monocouches. 2 plaques de 96 puits par substance chimique sont pré-incubées avec 8 différentes concentrations de la substance chimique pendant 1 heure. Ensuite une des 2 plaques est exposée à une dose non cytotoxique de lumière UVA visible à raison de 5J/cm^2, tandis que la seconde plaque n'est pas exposée à la lumière. Puis, le milieu traité est remplacé par un milieu de culture sur les 2 plaques, et la viabilité cellulaire est déterminée après 24 heures d'incubation par la méthode d'absorption au rouge neutre pendant 3 heures. La viabilité cellulaire, exprimée en pourcentage de contrôle négatif non

	traité, est calculé pour les 8 concentrations testées. Pour prédire le potentiel phototoxique, les réponses obtenues par concentration en présence ou en l'absence de traitement UV sont comparées, habituellement à la concentration EC50 (concentration inhibitrice de 50% de la viabilité cellulaire comparativement au contrôle négatif non traité).

Résumé de l'étude

Concentration (µg/ml)	**Présence rayonnement UV** % viabilité cellulaire	**Absence rayonnement UV** % viabilité cellulaire	**PIF** *1
0.00	100.00	100.00	
6.90	95.70	98.50	
20.55	93.01	96.45	
61.80	86.99	94.52	
100.00	81.26	94.45	

Conclusion	Le produit testé ne présente pas d'effet toxique après irradiation sur selon modèle expérimental. Il ne présente pas de potentiel phototoxiques.

Study	IN VITRO SAFETY STUDY 3T3 NRU PT – EVALUATION OF THE PHOTOTOXIC POTENTIAL OF A COSMETIC RAW MATERIAL
Study reference	TV.01.C_2015/1848
Study period	29/07/2015
Test method	3T3 NRU PT test method
Methodology abstract	Four mechanisms have been identified by which absorption of light by a (chemical) chromophore can result in a phototoxic response. All of them result in cell damage. Therefore, the in vitro 3T3 NRU phototoxicity test is based on a comparison of the cytotoxicity of a chemical when tested in the presence and in the absence of exposure to a non-cytotoxic dose of UVA/vis light. Cytotoxicity in this test is expressed as a concentration dependent reduction of the uptake of the vital dye, neutral red (NR) 24 hours after treatments with the test chemical and irradiation. Balb/c 3T3 cells are maintained in culture for 24 hours for the formation of monolayers. Two 96-well plates per test chemical are then preincubated with eight different concentration of the chemical for 1 hour. Thereafter one of the two plates is exposed to a non –cytotoxic UVA/vis light dose of 5J/cm² UVA (+ UV experiment), whereas the other plate is kept in the dark (-UV experiment). In both plates, the treatment medium is then replaced by culture medium and after another 24 hours of incubation, cell viability is determined by Neutral red uptake for 3 hours. Relative cell viability, expressed as percentage of untreated negative controls, is calculated for eight test concentration. To predict the phototoxic potential, the concentration responses obtained in the presence (+UV) and in the absence (-UV) of irradiation are compared, usually at the EC50 level, i.e. the concentation inhibiting cell viability by 50% CF. untreated controls.

Result

Concentration (µg/ml)	**+ UV experiment** % cell viability	**- UV experiment** % cell viability	**PIF** *1
0.00	100.00	100.00	
6.90	95.70	98.50	
20.55	93.01	96.45	
61.80	86.99	94.52	

	100.00	81.26	94.45
Conclusion	Tested product **does not show any toxic effect** after irradiation on experimental model. It **does not show a predictive photo-toxic potential.**		

MUTAGÉNICITÉ / MUTAGENICITY

Étude	ÉVALUATION DU POTENTIEL GENOTOXIQUE D'UNE MATIERE PREMIERE COSMETIQUE SELON LA METHODE DU TEST D'AMES
Référence de l'étude	MI.01.C_2015/1849
Période d'essai	03/09/2015
Méthode	Test d'Ames
Résumé de l'étude	L'objectif de cette étude est d'enquêter sur la possible activité génotoxique exercé par la substance testée sur les souches de *Salmonella typhimurium,* avec et sans activation métabolique avec S9. Le test d'Ames permet de détecter l'induction de point de mutation dans les bases nucléotidique, tel que des suppressions, insertions, transversions et erreurs de décalage, en utilisant les souches de *Salmonella typhimurium* modifiées. Ces souches portent un gène défectueux sur l'opéron histidine qui les rend auxotrophe pour cet acide aminé (mutant His- qui nécessite la présence d'histidine dans le milieu de culture pour sa croissance). Le principe de la méthode est basé sur le phénomène de backmutation par lequel une bactérie exposée à une substance mutagène peut changer et devenir prototrophe à l'histidine (His+), et donc les bactéries révertantes deviennent histidine dépendante. Les cellules bactériennes, en phase de croissance, sont exposées différentes concentrations de la substance testée et l'activité mutagène est déterminée par la capacité de la substance testée à induire une augmentation significative du nombre de colonie révertante (mutant indépendant histidine, His+) en comparaison aux réversions spontanées observées dans les cultures contrôle. Certaines substances chimiques n'ont pas d'activité mutagène directe mais le deviennent après transformation et activation métabolique survenant dans l'organisme par l'activité enzymatique hépatique. Afin d'étudier cet effet génotoxique, une fraction microsomial hépatique du rat (S9) est ajoutée à l'étude. L'utilisation du S9 est connue pour identifier les substances mutagènes indirectes.
Conclusion	Conformément au protocole expérimental et aux résultats obtenus lors de cette étude, le produit ne montre pas de preuve de potentiel mutagène.

Study	EVALUATION OF GENOTOXIC POTENTIAL OF A COSMETIC RAW MATERIAL BY MEANS OF AMES TEST
Study reference	MI.01.C_2015/1849
Study period	03/09/2015
Test method	Ames test
Methodology	Aim of the test is to investigate the possible genotoxic activity exerted by the

abstract	tested substance in strains of *Salmonella typhimurium*, with and without metabolic activation with S9. Ames test allows to detect the induction of point mutations in nucleotidic bases, such as deletions, insertions, transversions and frameshift errors by using modified *Salmonella typhimurium* strains. These strains carry a defective gene in the histidine operone making them auxotrophe for this aminoacid (mutants His- which require histidine in the culture medium for growth). The method guiding principle is based on the backmutation: phenomenon by which bacteria exposed to a mutagenic substance may change back and become again prototrophe concerning histidine (His+), so revertant bacteria become histidine-independent. The bacterial cells, in growth phase, are exposed to different concentrations of the test agent and mutagenic activity is determined by the capacity of the test substance to induce a significant increase in the number of reverted colonies (histidine-independent mutant, His+) in comparison to spontaneous reversions occurring in the control cultures. Some chemical agents are not directly mutagen but become so following transformation and metabolic activation occurring in the organism by liver enzyme activity. In order to study this genotoxic effect, rat liver microsomial fraction (S9) has been added. S9 employ admits to identify indirect mutagen substances.
Conclusion	In accordance with experimental protocol and the basis of the results from this investigations, the product did not show **any evidence of mutagenicity.**

Saint Thonan, 05/04/2016

Christophe Winckler

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 9, 2018

SUBJECT: Ascophyllum Nodosum Extract

Solabia Group. 2017. Manufacturing Process Invincity® (trade name mixture containing Ascophyllum Nodosum Extract).

Solabia Group. 2017. Ingredient composition Invincity® (trade name mixture containing Ascophyllum Nodosum Extract).

Solabia Group. 2017. Specifications data sheet Invincity® (trade name mixture containing Ascophyllum Nodosum Extract).

Solabia Group. 2017. Toxicological file Invincity® (trade name mixture containing Ascophyllum Nodosum Extract).

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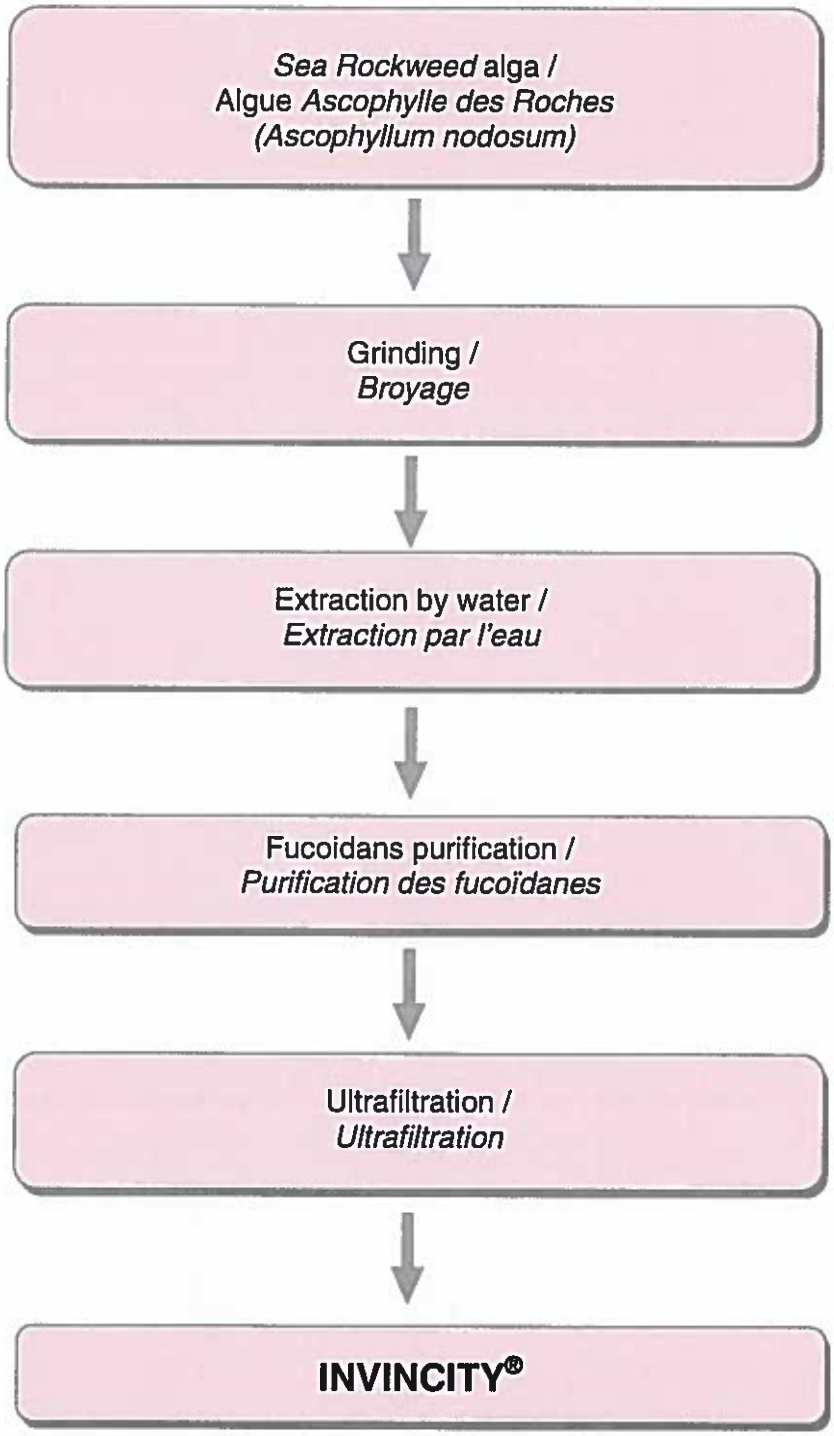
MANUFACTURING PROCESS
PROCEDE DE FABRICATION

INVINCITY®

Ref. M0006



Produced & Commercialized by Algues et Mer - SOLABIA Group
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INGREDIENT BREAKDOWN
COMPOSITION CENTESIMALE

INVINCITY®

Ref. M0006

Water	**94.50 %**
Ascophyllum nodosum extract *2g, 16 hours at 105°C*	**4.70 %**
Potassium sorbate	**0.30 %**
Sodium benzoate	**0.50 %**

Notes - *Remarques :*

- Because of the natural origin of the raw material, the centesimal composition is susceptible to slight variations.

  En raison de l'origine naturelle des matières premières, la composition centésimale est susceptible de subir une légère variation.

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SPECIFICATIONS DATA SHEET

INVINCITY®

Ref. M0006

DEFINITION

INVINCITY® is a concentrated form of fucoidans (sulphated polysaccharides) of high molecular weight (>100kDa), obtained from aqueous extraction of the intracellular polysaccharides of the alga Sea Rockweed (*Ascophyllum nodosum*), harvested on Ouessant island, and from their concentration by ultrafiltration.

PRESENTATION

• **Sample**	plastic flask - 125 mL
• **Code / Packaging** *to be mentioned with your order*	M0006KC - can 5 kg

ORGANOLEPTIC CHARACTERISTICS

• **Appearance**	translucent to opaque solution with possibly a slight precipitate
• **Color**	orange brown to brown
• **Odor**	characteristic

ANALYTICAL CHARACTERISTICS

• **pH at 20°C**	4.5 – 5.5
• **Density at 20°C**	0.9 – 1.1
• **Fucoidans (total sugars + total sulfate)** *Colorimetry + Turbidimetry*	≥ 2%
• **Dry matter** *Drying oven, 16h at 105°C*	5.0 – 6.0
• **Total ashes** *600°C*	≤ 2%
• **Heavy metals** *Eur. Ph. 9th ed. § 2.4.8*	≤ 20 ppm
• **Arsenic** *Eur. Ph. 9th ed. § 2.4.2*	≤ 2 ppm

MICROBIOLOGICAL CHARACTERISTICS

• **Total aerobic microbial count** *Eur. Ph. 9th ed. § 2.6.12 – 2.6.13*	≤ 100 C.F.U/g
• **Specified germs** *(Escherichia coli, Salmonella sp., Pseudomonas aeruginosa, Staphylococcus aureus)* *Eur. Ph. 9th ed. § 2.6.12 – 2.6.13*	absence
• **Total combined yeasts - molds count** *Eur. Ph. 9th ed. § 2.6.12 – 2.6.13*	≤ 10 C.F.U/g

INVINCITY®

- *Inhibits AhR pathway*
- *Reduces pollutant toxicity*
- *Prevents and corrects POLLUAGING®*

SOLUBILITIES (20% DILUTED)

• **Water**	soluble	• **Glycerin**	soluble
• **Alcohol 20% v/v**	non soluble	• **Mineral oils**	non soluble
• **Butylene glycol**	non soluble	• **Vegetal oils**	non soluble

SAFETY TESTS

- **In vitro ocular irritant potential** — practically non irritant
  Het-Cam - pure product
- **In vitro cutaneous irritation** — non irritant
  OECD 439 - pure product
- **Mutagenicity** — no mutagenic activity, no pro-mutagenic activity
  Ames test, OECD 471 – product diluted according to protocol
- **Phototoxicity** — no phototoxic activity
  OECD 432 – product diluted according to protocol

STORAGE AND USE

- **Shelf life** — 24 months in closed original packaging
- **Preservative system** — 0.3% of potassium sorbate and 0.5% sodium benzoate
- **Storage conditions** — store at room temperature
- **Use conditions** — mix before use if necessary

LEGISLATIVE INFORMATION

- **INCI** — Aqua / Ascophyllum nodosum extract
- **CTFA** — Water (and) Ascophyllum nodosum extract
- **CAS**

Aqua	7732-18-5
Ascophyllum nodosum extract	84775-78-0

- **EINECS**

Aqua	231-791-2
Ascophyllum nodosum extract	283-907-6

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TOXICOLOGICAL FILE

INVINCITY®

Ref. M0006

TOXICOLOGICAL PROFILE
INVINCITY®

Ref. M0006

IN VITRO OCULAR IRRITANT POTENTIAL [1]

Het-Cam - pure product — December 2015

Practically non irritant

IN VITRO CUTANEOUS IRRITATION [1]

OECD 439 - pure product — December 2015

Non irritant

MUTAGENICITY [1]

Ames test, OECD 471 – product diluted according to protocol — January 2016

No mutagenic activity, no pro-mutagenic activity

PHOTOTOXICITY [1]

OECD 432 - product diluted according to protocol — December 2015

No phototoxic activity

[1] *Tests realized by Bio-HC - Pessac (France)*

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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 20, 2018

SUBJECT: Sargassum Muticum Extract

Consumer Product Testing Co. 2014. Ophthalmological in-use safety evaluation - 50% sensitive eyes (eye cream containing 0.076% Sargassum Muticum Extract).

Consumer Product Testing Co. 2014. Repeated insult patch test (eye cream containing 0.076% Sargassum Muticum Extract).

Consumer Product Testing Co. 2016. Repeated insult patch test (skin care product containing 0.076% Sargassum Muticum Extract).

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

Consumer Product Testing Co.

FINAL REPORT

CLIENT: [redacted]

ATTENTION: [redacted] Ph.D., R.Ph.
Toxicologist

TEST: Ophthalmological In-Use Safety Evaluation - 50% Sensitive Eyes
Protocol No.: [redacted]

TEST MATERIAL: Eye Cream - [redacted] containing 0.076% Sargassum Muticum Extract

EXPERIMENT REFERENCE NUMBER: [redacted]

Reviewed by: Charles J. Kronengold, M.D.
Board Certified Ophthalmologist

Approved by: Michael Caswell, Ph.D., CCRA, CCRC
Vice President, Clinical Evaluations
31 Oct 2014

Approved by: Joy Frank, R.N.
Executive Vice President, Clinical Evaluations
10/31/14

70 New Dutch Lane • Fairfield, New Jersey 07004-2514 • (973) 808-7111 • Fax (973) 808-7234

Consumer Product Testing Co.

QUALITY ASSURANCE UNIT STATEMENT

Trial Number: [redacted]

The Consumer Product Testing Company, Incorporated (CPTC) Quality Assurance Unit (QAU) is responsible for auditing the conduct, content and reporting of all clinical trials that are conducted at CPTC.

This trial has been conducted in accordance with the Declaration of Helsinki, the ICH Guideline E6 for *Good Clinical Practice*, the requirements of 21 CFR Parts 50 and 56, other applicable laws and regulations, CPTC Standard Operating Procedures, and the approved protocol.

The CPTC QAU has reviewed all data, records, and documents relating to this trial and also this Final Report. The following QAU representative signature certifies that all data, records, and documents relating to this trial and also this Final Report have been reviewed and are deemed to be acceptable, and that the trial conforms to all of the requirements as indicated above.

All records and documents pertaining to the conduct of this trial shall be retained in the CPTC archives for a minimum of ten (10) years. At any time prior to the completion of the tenth archival year, a Sponsor may submit a written request to the CPTC QAU to obtain custody of trial records once the CPTC archive period has been completed. This transfer shall be performed at the Sponsor's expense. In the absence of a written request, trial-related records shall be destroyed at the end of the CPTC archive period in a manner that renders them useless.

William Cavaliere
Quality Assurance Representative

11/5/2014
Date

70 New Dutch Lane • Fairfield, New Jersey 07004-2514 • (973) 808-7111 • Fax (973) 808-7234
Clinical • Toxicology • Analytical Chemistry • Microbiology

Objective: To evaluate the safety and ocular irritation potential of an eye cream following repetitive, daily use conditions.

Participants: Thirty-three female subjects, ages 18 to 65 years, were recruited and qualified for this trial. Thirty-one subjects completed the trial. Subject #s 16 and 31 did not complete the trial due to personal reasons unrelated to test material use.

Inclusion Criteria:

a. Approximately 30 healthy female subjects, ages 18 to 65 years, inclusive;
b. Approximately 50% of the panel had self-perceived sensitive eyes;
c. Subjects who agreed to discontinue use of their current product with similar function and use only the test material;
d. Approximately 50% of the panel were soft contact lens wearers;
e. Subjects who agreed to arrive at the Testing Facility without eye makeup;
f. Subjects who were regular users of a product with similar function;
g. Subjects who agreed to avoid introducing the use of any new cosmetic, toiletry or personal care products during the course of the trial;
h. Subjects who had an acceptable ophthalmic examination to ensure eye health and, if appropriate, the correct fit and condition of their contact lenses;
i. Subjects who read, understood and signed an Informed Consent Form; and
j. Subjects who were considered dependable and able to follow directions as outlined in the protocol.

Exclusion Criteria:

a. Subjects in ill health or taking medication, other than birth control, which could have influenced the purpose, integrity or outcome of the trial;
b. Subjects using any systemic or topical corticosteroids, anti-inflammatory drugs, antihistamines, retinoids or other medication that, in the opinion of the Investigator, may have influenced the outcome of the trial;
c. Females who were pregnant, nursing or planning on becoming pregnant during the course of the trial;
d. Subjects with a history of adverse reactions to similar products being tested; or
e. Subjects with any visible skin or eye disease that might have been confused with a reaction to the test material.

Test Material: Eye Cream [redacted]

Trial Schedule:

Initiation Date	Completion Date
September 29, 2014	October 27, 2014

Methodology:

Each subject received a qualifying ophthalmic examination by a Board Certified Ophthalmologist to ensure eye health and, if appropriate, the correct fit of their contact lenses.

The Ophthalmologist studied and evaluated by gross and/or slit lamp examination the subjects' eyelids, conjunctivae, corneas, irises, lenses, anterior chambers and pupillary reactions, as well as measured visual acuity.

Findings were noted on subjects' Ocular Case Report Forms.

The panel was comprised of 14 soft contact lens wearers. The remaining 19 subjects were non-contact lens wearers.

After completion of the ophthalmic examination, qualified subjects received the test material and were instructed to use the test material twice daily for 4 weeks, according to the following directions:

Instructions:

Discontinue the use of your current eye cream/treatment and use only the test material provided for the duration of this trial. You are permitted to use your own makeup products for the duration of this trial. Do not introduce any new cleansing products, moisturizers or other cosmetics during the trial interval.

Contact wearers, please wear your contacts on examination days. Do not wear eye makeup to Testing Facility visits.

Usage Directions:

Twice a day (morning and evening). Apply the test material at eye contour, excluding eyelids, as much as necessary, under normal conditions of use: on clean and dry skin, by slight massages until complete penetration.

Applications must be recorded on the daily diary.

Keep out of reach of children. Do not let anyone else use the test material.

Methodology (continued):

Report any adverse reactions or problems immediately to the Testing Facility staff.

To document compliance, subjects were required to maintain a daily diary to record each use.

A comprehensive ocular examination, as previously described, was conducted for each subject after 4 weeks of test material usage.

All unused test material and daily diaries were returned to the Testing Facility at the final visit.

Daily diaries were reviewed for completeness, prior to dismissal of the subjects.

Amendments: There were no amendments.

Deviations: There were no deviations.

Adverse Events: There were no adverse events.

Results: All ophthalmologic examinations remained within normal limits throughout the test interval.

Subject demographics are presented in Table 1.

All ophthalmological examination Case Report Forms and daily diaries are provided under separate cover.

Summary: Under the conditions of this trial, test material, Eye Cream - [redacted] did not indicate a potential for ophthalmologic irritation. This test material can be considered safe for use by both contact and non-contact lens wearers, as well as individuals with normal or self-perceived sensitive eyes.

Table 1

Subject Demographics

Subject Number	Initials	Age	Contact Lens	Eye Sensitivity
1	JRW	62	Non	No
2	LLR	46	Non	No
3	A-C	20	Soft	Yes
4	M-H	63	Non	Yes
5	LLM	24	Non	No
6	J-N	27	Non	No
7	R-A	42	Soft	Yes
8	KSC	59	Non	Yes
9	BRK	53	Soft	Yes
10	C-S	65	Non	Yes
11	AMA	23	Soft	Yes
12	A-M	60	Soft	Yes
13	MEH	62	Soft	Yes
14	DLT	52	Non	Yes
15	C-D	50	Soft	No
16	CAR	37	Soft	Yes
17	TAB	24	Non	No
18	NKK	56	Soft	Yes
19	R-B	50	Soft	Yes
20	EMB	21	Soft	Yes
21	PJB	42	Soft	No
22	LSC	63	Non	No
23	LMM	51	Non	No
24	DAV	47	Soft	Yes
25	A-A	61	Non	Yes
26	A-F	42	Soft	No
27	V-B	21	Non	Yes
28	S-O	54	Non	No
29	T-Z	50	Non	No
30	JID	52	Non	No
31	LMC	51	Non	No
32	HES	18	Non	Yes
33	ECC	37	Non	No

Did Not Complete: Subject #'s 16 and 31

Consumer Product Testing Co.

ESE 1075

FINAL REPORT

CLIENT: [redacted]

ATTENTION: [redacted]

TEST: Repeated Insult Patch Test
Protocol No.: [redacted]

TEST MATERIAL: EYE CREAM-[redacted]
containing 0.076% Sargassum Muticum Extract

EXPERIMENT REFERENCE NUMBER: [redacted]

Reviewed by: Richard R. Eisenberg, M.D.
Medical Director
Board Certified Dermatologist

Approved by: Michael Caswell, Ph.D., CCRA, CCRC
Vice President, Clinical Evaluations
05 Sept 2014

Approved by: Joy Frank, R.N.
Executive Vice President, Clinical Evaluations
9/5/14

70 New Dutch Lane • Fairfield, New Jersey 07004-2514 • (973) 808-7111 • Fax (973) 808-7234

Consumer Product Testing Co.

Est. 1975

QUALITY ASSURANCE UNIT STATEMENT

Study Number: [redacted]

The Consumer Product Testing Company, Incorporated (CPTC) Quality Assurance Unit (QAU) is responsible for auditing the conduct, content and reporting of all clinical trials that are conducted at CPTC.

This trial has been conducted in accordance with the Declaration of Helsinki, the ICH Guideline E6 for *Good Clinical Practice*, the requirements of 21 CFR Parts 50 and 56, other applicable laws and regulations, CPTC Standard Operating Procedures, and the approved protocol.

The CPTC QAU has reviewed all data, records, and documents relating to this trial and also this Final Report. The following QAU representative signature certifies that all data, records, and documents relating to this trial and also this Final Report have been reviewed and are deemed to be acceptable, and that the trial conforms to all of the requirements as indicated above.

All records and documents pertaining to the conduct of this trial shall be retained in the CPTC archives for a minimum of ten (10) years. At any time prior to the completion of the tenth archival year, a Sponsor may submit a written request to the CPTC QAU to obtain custody of trial records once the CPTC archive period has been completed. This transfer shall be performed at the Sponsor's expense. In the absence of a written request, trial-related records shall be destroyed at the end of the CPTC archive period in a manner that renders them useless.

William Cavaliere
Quality Assurance Representative

9/9/14
Date

70 New Dutch Lane • Fairfield, New Jersey 07004-2514 • (973) 808-7111 • Fax (973) 808-7234
Clinical • Toxicology • Analytical Chemistry • Microbiology

Objective: To determine by repetitive epidermal contact the potential of a test material to induce primary or cumulative irritation and/or allergic contact sensitization.

Participants: One hundred fourteen (114) qualified subjects, male and female, ranging in age from 16 to 74 years, were selected for this evaluation. One hundred three (103) subjects completed this study. The remaining subjects discontinued their participation for various reasons, none of which were related to the application of the test material.

Inclusion Criteria:

a. Male and female subjects, age 16[a] to 79 years.
b. Absence of any visible skin disease which might be confused with a skin reaction from the test material.
c. Prohibition of use of topical or systemic steroids and/or antihistamines for at least seven days prior to study initiation.
d. Completion of a Medical History form and the understanding and signing of an Informed Consent form.
e. Considered reliable and capable of following directions.

Exclusion Criteria:

a. Ill health.
b. Under a doctor's care or taking medication(s) which could influence the outcome of the study.
c. Females who are pregnant or nursing.
d. A history of adverse reactions to cosmetics or other personal care products.

Test Material: EYE CREAM-[redacted]

Study Schedule:

Panel #	Initiation Date	Completion Date
20140276	July 21, 2014	August 28, 2014
20140277	July 21, 2014	August 29, 2014

[a]With parental or guardian consent

Methodology:

The upper back between the scapulae served as the treatment area. Approximately 0.2 g of the test material, or an amount sufficient to cover the contact surface, was applied to the 1" x 1" absorbent pad portion of a clear adhesive dressing. This was then applied to the appropriate treatment site to form a semi-occlusive patch.

Induction Phase:

Patches were applied three (3) times per week (e.g., Monday, Wednesday, and Friday) for a total of nine (9) applications. The site was marked to ensure the continuity of patch application. Following supervised removal and scoring of the first Induction patch, participants were instructed to remove all subsequent Induction patches at home, twenty-four hours after application. The evaluation of this site was made again just prior to re-application. If a participant was unable to report for an assigned test day, one (1) makeup day was permitted. This day was added to the Induction period.

With the exception of the first supervised Induction Patch reading, if any test site exhibited a moderate (2-level) reaction during the Induction Phase, application was moved to an adjacent area. Applications were discontinued for the remainder of this test phase, if a moderate (2-level) reaction was observed on this new test site. Applications would also be discontinued if marked (3-level) or severe (4-level) reactivity was noted.

Rest periods consisted of twenty-four hours following each Tuesday and Thursday removal, and forty-eight hours following each Saturday removal.

Challenge Phase:

Approximately two (2) weeks after the final Induction patch application, a Challenge patch was applied to a virgin test site adjacent to the original Induction patch site, following the same procedure described for Induction. The patch was removed and the site scored at the clinic twenty-four and seventy-two hours post-application.

Methodology (continued):

Evaluation Criteria (Erythema and additional Dermal Sequelae):

0	=	No visible skin reaction	E	=	Edema
0.5	=	Barely perceptible	D	=	Dryness
1	=	Mild	S	=	Staining
2	=	Moderate	P	=	Papules
3	=	Marked	V	=	Vesicles
4	=	Severe	B	=	Bullae
			U	=	Ulceration
			Sp	=	Spreading

Erythema was scored numerically according to this key. If present, additional Dermal Sequelae were indicated by the appropriate letter code and a numerical value for severity.

Adverse Events:

Subject #16, Panel 20140277, experienced overall body pain due to an automobile accident; an examination revealed bruising due to the activation of the air bag.

Subject #17, Panel 20140277, experienced back pain due to an automobile accident; however, x-rays of her back and left knee were negative. Areas were bruised.

Subject #54, Panel 20140277, experienced chest pain on July 23, 2014; however, on July 24, 2014 she reported that she was feeling better and did not seek medical attention.

It was the Principal Investigator's opinion that these occurrences were unlikely related to the test material.

Amendments:

There were no amendments.

Deviations:

There were no deviations.

Results:

The results of each participant are appended (Table 1).

Observations remained negative throughout the test interval.

Subject demographics are presented in Table 2.

Summary:

Under the conditions of this study, test material, EYE CREAM-[redacted] did not indicate a potential for dermal irritation or allergic contact sensitization.

Table 1
Panel #20140276

Individual Results

EYE CREAM-[redacted]

Subject Number	24*hr	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site 24*hr	72 hr
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	----------DID NOT COMPLETE STUDY----------						
11	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0	0
16	----------DID NOT COMPLETE STUDY----------											
17	0	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0	0	0	0	0
21	0	0	0	0	0	0	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0	0	0	0	0
25	0	0	0	0	0	0	0	0	0	0	0	0
26	0	0	0	0	0	0	0	0	0	0	0	0
27	0	0	0	0	0	0	0	0	0	0	0	0
28	0	0	0	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0	0	0	0	0

24* = Supervised removal of 1st Induction and Challenge Patch

Table 1
(continued)
Panel #20140276

Individual Results

EYE CREAM-[redacted]

Subject Number	24*hr	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site 24*hr	72 hr
30	0	0	0	0	0	0	0	0	0	0	0	0
31	0	0	0	0	0	0	0	0	0	0	0	0
32	0	0	DID NOT COMPLETE STUDY									
33	0	0	0	0	0	0	0	0	0	0	0	0
34	0	0	0	0	0	0	0	0	0	0	0	0
35	0	0	0	0	0	0	0	0	0	0	0	0
36	0	0	0	DID NOT COMPLETE STUDY								
37	DID NOT COMPLETE STUDY											
38	0	0	0	0	0	0	0	0	0	0	0	0
39	0	0	0	0	0	0	0	0	0	0	0	0
40	0	0	0	0	0	0	0	DID NOT COMPLETE STUDY				
41	0	0	0	0	0	0	0	0	0	0	0	0
42	0	0	0	0	0	0	0	0	0	0	0	0
43	DID NOT COMPLETE STUDY											
44	0	0	0	0	0	0	0	0	0	0	0	0
45	0	0	0	0	0	0	0	0	0	0	0	0
46	0	0	0	0	0	0	0	0	0	0	0	0
47	0	0	0	0	0	0	0	0	0	0	0	0
48	0	0	0	0	0	0	0	0	0	0	0	0
49	0	0	0	0	0	0	0	0	0	0	0	0
50	0	0	0	0	0	0	0	0	0	0	0	0
51	0	0	0	0	0	0	0	0	0	0	0	0
52	0	0	0	0	0	0	0	0	0	0	0	0
53	0	0	0	0	0	0	0	0	0	0	0	0
54	0	0	0	0	0	0	0	0	0	0	0	0
55	0	0	0	0	0	0	0	0	0	0	0	0
56	0	0	0	0	0	0	0	0	0	0	0	0
57	0	0	0	0	0	0	0	0	0	0	0	0

24* = Supervised removal of 1st Induction and Challenge Patch

Table 1
Panel #20140277

Individual Results

EYE CREAM-[redacted]

Subject Number	24*hr	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site 24*hr	72 hr
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	----------DID NOT COMPLETE STUDY----------						
15	0	0	0	0[m]	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0	0	0	0	0
21	0	0	0	0	0	0	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0	0	0	0	0
25	----------DID NOT COMPLETE STUDY----------											
26	0	0	0	0	0	0	0	0	0	0	0	0
27	0	0	0	0	0	0	0	0	0	0	0	0
28	0	0	0	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0	0	0	0	0

24* = Supervised removal of 1st Induction and Challenge Patch
m = Additional makeup day granted at the discretion of the clinic supervisor

Table 1
(continued)
Panel #20140277

Individual Results

EYE CREAM-[redacted]

Subject Number	24*hr	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site 24*hr	72 hr
30	0	0	0	0	0	0	0	0	0	0	0	0
31	0	0	0	0	0	0	0	0	0	0	0	0
32	0	0	0	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0	0	0
34	0	0	0	0	0	0	0	0	0	0	0	0
35	0	0	0	0	0	0	0	0	0	0	0	0
36	0	0	0	0	0	0	0	0	0	0	0	0
37	0	0	0	0	0	0	0	0	0	0	0	0
38	0	0	0	0	0	0	0	0	0	0	0	0
39	0	0	0	0	0	0	0	0	0	0	0	0
40	0	0	0	0	0	0	0	0	0	0	0	0
41	0	0	0	0	0	0	0	0	0	0	0	0
42	0	0	0	0	0	0	0	0	0	0	0	0
43	0	0	0	0	0	0	0	0	0	0	0	0
44	0	0	0	0	0	0	0	0	0	0	0	0
45	0	0	0	0	0	0	0	0	0	0	0	0
46	0	0	0	0	0	0	0	0	0	0	0	0
47	0	0	0	0	0	0	0	0	0	0	0	0
48	0	0	0	0	0	0	0	0	0	0	0	0
49	0	0	0	0	0	0	0	0	0	0	0	0
50	0	0	0	0	0	0	0	0	0	0	0	0
51	0	0	0	0	0	0	0	0	0	0	0	0
52	0	0	0	0	0	0	0	0	0	0	0	0
53	0	0	0	0	0	0	------DID NOT COMPLETE STUDY----------					
54	0	----------DID NOT COMPLETE STUDY----------										
55	0	0	0	0	0	0	0	0	0	0	0	0
56	0	0	0	0	0	0	0	0	0	0	0	0
57	0	0	0	0	0	0	0	0	0	0	0	0

24* = Supervised removal of 1st Induction and Challenge Patch

Table 2
Panel #20140276

Subject Demographics

Subject Number	Initials	Age	Gender
1	J-M	69	F
2	LOF	63	M
3	C-W	54	F
4	GVW	43	F
5	RDH	63	M
6	M-B	62	F
7	JAO	57	M
8	BPJ	22	F
9	SCF	44	F
10	SAM	41	F
11	D-V	60	F
12	J-J	44	F
13	J-O	45	F
14	PJM	58	M
15	CAC	65	M
16	SAF	62	M
17	SGF	59	M
18	HAH	53	F
19	RWS	56	M
20	TAP	46	F
21	C-V	67	F
22	JPP	60	M
23	D-C	45	F
24	J-M	18	M
25	LVT	35	F
26	AWW	65	M
27	WJS	49	F
28	JGC	57	M
29	G-Z	44	F

Table 2
(continued)
Panel #20140276

Subject Demographics

Subject Number	Initials	Age	Gender
30	EMJ	35	M
31	SLC	19	F
32	DMS	43	F
33	KAN	59	F
34	MLL	45	F
35	ADB	38	F
36	G-V	41	M
37	RMS	42	F
38	CYB	37	F
39	EAM	52	F
40	DAF	37	F
41	DRH	20	M
42	J-K	57	F
43	JDJ	39	F
44	LPD	53	F
45	G-B	65	F
46	ZIR	34	F
47	EVP	40	F
48	CRB	40	F
49	ADD	37	M
50	LCO	55	F
51	MFC	38	F
52	SLB	64	F
53	JWB	37	M
54	SAS	45	F
55	LMB	54	F
56	RJT	55	F
57	LAC	53	F

Table 2
Panel #20140277

Subject Demographics

Subject Number	Initials	Age	Gender
1	JHB	53	F
2	SHZ	74	M
3	J-C	54	F
4	SEC	62	F
5	NVR	65	M
6	KNS	36	F
7	LKD	68	F
8	M-N	66	F
9	RAC	71	M
10	J-M	16	M
11	KTP	56	F
12	J-B	52	M
13	CAC	40	F
14	JAP	73	F
15	ETW	61	M
16	LRC	44	F
17	EHV	52	F
18	MCV	51	F
19	DLF	54	F
20	F-V	53	M
21	PAD	47	F
22	MMJ	16	F
23	DLT	51	F
24	DRA	57	F
25	R-G	71	F
26	PAB	63	F
27	DAC	60	F
28	SAM	17	F
29	V-C	16	F

Table 2
(continued)
Panel #20140277

Subject Demographics

Subject Number	Initials	Age	Gender
30	LGM	56	F
31	LDS	44	F
32	JLM	21	M
33	MHS	58	M
34	TEH	37	F
35	MCP	43	M
36	LEH	18	F
37	M-P	64	F
38	J-S	37	F
39	ELB	49	F
40	MTZ	25	M
41	DLW	29	M
42	WM	65	F
43	KSC	26	F
44	LRA	22	M
45	KSV	23	F
46	J-O	71	F
47	JAO	72	M
48	CJC	53	M
49	DW	57	M
50	BST	21	F
51	TAM	48	F
52	RBL	56	M
53	JMJ	34	M
54	BEZ	40	F
55	NPM	52	M
56	JAZ	56	M
57	SAR	30	F

Consumer Product Testing Co

FINAL REPORT

CLIENT: [redacted]

ATTENTION: [redacted] Pharm D, PhD.

TEST: Repeated Insult Patch Test
Protocol No.: [redacted]

TEST MATERIAL: Skin Care - [redacted]
containing 0.076% Sargassum Muticum Extract

EXPERIMENT REFERENCE NUMBER: [redacted]

Reviewed by: Richard R. Eisenberg, M.D.
Medical Director
Board Certified Dermatologist

Approved by: Michael Caswell, Ph.D., CCRA, CCRC
Vice President, Clinical Evaluations
24Mar2016

Approved by: Joy Frank, R.N.
Executive Vice President, Clinical Evaluations
3/25/2016 3/25/16

70 New Dutch Lane • Fairfield, New Jersey 07004-2514 • (973) 808-7111 • Fax (973) 808-7234

Consumer Product Testing Co.

QUALITY ASSURANCE UNIT STATEMENT

Study Number: [redacted]

The Consumer Product Testing Company, Incorporated (CPTC) Quality Assurance Unit (QAU) is responsible for auditing the conduct, content and reporting of all clinical trials that are conducted at CPTC.

This trial has been conducted in accordance with the Declaration of Helsinki, the ICH Guideline E6 for *Good Clinical Practice*, the requirements of 21 CFR Parts 50 and 56, other applicable laws and regulations, CPTC Standard Operating Procedures, and the approved protocol.

The CPTC QAU has reviewed all data, records, and documents relating to this trial and also this Final Report. The following QAU representative signature certifies that all data, records, and documents relating to this trial and also this Final Report have been reviewed and are deemed to be acceptable, and that the trial conforms to all of the requirements as indicated above.

All records and documents pertaining to the conduct of this trial shall be retained in the CPTC archives for a minimum of ten (10) years. At any time prior to the completion of the tenth archival year, a Sponsor may submit a written request to the CPTC QAU to obtain custody of trial records once the CPTC archive period has been completed. This transfer shall be performed at the Sponsor's expense. In the absence of a written request, trial-related records shall be destroyed at the end of the CPTC archive period in a manner that renders them useless.

William Cavaliere
Quality Assurance Representative

3/28/2016
Date

70 New Dutch Lane • Fairfield, New Jersey 07004-2514 • (973) 808-7111 • Fax (973) 808-7234
Clinical • Toxicology • Analytical Chemistry • Microbiology

Objective: To determine by repetitive epidermal contact the potential of a test material to induce primary or cumulative irritation and/or allergic contact sensitization.

Participants: One hundred twelve (112) qualified subjects, male and female, ranging in age from 18 to 70 years, were selected for this evaluation. One hundred four (104) subjects completed this study. The remaining subjects discontinued their participation for various reasons, none of which were related to the application of the test material.

Inclusion Criteria:

a. Male and female subjects, age 16[a] to 79 years.
b. Absence of any visible skin disease which might be confused with a skin reaction from the test material.
c. Prohibition of use of topical or systemic steroids and/or antihistamines for at least seven days prior to study initiation.
d. Completion of a Medical History form and the understanding and signing of an Informed Consent form.
e. Considered reliable and capable of following directions.

Exclusion Criteria:

a. Ill health.
b. Under a doctor's care or taking medication(s) which could influence the outcome of the study.
c. Females who are pregnant or nursing.
d. A history of adverse reactions to cosmetics or other personal care products.

Test Material: Skin Care - [redacted]

Study Schedule:

Panel #	Initiation Date	Completion Date
20160028	February 8, 2016	March 17, 2016
20160033	February 8, 2016	March 18, 2016

[a]With parental or guardian consent

Methodology:

The upper back between the scapulae served as the treatment area. Approximately 0.2 ml of the test material, or an amount sufficient to cover the contact surface, was applied to the 1" x 1" absorbent pad portion of a clear adhesive dressing. This was then applied to the appropriate treatment site to form a semi-occlusive patch.

Induction Phase:

Patches were applied three (3) times per week (e.g., Monday, Wednesday, and Friday) for a total of nine (9) applications. The site was marked to ensure the continuity of patch application. Following supervised removal and scoring of the first Induction patch, participants were instructed to remove all subsequent Induction patches at home, twenty-four hours after application. The evaluation of this site was made again just prior to re-application. If a participant was unable to report for an assigned test day, one (1) makeup day was permitted. This day was added to the Induction period.

With the exception of the first supervised Induction Patch reading, if any test site exhibited a moderate (2-level) reaction during the Induction Phase, application was moved to an adjacent area. Applications were discontinued for the remainder of this test phase, if a moderate (2-level) reaction was observed on this new test site. Applications would also be discontinued if marked (3-level) or severe (4-level) reactivity was noted.

Rest periods consisted of one day following each Tuesday and Thursday removal, and two days following each Saturday removal.

Challenge Phase:

Approximately two (2) weeks after the final Induction patch application, a Challenge patch was applied to a virgin test site adjacent to the original Induction patch site, following the same procedure described for Induction. The patch was removed and the site scored at the clinic Day 1 and Day 3 post-application.

Methodology (continued):

Evaluation Criteria (Erythema and additional Dermal Sequelae):

0	=	No visible skin reaction	E	=	Edema
0.5	=	Barely perceptible	D	=	Dryness
1	=	Mild	S	=	Staining
2	=	Moderate	P	=	Papules
3	=	Marked	V	=	Vesicles
4	=	Severe	B	=	Bullae
			U	=	Ulceration
			Sp	=	Spreading

Erythema was scored numerically according to this key. If present, additional Dermal Sequelae were indicated by the appropriate letter code and a numerical value for severity.

Adverse Events: There were no adverse events.

Amendments: There were no amendments.

Deviations: Subject #37, Panel 20160033, reported to the Testing Facility on Day 1 post challenge application without her patches. She had removed the patches in error and was repatched. It was the Principal Investigator's opinion that this occurrence would have no impact on final results since the challenge patch procedure was repeated.

Results: The results of each participant are appended (Table 1).

Observations remained negative throughout the test interval.

Subject demographics are presented in Table 2.

Summary: Under the conditions of this study, test material, Skin Care - [redacted] indicated no potential for dermal irritation or allergic contact sensitization.

Table 1
Panel #20160028

Individual Results

Skin Care - [redacted]

Subject Number	Day 1*	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site Day 1*	Day 3
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	DID NOT COMPLETE STUDY							
14	0	0	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0	0	0	0	0
21	0	0	0	0	0	0	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0	0	0	0	0
25	0	0	0	0	0	0	0	0	0	0	0	0
26	0	0	DID NOT COMPLETE STUDY									
27	0	0	0	0	0	0	0	0	0	0	0	0
28	0	0	0	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0	0	0	0	0

Day 1* = Supervised removal

Table 1
(continued)
Panel #20160028

Individual Results

Skin Care - [redacted]

Subject Number	Day 1*	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site Day 1*	Day 3
30	0	0	0	0	0	0	0	0	0	0	0	0
31	0	0	0	0	0	0	0	0	0	0	0	0
32	0	0	0	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0	0	0
34	0	0	0	0	0	0	0	0	0	0	0	0
35	0	0	0	0	0	0	0	0	0	0	0	0
36	0	0	0	0	0	0	0	0	0	0	0	0
37	0	0	0	0	0	0	0	0	0	0	0	0
38	0	0	0	0	0	0	0	0	0	0	0	0
39	0	0	0	0	0	0	0	0	0	0	0	0
40	0	0	0	0	0	0	0	0	0	0	0	0
41	0	0	0	0	0	0	0	0	0	0	0	0
42	0	----------DID NOT COMPLETE STUDY----------										
43	0	----------DID NOT COMPLETE STUDY----------										
44	0	0	0	0	0	0	0	0	0	0	0	0
45	0	0	0	0	0	0	0	0	0	0	0	0
46	0	0	0	0	0	0	0	0	0	0	0	0
47	0	0	0	0	0	0	0	0	0	0	0	0
48	0	0	0	0	0	0	0	0	0	0	0	0
49	0	0	0	0	0	0	0	0	0	0	0	0
50	----------DID NOT COMPLETE STUDY----------											
51	0	0	0	0	0	0	0	0	0	0	0	0
52	0	0	0	0	0	0	0	0	0	0	0	0
53	0	0	0	0	0	0	0	0	0	0	0	0
54	0	0	0	0	0	0	0	0	0	0	0	0
55	0	0	0	0	0	0	0	0	0	0	0	0
56	0	0	0	0	0	0	0	0	0	0	0	0

Day 1* = Supervised removal

Table 1
(continued)
Panel #20160033

Individual Results

Skin Care - [redacted]

Subject Number	Day 1*	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site Day 1*	Day 3
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0	0	0	0	0
21	0	0	0	0	0	0	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0	0	0	0	0
25	0	0	0	0	0	0	0	0	0	0	0	0
26	0	0	0	0	0	0	0	0	0	0	0	0
27	0	0	0	0	0	0	0	0	0	0	0	0
28	0	0	0	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0	0	0	0	0

Day 1* = Supervised removal

Table 1
(continued)
Panel #20160033

Individual Results

Skin Care - [redacted]

Subject Number	Induction Phase									Virgin Challenge Site	
	Day 1*	1	2	3	4	5	6	7	8	9	Day 1*	Day 3
30	0	0	0	0	0	0	0	0	0	0	0	0
31	0	0	0	0	0	0	0	0	0	0	0	0
32	0	0	0	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0	0	0
34	0	0	0	DID NOT COMPLETE STUDY								
35	0	0	0	0	0	0	0	0	0	0	0	0
36	0	0	0	DID NOT COMPLETE STUDY								
37	0	0	0	0	0	0	0	0	0	0	0	0
38	0	0	0	0	0	0	0	0	0	0	0	0
39	0	0	0	0	0	0	0	0	0	0	0	0
40	0	0	0	0	0	0	0	0	0	0	0	0
41	0	0	0	0	0	0	0	0	0	0	0	0
42	0	0	0	0	0	0	0	0	0	0	0	0
43	DID NOT COMPLETE STUDY											
44	0	0	0	0	0	0	0	0	0	0	0	0
45	0	0	0	0	0	0	0	0	0	0	0	0
46	0	0	0	0	0	0	0	0	0	0	0	0
47	0	0	0	0	0	0	0	0	0	0	0	0
48	0	0	0	0	0	0	0	0	0	0	0	0
49	0	0	0	0	0	0	0	0	0	0	0	0
50	0	0	0	0	0	0	0	0	0	0	0	0
51	0	0	0	0	0	0	0	0	0	0	0	0
52	0	0	0	0	0	0	0	0	0	0	0	0
53	0	0	0	0	0	0	0	0	0	0	0	0
54	0	0	0	0	0	0	0	0	0	0	0	0
55	0	0	0	0	0	0	0	0	0	0	0	0
56	0	0	0	0	0	0	0	0	0	0	0	0

Day 1* = Supervised removal

Table 2
Panel #20160028

Subject Demographics

Subject Number	Initials	Age	Gender
1	R-B	63	F
2	PLL	26	M
3	SEM	30	F
4	RRC	51	M
5	ASK	26	F
6	TAK	44	F
7	C-P	18	F
8	CAG	25	F
9	NJN	24	M
10	KPD	42	F
11	VMB	62	F
12	JCC	67	F
13	BJR	20	F
14	JLM	40	F
15	G-V	42	F
16	DEG	61	F
17	DJB	44	M
18	BMM	51	F
19	VDS	47	F
20	RDP	42	M
21	WAM	47	F
22	SAD	37	F
23	GKV	57	F
24	VGC	44	F
25	ALP	59	F
26	G-V	52	F
27	ESF	58	F
28	MRM	60	F
29	MEG	69	M

Table 2
(continued)
Panel #20160028

Subject Demographics

Subject Number	Initials	Age	Gender
30	J-O	44	F
31	RNC	52	F
32	SNM	19	F
33	PCR	37	F
34	AFR	37	M
35	GMB	46	F
36	CJW	40	M
37	D-H	18	F
38	IMM	40	F
39	MRS	38	F
40	LSZ	45	F
41	VVL	22	F
42	MMM	20	F
43	KAM	19	F
44	CRD	45	F
45	RAD	42	M
46	DLR	18	F
47	DRR	18	F
48	ECC	39	F
49	W-U	62	M
50	P-S	38	F
51	D-M	64	F
52	BAM	56	F
53	S-H	58	F
54	G-S	56	M
55	CRR	41	F
56	JJP	42	M

Table 2
(continued)
Panel #20160033

Subject Demographics

Subject Number	Initials	Age	Gender
1	SDR	44	F
2	MCO	64	F
3	PJG	69	M
4	RSG	70	F
5	M-W	52	M
6	DAC	30	F
7	M-A	69	M
8	V-G	51	M
9	O-C	53	M
10	SLB	62	F
11	A-S	54	F
12	CLA	42	F
13	N-A	64	F
14	MLO	66	F
15	SMB	35	F
16	AVR	20	F
17	JVL	51	M
18	A-S	48	F
19	E-B	31	F
20	NLB	58	F
21	A-R	66	F
22	EPM	56	F
23	NRH	59	M
24	TLS	44	F
25	MJK	52	M
26	JAM	54	F
27	LSH	50	F
28	M-R	59	M
29	MAG	69	M

Table 2
(continued)
Panel #20160033

Subject Demographics

Subject Number	Initials	Age	Gender
30	LDP	68	F
31	I-T	69	F
32	R-B	51	F
33	FCM	24	M
34	L-V	19	F
35	E-V	50	F
36	E-G	21	M
37	VAO	25	F
38	DLB	41	F
39	HDK	49	F
40	A-R	46	F
41	K-N	46	F
42	BML	68	F
43	D-S	18	M
44	J-S	40	F
45	KJM	52	M
46	CPL	68	F
47	RBC	49	F
48	LAT	52	F
49	PAB	46	F
50	SNB	36	F
51	PED	45	M
52	P-D	45	F
53	NAD	18	F
54	JNC	34	F
55	EHB	70	F
56	DAG	50	F

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 20, 2018

SUBJECT: Alaria Esculenta Extract

Consumer Product Testing Co. 2013. Repeated insult patch test - night moisturizer containing 0.05% Alaria Esculenta Extract.

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

Consumer Product Testing Co.

FINAL REPORT

CLIENT: [redacted]

ATTENTION: [redacted]

TEST: Repeated Insult Patch Test
Protocol No.: [redacted]

TEST MATERIAL: NIGHT MOISTURIZER- [redacted]
containing 0.05% Alaria Esculenta Extract

EXPERIMENT REFERENCE NUMBER: [redacted]

Reviewed by: Richard R. Eisenberg, M.D.
Medical Director
Board Certified Dermatologist

Approved by: Michael Caswell, Ph.D., CCRA, CCRC
Vice President, Clinical Evaluations
05 Jun 2013

Approved by: Joy Frank, R.N.
Executive Vice President, Clinical Evaluations
6/6/13

70 New Dutch Lane • Fairfield, New Jersey 07004-2514 • (973) 808-7111 • Fax (973) 808-7234

Consumer Product Testing Co.

QUALITY ASSURANCE UNIT STATEMENT

Study Number: [redacted]

The Consumer Product Testing Company, Incorporated (CPTC) Quality Assurance Unit (QAU) is responsible for auditing the conduct, content and reporting of all clinical trials that are conducted at CPTC.

This trial has been conducted in accordance with the Declaration of Helsinki, the ICH Guideline E6 for *Good Clinical Practice*, the requirements of 21 CFR Parts 50 and 56, other applicable laws and regulations, CPTC Standard Operating Procedures, and the approved protocol.

The CPTC QAU has reviewed all data, records, and documents relating to this trial and also this Final Report. The following QAU representative signature certifies that all data, records, and documents relating to this trial and also this Final Report have been reviewed and are deemed to be acceptable, and that the trial conforms to all of the requirements as indicated above.

All records and documents pertaining to the conduct of this trial shall be retained in the CPTC archives for a minimum of ten (10) years. At any time prior to the completion of the tenth archival year, a Sponsor may submit a written request to the CPTC QAU to obtain custody of trial records once the CPTC archive period has been completed. This transfer shall be performed at the Sponsor's expense. In the absence of a written request, trial-related records shall be destroyed at the end of the CPTC archive period in a manner that renders them useless.

Quality Assurance Representative

6/7/13
Date

70 New Dutch Lane • Fairfield, New Jersey 07004-2514 • (973) 808-7111 • Fax (973) 808-7234
Clinical • Toxicology • Analytical Chemistry • Microbiology

Objective: To determine by repetitive epidermal contact the potential of a test material to induce primary or cumulative irritation and/or allergic contact sensitization.

Participants: One hundred thirteen (113) qualified subjects, male and female, ranging in age from 19 to 70 years, were selected for this evaluation. One hundred five (105) subjects completed this study. The remaining subjects discontinued their participation for various reasons, none of which were related to the application of the test material.

Inclusion Criteria:

a. Male and female subjects, age 16[a] and over.
b. Absence of any visible skin disease which might be confused with a skin reaction from the test material.
c. Prohibition of use of topical or systemic steroids and/or antihistamines for at least seven days prior to study initiation.
d. Completion of a Medical History form and the understanding and signing of an Informed Consent form.
e. Considered reliable and capable of following directions.

Exclusion Criteria:

a. Ill health.
b. Under a doctor's care or taking medication(s) which could influence the outcome of the study.
c. Females who are pregnant or nursing.
d. A history of adverse reactions to cosmetics or other personal care products.

Test Material: NIGHT MOISTURIZER- [redacted]

Study Schedule:

Panel #	Initiation Date	Completion Date
20130141	April 15, 2013	May 23, 2013
20130145	April 22, 2013	May 31, 2013

[a]With parental or guardian consent

Methodology:

The upper back between the scapulae served as the treatment area. Approximately 0.2 g of the test material, or an amount sufficient to cover the contact surface, was applied to the 1" x 1" absorbent pad portion of a clear adhesive dressing. This was then applied to the appropriate treatment site to form a semi-occlusive patch.

Induction Phase:

Patches were applied three (3) times per week (e.g., Monday, Wednesday, and Friday) for a total of nine (9) applications. The site was marked to ensure the continuity of patch application. Following supervised removal and scoring of the first Induction patch, participants were instructed to remove all subsequent Induction patches at home, twenty-four hours after application. The evaluation of this site was made again just prior to re-application. If a participant was unable to report for an assigned test day, one (1) makeup day was permitted. This day was added to the Induction period.

With the exception of the first supervised Induction Patch reading, if any test site exhibited a moderate (2-level) reaction during the Induction Phase, application was moved to an adjacent area. Applications were discontinued for the remainder of this test phase, if a moderate (2-level) reaction was observed on this new test site. Applications would also be discontinued if marked (3-level) or severe (4-level) reactivity was noted.

Rest periods consisted of twenty-four hours following each Tuesday and Thursday removal, and forty-eight hours following each Saturday removal.

Challenge Phase:

Approximately two (2) weeks after the final Induction patch application, a Challenge patch was applied to a virgin test site adjacent to the original Induction patch site, following the same procedure described for Induction. The patch was removed and the site scored at the clinic twenty-four and seventy-two hours post-application.

Methodology (continued):

Evaluation Criteria (Erythema and additional Dermal Sequelae):

0	=	No visible skin reaction	E	=	Edema
0.5	=	Barely perceptible	D	=	Dryness
1	=	Mild	S	=	Staining
2	=	Moderate	P	=	Papules
3	=	Marked	V	=	Vesicles
4	=	Severe	B	=	Bullae
			U	=	Ulceration
			Sp	=	Spreading

Erythema was scored numerically according to this key. If present, additional Dermal Sequelae were indicated by the appropriate letter code and a numerical value for severity.

Adverse Events: There were no adverse events.

Amendments: There were no amendments.

Deviations: There were no deviations.

Results: The results of each participant are appended (Table 1).

Observations remained within normal limits throughout the test interval.

Subject demographics are presented in Table 2.

Summary: Under the conditions of this study, test material, NIGHT MOISTURIZER-[redacted] did not indicate a potential for dermal irritation or allergic contact sensitization.

Table 1
Panel #20130141

Individual Results

NIGHT MOISTURIZER- [redacted]

Subject Number	24*hr	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site 24*hr	72 hr
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	----------DID NOT COMPLETE STUDY----------					
6	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	----------DID NOT COMPLETE STUDY----------									
11	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0	0	0	0	0
21	0	0	0	0	0	0	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0	0	0	0	0
25	0	0	0	0	0	0	0	0	0	0	0	0
26	0	0	0	0	0	0	0	0	0	0	0	0
27	0	0	0	0	0	0	0	0	0	0	0	0
28	0	0	0	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0	0	0	0	0

24* = Supervised removal of 1st Induction and Challenge Patch

Table 1
(continued)
Panel #20130141

Individual Results

NIGHT MOISTURIZER-[redacted]

Subject Number	24*hr	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site 24*hr	72 hr
30	0	0	0	0	0	0	0	0	0	0	0	0
31	0	0	0	0	0	----------DID NOT COMPLETE STUDY----------						
32	0	0	0	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0	0	0
34	0	0	0	0	0	0	0	0	0	0	0	0
35	0	0	0	0	0	0	0	0	0	0	0	0
36	0	0.5	0.5	0	0.5	0	0	0	0	0	0	0
37	0	0	0	0	0	0	0	0	0	0	0	0
38	0	0	0	0	0	0	0	0	0	0	0	0
39	0	0	0	0	0	0	0	0	0	0	0	0
40	0	0	0	0	0	0	0	0	0	0	0	0
41	0	0	0	0	0	0	0	0	0	0	0	0
42	0	0	0	0	0	0	0	0	0	0	0	0
43	0	0	0	0	0	0	0	0	0	0	0	0
44	0	0	0	0	0	0	0	0	0	0	0	0
45	0	0	0	0	0	0	0	0	0	0	0	0
46	0	0	0	0	0	0	0	0	0	0	0	0
47	0	0	0	0	0	0	0	0	0	0	0	0
48	0	0	0	0	0	0	0	0	0	0	0	0
49	0	0	0	0	0	0	0	0	0	0	0	0
50	0	0	0	0	0	0	0	0	0	0	0	0
51	0	0	0	0	0	0	0	0	0	0	0	0
52	0	0	0	0	0	0	0	0	0	0	0	0
53	0	0	0	0	0[m]	0	0	0	0	0	0	0
54	0	0	0	0	0	0	0	0	0	0	0	0
55	0	0	0	0	0	0	0	0	0	0	0	0
56	0	0	0	0	0	0	0	0	0	0	0	0

24* = Supervised removal of 1st Induction and Challenge Patch
m = Additional makeup day granted at the discretion of the clinic supervisor

Table 1
(continued)
Panel #20130145

Individual Results

NIGHT MOISTURIZER- [redacted]

Subject Number	24*hr	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site 24*hr	72 hr
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	----------DID NOT COMPLETE STUDY---------					
6	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0	0
11	-	0	0	0	0	0	0	0	0	0	0	0
12	-	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0	0	0	0	0
20	----------DID NOT COMPLETE STUDY----------											
21	-	0	0	0	0	0	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0	0	0	0	0
25	0	0	0	0	0	0	0	0	0	0	0	0
26	-	0	0	----------DID NOT COMPLETE STUDY----------								
27	0	0	0	0	0	0	0	0	0	0	0	0
28	0	0	0	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0	0	0	0	0

24* = Supervised removal of 1st Induction and Challenge Patch
- = Subject not present for supervised removal

[redacted]

Table 1
(continued)
Panel #20130145

Individual Results

NIGHT MOISTURIZER-[redacted]

Subject Number	24*hr	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site 24*hr	72 hr
30	DID NOT COMPLETE STUDY											
31	0	0	0	0	0	0	0	0	0	0	0	0
32	0	0	0	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0	0	0
34	0	0	0	0	0	0	0	0	0	0	0	0
35	0	0	0	0	0	0	0	0	0	0	0	0
36	0	0	0	0	0	0	0	0	0	0	0	0
37	0	0	0	0	0	0	0	0	0	0	0	0
38	0	0	0	0	0	0	0	0	0	0	0	0
39	0	0	0	0	0	0	0	0	0	0	0	0
40	0	0	0	0	0	0	0	0	0	0	0	0
41	0	0	0	0	0	0	0	0	0	0	0	0
42	0	0	0	0	0	0	0	0	0	0	0	0
43	0	0	0	0	0	0	0	0	0	0	0	0
44	0	0	0	0	0	0	0	0	0	0	0	0
45	0	0	0	0	0	0	0	0	0	0	0	0
46	0	0	0	0	0	0	0	0	0	0	0	0
47	0	0	0	0	0	0	0	0	DID NOT COMPLETE STUDY			
48	-	0	0	0	0	0	0	0	0	0	0	0
49	0	0	0	0	0	0	0	0	0	0	0	0
50	0	0	0	0	0	0	0	0	0	0	0	0
51	0	0	0	0	0	0	0	0	0	0	0	0
52	0	0	0	0	0	0	0	0	0	0	0	0
53	0	0	0	0	0	0	0	0	0	0	0	0
54	0	0	0	0	0	0	0	0	0	0	0	0
55	0	0	0	0	0	0	0	0	0	0	0	0
56	0	0	0	0	0	0	0	0	0	0	0	0
57	0	0	0	0	0	0	0	0	0	0	0	0

24* = Supervised removal of 1st Induction and Challenge Patch
- = Subject not present for supervised removal

Table 2
Panel #20130141

Subject Demographics

Subject Number	Initials	Age	Sex
1	JFH	44	M
2	AMC	35	F
3	AJC	30	F
4	CJC	52	M
5	JLV	41	F
6	DMD	53	F
7	DPB	65	M
8	H-B	54	M
9	SEV	68	F
10	JAT	48	M
11	ADC	39	M
12	M-Z	51	F
13	L-W	47	M
14	MRH	22	F
15	M-D	54	F
16	A-M	47	M
17	RAD	41	M
18	D-M	46	F
19	C-S	45	F
20	LAK	48	F
21	PVO	41	F
22	NHB	45	F
23	LMO	46	F
24	NLJ	57	F
25	RVD	55	M
26	E-M	54	F
27	ELM	32	F
28	PGH	48	F
29	QLD	33	F

Table 2
(continued)
Panel #20130141

Subject Demographics

Subject Number	Initials	Age	Sex
30	JGM	50	F
31	R-M	28	M
32	DPC	57	F
33	D-R	61	F
34	MAE	46	M
35	MSL	60	F
36	DWM	52	M
37	CPW	57	M
38	B-C	49	F
39	SCF	43	F
40	RDF	44	M
41	EAS	58	F
42	MEP	70	F
43	J-B	52	M
44	MPF	52	M
45	L-C	57	M
46	JMN	54	F
47	JMC	25	F
48	MLA	55	F
49	DMJ	47	F
50	JFK	69	F
51	L-H	25	F
52	BWC	52	M
53	SAM	19	M
54	BJS	43	F
55	D-N	27	F
56	DSP	41	F

Table 2
(continued)
Panel #20130145

Subject Demographics

Subject Number	Initials	Age	Sex
1	AMS	66	M
2	H-H	52	M
3	JJR	23	F
4	DMR	62	F
5	SLR	31	F
6	T-H	35	F
7	ISM	22	F
8	E-W	47	F
9	MTR	52	F
10	M-G	67	F
11	CSG	26	F
12	MAM	36	F
13	RLA	44	M
14	LMP	61	F
15	L-R	45	F
16	YYM	31	F
17	SAR	37	F
18	LAM	47	F
19	DMB	42	F
20	SMR	33	F
21	SAM	43	M
22	L-F	65	F
23	R-F	67	M
24	SKC	28	F
25	AMR	23	F
26	BMJ	28	M
27	MYS	34	M
28	E-B	65	F
29	NMD	27	F

Table 2
(continued)
Panel #20130145

Subject Demographics

Subject Number	Initials	Age	Sex
30	UPP	62	F
31	DAW	48	F
32	EJG	22	M
33	L-S	39	F
34	BWP	53	M
35	BLA	59	F
36	RLS	56	F
37	SMH	51	F
38	M-C	48	F
39	S-R	53	F
40	DSP	21	F
41	C-S	28	F
42	TOK	28	M
43	E-B	43	F
44	S-K	57	F
45	SLK	34	F
46	DVJ	40	F
47	JEJ	29	M
48	LDS	27	F
49	A-A	61	F
50	DRB	69	M
51	LCO	54	F
52	E-F	38	F
53	A-S	45	M
54	M-D	43	M
55	A-G	48	M
56	EAS	20	M
57	GJG	49	M

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: August 13, 2018

SUBJECT: Scientific Literature Review: Safety Assessment of Brown Algae-Derived Ingredients as Used in Cosmetics (release date: July 26, 2018)

The Council has no suppliers for the following ingredients included in the report on brown algae-derived ingredients:

Durvilleae Antarctica Extract
Laminaria Japonica Powder
Laminaria Longissima Extract
Macrocystis Pyrifera (Kelp) Protein
Sargassum Vulgare Extract

The Council respectfully submits the following comments on the Scientific Literature Review: Safety Assessment of Brown Algae-Derived Ingredients as Used in Cosmetics.

Key Issues

Three ingredients, Asterionellopsis Glacialis Extract, Rissoella Verruculosa Extract and Sahel Scenedesmus Extract do not belong in this report because they are not derived from species of brown algae. Dr. Lena Struwe, Rutgers University was asked if these species were brown algae, her responses are provided below.

Asterionellopsis glacialis: "definitely a diatom and not a brown algae. Diatoms are Bacillariophyta, brown algae are Ochrophyta (in the Algaebase classification). The species name is accepted."

Rissoella verruculosa - "red algae (Rhodophyta). The species name is accepted."

"Brown algae are classified in Algaebase as:

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

Empire Eukaryota
Kingdom Chromista
Phylum Ochrophyta
Class Phaeophyceae
and are in a different phylum from diatoms and red algae, so very distantly related."

Sahel Scenedesmus - "A strain of *Scenedesmus* (a green algae, Chlorophyta) was extracted from Sahel (an African area), and called *Scenedesmus* Sahel strain. The genus name is Scenedesmus, and Sahel is an informal name (not a species name). For INCI this is best listed as "Scenedesmus spp. Sahel strain" or "Scenedesmus spp. Sahel extract". (Spp. indicates that it might be several species, not just one. It can be excluded [as a brown algae] as well. It would be great if the source could provide a species identification for their strain, since there are many (at least 120) species in the genus *Scenedesmus*. It should DEFINITELY not be called "Sahel scenedesmus" in the INCI database. (For the record, there is no genus of any organism named Sahel...)"

As noted above, brown algae are currently considered to be in the Class Phaeophyceae not the phylum Phaeophyta as stated in the Introduction to the CIR report and in Table 3. The Summary says they are in the "class *Phaeophyta*" - it is correct that they are in a class, but the name needs to be corrected to Phaeophyceae.

Although it may be useful for the CIR Expert Panel, the first paragraph of the Algae Identification section and Table 3, Descriptions of the major groups of algae, is not necessary for the brown algae report. If left in the report, Table 3 needs to be corrected. For example, kingdom should be presented before phylum, and both Rhodophyta (red) and Chlorophyta (green) are in the Kingdom Plantae. Another example is that diatoms are now considered to be in the class Bacillariophyceae rather than the phylum Bacillariophyta as stated in the CIR report.

Rather than strictly presenting the ingredient names alphabetically, it would be helpful to add the attached table (Brown Algae Taxonomy for Genuses Included in the CIR Report on Brown Algae-Derived Ingredients) that presents the various genuses included in the report by taxonomic classification. This type of presentation may be helpful to determine whether or not all of the ingredients should be included in one report, or if information on one species can be used to support the safety of another species.

Since brown algae are not in the plant kingdom, in the CIR report they should not be called plants (as in Tables 4 and 6) or "botanicals".

It is not clear why some sections have ingredient named subsections e.g., Irritation, while other sections, e.g., Genotoxicity, do not have ingredient named subsections.

Table 4 - It is not clear why all of the brown algae species included in INCI names are not presented in this table. For example, there is no description of *Asterionellopsis glacialis*.

<u>Additional Considerations</u>

Composition - Please correct the spelling of "xanthophyls"

Impurities/Constituents of Concern - What were the concentrations of phthalates found in *Undaria pinnatifida* and *Laminaria japonica*?

Cosmetic Use - Please state the highest concentration and the product category in which Fucus Vesiculosis was reported to be used.

Short-Term, Subchronic, and Chronic, Oral - What were the effects (increased or decreased) on body weight gain and organ weights in the 13-week rat study of an alcohol extract of *Ecklonia cava*.

Although some reports may have used "alcohol" and other reports "ethanol", it would be helpful to use either alcohol or ethanol throughout the CIR report.

What was the NOEL (or NOAEL) dose in the 3-month rat study of Cladosiphon Okamuranus Extract?

Tumor Promotion, dermal - What was the duration of the study of Undaria Pinnatifida Extract?

Tumor Promotion, Oral - Please correct the spelling of "malondialhehyde"

Estrogenic Effects - As progesterone receptor binding was also studied, it is not clear why this subsection is being called "Estrogenic Effects".

Irritation - As the dose, 0.5 g, is stated, "dose not specified" should be deleted. It should be added that the extract was placed on an area between 12-20 cm^2.

Photoprotection, Summary - What was the concentration of the *Sargassum muticum* extract used in this study? What durations of exposure were used?

Clinical Trials. Oral - Were thyroid-stimulating hormone levels increased or decreased?

It is not necessary to state that the Fucus Vesiculosis powder "increased the menstrual cycle length and reduced the days of menstruation" twice in the same paragraph.

Summary - How many ingredients are in this report? The Introduction says 84, the Summary says 85. If the three ingredients that are not actually brown algae-derived are removed from the report, there are 82 ingredients in this report.

In the Summary, it would be helpful if the highest doses causing no adverse effects were stated.

Please revise the following sentence: "There were increased liver weights in two ethanol Fucus Vesiculosus Extracts (starting at 200 mg/kg/day) administered by gavage for 4 weeks in male, but not female rats." The increased liver weights were seen in rats treated with the extract (not in the extract as currently stated).

Although TPA was used as a promoter, it was not used as a promoter with Undaria Pinnatifida Extract. TPA was a control promoter. This is not clear in the Summary.

Table 1 - Hard returns are needed between Fucus Spiralis Extract and Fucus Vesiculosus, and Macrocystis Pyrifera (Kelp) Juice and Macrocystis Pyrifera (Kelp) Protein.

Table 6 - Please correct "digitate" (to digitata)

Table 21 - Please include the results of the Irwin test (reference 23) in the Results column.

Table 22 - Were reproductive organs examined in the 13-week study of Ecklonia Cava Extract (reference 9)?

Tables 22 and 24, reference 66 - The concentration (1.5 g in 1000 ml distilled water) should be stated in the Dose/Concentration column. The concentration of 1.5 g in 1000 ml is 0.15% not "100% for water" as currently stated in the Dose/Concentration columns of these two tables.

Table 23 - Although the extraction solvent/method may not have been stated, reference 9 indicates that the *Ascophyllum nodosum* extract studied was a fertilizer. This should be stated in Table 23.

Brown Algae Taxonomy for Genuses Included in the CIR Report on Brown Algae-Derived Ingredients*
(all subclasses listed in the table are in the kingdom Chromista, phylum Ochrophyta, class Phaeophyceae)

Subclass	Order	Family	Genus
Dictyotophycidae	Dictyotales	Dictyotaceae	Dictyopteris
Dictyotophycidae	Dictyotales	Dictyotaceae	Dictyota
Dictyotophycidae	Sphacelariales	Sphacelariaceae	Sphacelaria
Dictyotophycidae	Sphacelariales	Stypocaulaceae	Halopteris
Fucophycidae	Ectocarpales	Chordariaceae	Cladosiphon
Fucophycidae	Fucales	Durvillaeaceae	Durvillaea
Fucophycidae	Fucales	Fucaceae	Ascophyllum
Fucophycidae	Fucales	Fucaceae	Fucus
Fucophycidae	Fucales	Fucaceae	Pelvetia
Fucophycidae	Fucales	Himanthaliaceae	Himanthalia
Fucophycidae	Fucales	Sargassaceae	Cystoseira
Fucophycidae	Fucales	Sargassaceae	Halidrys
Fucophycidae	Fucales	Sargassaceae	Hizikia
Fucophycidae	Fucales	Sargassaceae	Phyllacantha
Fucophycidae	Fucales	Sargassaceae	Sargassum
Fucophycidae	Laminariales	Agaraceae	Agarum
Fucophycidae	Laminariales	Alariaceae	Alaria
Fucophycidae	Laminariales	Alariaceae	Undaria
Fucophycidae	Laminariales	Laminariaceae	Laminaria
Fucophycidae	Laminariales	Laminariaceae	Macrocystis
Fucophycidae	Laminariales	Laminariaceae	Nereocystis
Fucophycidae	Laminariales	Laminariaceae	Saccharina
Fucophycidae	Laminariales	Lessoniaceae	Ecklonia
Fucophycidae	Laminariales	Lessoniaceae	Eisenia
Fucophycidae	Laminariales	Lessoniaceae	Lessonia

*from: Guiry, MD and Guiry, G.M. 2018. AlgaeBase. World-wide electronic publication, National University of Ireland, Galway. http://www.algaebase.org ; searched on 09 August 2018.

Taxonomy of Genuses Included in the CIR Report of Brown Algae Which are Not brown algae*
(ingredients derived from these genuses should be deleted from the brown algae CIR report)

Class	Subclass	Order	Family	Genus
Bacillariophyceae	Umeidophycidae	Rhaphoneidales	Asterionellosidaceae	Asterionellopsis
Florideophyceae	Rhodymeniophycidae	Gigartinales	Rissoellaceae	Rissoella

*from: Guiry, MD and Guiry, G.M. 2018. AlgaeBase. World-wide electronic publication, National University of Ireland, Galway. http://www.algaebase.org ; searched on 09 August 2018.