SUPPLEMENT

Wave 2 Data

- Alkane Diols
- Eucalyptus
- Fluoropolymers
- Ginkgo Biloba
- Malic Acid
- Mentha Piperita (Peppermint)
- Polyol Phosphates
- Sultaines
- Witch Hazel
- Zinc Salts

CIR EXPERT PANEL MEETING

MARCH 5-6, 2018

Cosmetic Ingredient Review

Commitment & Credibility since 1976

Memorandum

To: CIR Expert Panel Members and Liaisons
From: Monice M. Fiume MMF
Senior Director, CIR
Date: February 23, 2018
Subject: Wave 2 – updated VCRP data for Alkane Diols

Updated VCRP data were received after the March Panel materials were distributed. Because Alkane Diols is a draft Final Report, this updated information is being provided to the Panel to inform you of any frequency of use changes resulting from the most recent VCRP data. Most (but not all) of the in-use ingredients had increases in the reported frequency of use, but nothing significant was noted. The greatest number of uses (Propanediol) increased from 1138 to 1528.

An updated use table is included with this submission, and it contains track changes so that the changes in frequencies of use are obvious (*aldiol032018w2_use table*). Also included are the 2018 FDA raw data (*aldiol032018w2_FDA 2018*).

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Table 1. Frequency and concentration of use of alkane diols

	# of Uses[50]	Max Conc Use (%)[51]	# of Uses[50]	Max Conc Use (%)[51]	# of Uses[50]	Max Conc Use (%)[51]
	Propanediol		**1,4-Butanediol**		**Hexanediol**	
Totals*	~~1138~~1528	**0.0001-39.9**	~~45~~	**NR**	~~13~~	**0.011-0.5**
Duration of Use						
Leave-On	~~453~~688	*0.0001-39.9*	~~45~~	*NR*	~~13~~	*0.011-0.5*
Rinse-Off	~~685~~840	*0.005-12*	*NR*	*NR*	*NR*	*0.02-0.45*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Eye Area	~~43~~66	0.002-10	~~1~~2	NR	~~NR~~1	0.011-0.08
Incidental Ingestion	~~1~~6	3-10	NR	NR	NR	NR
Incidental Inhalation-Spray	spray: ~~18~~–21 possible: ~~171~~[a]266[a]; ~~145~~[b]211[b]	spray: 0.0001-3 possible: 2-38[a]	possible: 3[a]	NR	~~NR~~possible: 1[a]	NR
Incidental Inhalation-Powder	possible: ~~145~~[b]211[b]; 4[c]5[c]	possible: 0.0071-24[c]	NR	NR	NR	possible: 0.38[c]
Dermal Contact	~~1066~~1430	0.0001-39.9	~~4~~5	NR	~~NR~~2	0.011-0.5
Deodorant (underarm)	~~11~~[a]12[a]	not spray: 5-39.9	NR	NR	NR	NR
Hair - Non-Coloring	~~56~~74	0.005-38	NR	NR	NR	NR
Hair-Coloring	~~9~~11	0.17-12	NR	NR	NR	NR
Nail	NR	5	NR	NR	1	NR
Mucous Membrane	~~562~~680	0.5-10	NR	NR	NR	NR
Baby Products	~~7~~8	NR	NR	NR	NR	NR
	Octanediol		**1,10-Decanediol**		**Methylpropanediol**	
Totals*	**3**	**NR**	~~15~~6	**0.006**	~~541~~570	**0.025-21.2**
Duration of Use						
Leave-On	*3*	*NR*	~~14~~5	*0.006*	~~336~~360	*0.025-21.2*
Rinse-Off	*NR*	*NR*	*1*	*NR*	~~203~~209	*5-12*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	~~2~~1	*NR*
Exposure Type						
Eye Area	NR	NR	NR	NR	~~47~~45	0.71-5
Incidental Ingestion	NR	NR	NR	NR	2	NR
Incidental Inhalation-Spray	possible: 3[a]	NR	possible: ~~12~~[a]3[a]; 2[b]	NR	spray: ~~6~~5 possible: ~~100~~[a]117[a]; ~~140~~[b]147[b]	NR
Incidental Inhalation-Powder	NR	NR	possible: 2[b]	possible: 0.006[c]	possible: ~~140~~[b]147[b]	possible: 0.8-21.2[c]
Dermal Contact	3	NR	~~15~~6	0.006	~~504~~534	0.025-21.2
Deodorant (underarm)	NR	NR	NR	NR	NR	not spray: 0.025
Hair - Non-Coloring	NR	NR	NR	NR	~~15~~16	NR
Hair-Coloring	NR	NR	NR	NR	8	NR
Nail	NR	NR	NR	NR	1	0.04-12
Mucous Membrane	NR	NR	NR	NR	~~124~~116	5
Baby Products	NR	NR	NR	NR	NR	NR
	Butyl Ethyl Propanediol		**Isopentyldiol**			
Totals*	**NR**	**0.29**	~~135~~160	**0.13-15**		
Duration of Use						
Leave-On	*NR*	*0.29*	~~132~~155	*0.13-15*		
Rinse-Off	*NR*	*NR*	~~3~~5	*3-15*		
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*		
Exposure Type						
Eye Area	NR	NR	~~25~~27	0.13-5		
Incidental Ingestion	NR	NR	NR	NR		
Incidental Inhalation-Spray	NR	possible: 0.29[a]	spray: 4 possible: ~~74~~[a]91[a]; ~~10~~[b]12[b]	spray: 3-5 possible: 2-5[a]		
Incidental Inhalation-Powder	NR	NR	powder: 3 possible: ~~10~~[b]12[b]	powder: 0.33 possible: 1-10[c]		
Dermal Contact	NR	NR	~~133~~156	0.33-10		
Deodorant (underarm)	NR	NR	NR	spray: 1		
Hair - Non-Coloring	NR	0.29	~~1~~3	3-15		
Hair-Coloring	NR	NR	NR	5		
Nail	NR	NR	NR	NR		
Mucous Membrane	NR	NR	NR	NR		
Baby Products	NR	NR	NR	NR		

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

[a]Includes products that can be sprays, but it is not known whether the reported uses are sprays

[b]Not specified whether this product is a spray or a powder or neither, but it is possible it may be a spray or a powder, so this information is captured for both categories of incidental inhalation

[c]Includes products that can be powders, but it is not known whether the reported uses are powders

NR – no reported use

Propanediol

01A - Baby Shampoos	2
01B - Baby Lotions, Oils, Powders, and Creams	5
01C - Other Baby Products	1
03B - Eyeliner	3
03C - Eye Shadow	3
03D - Eye Lotion	20
03E - Eye Makeup Remover	4
03F - Mascara	7
03G - Other Eye Makeup Preparations	29
04A - Cologne and Toilet waters	1
04E - Other Fragrance Preparation	14
05A - Hair Conditioner	15
05B - Hair Spray (aerosol fixatives)	1
05C - Hair Straighteners	3
05F - Shampoos (non-coloring)	16
05G - Tonics, Dressings, and Other Hair Grooming Aids	23
05H - Wave Sets	1
05I - Other Hair Preparations	13
06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	3
06B - Hair Tints	2
06D - Hair Shampoos (coloring)	1
06E - Hair Color Sprays (aerosol)	5
07C - Foundations	18
07E - Lipstick	3
07F - Makeup Bases	10
07H - Makeup Fixatives	1
07I - Other Makeup Preparations	6
09A - Dentifrices	1
09B - Mouthwashes and Breath Fresheners	1
09C - Other Oral Hygiene Products	1
10A - Bath Soaps and Detergents	669
10B - Deodorants (underarm)	12
10E - Other Personal Cleanliness Products	5
11A - Aftershave Lotion	4
11G - Other Shaving Preparation Products	2
12A - Cleansing	54
12B - Depilatories	1
12C - Face and Neck (exc shave)	184
12D - Body and Hand (exc shave)	26
12E - Foot Powders and Sprays	1
12F - Moisturizing	204
12G - Night	29
12H - Paste Masks (mud packs)	59
12I - Skin Fresheners	5
12J - Other Skin Care Preps	56
13A - Suntan Gels, Creams, and Liquids	1
13B - Indoor Tanning Preparations	2
13C - Other Suntan Preparations	1

1,4-Butanediol

03D - Eye Lotion	1
03G - Other Eye Makeup Preparations	1
12F - Moisturizing	1
12I - Skin Fresheners	1
13B - Indoor Tanning Preparations	1

2,3-Butanediol

None

1,5-Pentanediol

None

Hexanediol

03G - Other Eye Makeup Preparations	1
08G - Other Manicuring Preparations	1
12F - Moisturizing	1

Octanediol

12I - Skin Fresheners	3

1,10-Decanediol

12A - Cleansing	1
12C - Face and Neck (exc shave)	1
12D - Body and Hand (exc shave)	1
12F - Moisturizing	1
12G - Night	2

Methylpropanediol

02D - Other Bath Preparations	1
03A - Eyebrow Pencil	2
03B - Eyeliner	4
03C - Eye Shadow	10
03D - Eye Lotion	13
03E - Eye Makeup Remover	2
03F - Mascara	9
03G - Other Eye Makeup Preparations	5
04A - Cologne and Toilet waters	1
05A - Hair Conditioner	5
05B - Hair Spray (aerosol fixatives)	4
05E - Rinses (non-coloring)	1
05F - Shampoos (non-coloring)	3
05G - Tonics, Dressings, and Other Hair Grooming Aids	2
05H - Wave Sets	1
06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	5
06D - Hair Shampoos (coloring)	1
06H - Other Hair Coloring Preparation	2
07A - Blushers (all types)	2
07C - Foundations	19
07E - Lipstick	2
07F - Makeup Bases	4
07H - Makeup Fixatives	1
07I - Other Makeup Preparations	1
08B - Cuticle Softeners	1
10A - Bath Soaps and Detergents	92
10E - Other Personal Cleanliness Products	21
11A - Aftershave Lotion	5
11E - Shaving Cream	1
11G - Other Shaving Preparation Products	1
12A - Cleansing	42
12C - Face and Neck (exc shave)	71
12D - Body and Hand (exc shave)	76
12F - Moisturizing	95
12G - Night	9
12H - Paste Masks (mud packs)	32
12I - Skin Fresheners	5
12J - Other Skin Care Preps	13
13A - Suntan Gels, Creams, and Liquids	2
13B - Indoor Tanning Preparations	4

Butyl Ethyl Propanediol

none

Isopentyldiol

03A - Eyebrow Pencil	2
03B - Eyeliner	2
03C - Eye Shadow	9
03D - Eye Lotion	9
03F - Mascara	1
03G - Other Eye Makeup Preparations	4
04E - Other Fragrance Preparation	4
05G - Tonics, Dressings, and Other Hair Grooming Aids	1
05I - Other Hair Preparations	2
07A - Blushers (all types)	8
07B - Face Powders	3
07C - Foundations	1
07I - Other Makeup Preparations	5
12A - Cleansing	3
12C - Face and Neck (exc shave)	11
12D - Body and Hand (exc shave)	1
12F - Moisturizing	74
12H - Paste Masks (mud packs)	2
12J - Other Skin Care Preps	2
13B - Indoor Tanning Preparations	15
13C - Other Suntan Preparations	1

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MEMORANDUM

To: CIR Expert Panel and Liaisons

From: Lillian C. Becker, M.S.
Scientific Analyst and Writer

Date: February 23, 2018

Subject: Wave 2 for *Eucalyptus globulus*-Derived Ingredients As Used In Cosmetics

Attached are additional data submitted by the Council on method of manufacture, specifications for impurities (including heavy metals and allergens), and specifications for chemical and physical properties of Eucalyptus Globulus Leaf Extract. [*eucaly032018w2_data 1*]

Also included are updated concentration of use data [*eucaly032018w2_data 2*]. The maximum use concentration of Eucalyptus Globulus Leaf Oil in body and hand preparations (not spray) was corrected from 5.5% to 0.1%. Therefore, the highest maximum concentration for leave-on use (with dermal contact) is now 0.4%. The highest concentration for incidental inhalation that may be powder is now 0.27%.

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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: February 2, 2018

SUBJECT: Eucalyptus Globulus Leaf Extract

Anonymous. 2018. Eucalyptus Globulus Leaf Extract: Summary specification information.

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- **Eucalyptus Globulus Leaf Extract**

Manufacturing Process:

The fresh/dried leaf is extracted with specified eluent(s) under appropriate temperature conditions, to yield a concentrate. The concentrate containing the phytochemical constituents is then blended with the desired diluent(s) and preservation system to produce the final ingredient. The ingredient is evaluated for physiochemical properties according to the specification requirements for the batch to be released. In addition, the concentrate is also evaluated for contaminants and physiochemical properties as needed.

Heavy Metal & Pesticides/ Allergens/ Impurities:

The following heavy metal testing was conducted on the concentrate in a propylene glycol base:

	Heavy Metal	Detection	Reporting Limit	Heavy Metal	Detection	Reporting Limit
Heavy metals:	Antimony	Not Detected	0.051 mg/l	Iron	Not Detected	0.087 mg/l
	Arsenic	Not Detected	0.055 mg/l	Lead	Not Detected	0.015 mg/l
	Cadmium	Not Detected	0.004 mg/l	Mercury	Not Detected	0.0002 mg/l
	Chromium	Not Detected	0.010 mg/l	Nickel	Not Detected	0.016 mg/l

Pesticides: There were no residual pesticides detected. (Parameters: 8081 GCS Pesticides and 8141 GCS, O/P Pesticides) .

The following Allergen testing was conducted on the concentrate in an alcohol base:

	Fragrance Ingredient	Threshold	Fragrance Ingredient	Threshold
Presence of the 26 allergens defined by the 7th amendment to the EU Cosmetic Directive:	Amyl Cinnamal	<10ppm-0.001%	Anise Alcohol	<10ppm-0.001%
	Benzyl Alcohol	<10ppm-0.001%	Benzyl Cinnamate	<10ppm-0.001%
	Cinnamyl Alcohol	<10ppm-0.001%	Farnesol	<10ppm-0.001%
	Citral	<10ppm-0.001%	Butylphenyl Methylpropional	<10ppm-0.001%
	Eugenol	<10ppm-0.001%	Linalool	<10ppm-0.001%
	Hydroxycitronellal	<10ppm-0.001%	Benzyl Benzoate	<10ppm-0.001%
	Isoeugenol	<10ppm-0.001%	Citronellol	<10ppm-0.001%
	Amylcinnamyl Alcohol	<10ppm-0.001%	Hexyl Cinnamal	<10ppm-0.001%
	Benzyl Salicylate	<10ppm-0.001%	Limonene	<10ppm-0.001%
	Cinnamal	<10ppm-0.001%	Methyl l2-octynoate	<10ppm-0.001%
	Hydroxyisohexyl 3-Cyclohexene Carboxaldehyde	<10ppm-0.001%	Alpha-Isomethyl Inone (Other Name: Methyl Lonone Gamma)	<10ppm-0.001%
	Coumarin	<10ppm-0.001%	Evernia Prunastri (Oak Moss) Extract	Not Tested
	Geraniol	<10ppm-0.001%	Evernia Furfuracea (Tree Moss) Extract	Not Tested

*The given values correspond to the limit of determination OR *Results have been calculated form highest reported values published.

Additional information:

- A typical product with the **Eucalyptus Globulus Leaf Extract** prepared in water has the following specifications:

Analysis:

Specification	Range	Actual
APPEARANCE	Light to medium amber liquid	PASS
MICROBIAL PLATE COUNT	Less than 100 organisms per gram	PASS
ODOR	Characteristic	PASS
PH	4.0 - 6.5 at 25° C	4.8
PRESERVATIVE - PHENOXYETHANOL	1.0%	PASS
REFRACTIVE INDEX	1.3250 - 1.3450 at 25° C	1.3352
SOLUBILITY	Soluble in any proportion in water	PASS
SPECIFIC GRAVITY	0.99 - 1.01 at 25° C	1.00

Concentration of Use by FDA Product Category – *Eucalyptus globulus*-Derived Ingredients*

Eucalyptus Globlulus Leaf Oil
Eucalyptus Globluuls Leaf
Eucalyptus Globlulus Leaf Extract
Eucalyptus Globulus Leaf Powder
Eucalyptus Globulus Leaf/Twig Oil
Eucalyptus Globulus Leaf Water

Ingredient	Product Category	Maximum Concentration of Use
Eucalyptus Globlulus Leaf Oil	Baby shampoo	0.000019%
Eucalyptus Globlulus Leaf Oil	Baby lotions, oils and creams Not powder	 0.00067%
Eucalyptus Globlulus Leaf Oil	Other baby products	0.000002%
Eucalyptus Globlulus Leaf Oil	Bath oils, tablets and salts	0.13%
Eucalyptus Globlulus Leaf Oil	Bubble baths	0.2%
Eucalyptus Globlulus Leaf Oil	Eye shadows	0.00021%
Eucalyptus Globlulus Leaf Oil	Eye lotions	0.038%
Eucalyptus Globlulus Leaf Oil	Eye makeup removers	0.00001%
Eucalyptus Globlulus Leaf Oil	Colognes and toilet waters	0.4%
Eucalyptus Globlulus Leaf Oil	Other fragrance preparations	0.2%
Eucalyptus Globlulus Leaf Oil	Hair conditioners	0.00001-0.011%
Eucalyptus Globlulus Leaf Oil	Hair sprays Aerosol	 0.002%
Eucalyptus Globlulus Leaf Oil	Shampoos (noncoloring)	0.00001-0.12%
Eucalyptus Globlulus Leaf Oil	Tonics, dressings and other hair grooming aids	0.0031-0.04%
Eucalyptus Globlulus Leaf Oil	Hair dyes and colors	0.005%
Eucalyptus Globlulus Leaf Oil	Foundations	0.001%
Eucalyptus Globlulus Leaf Oil	Lipstick	0.008-0.35%
Eucalyptus Globlulus Leaf Oil	Other makeup preparations	0.0001%
Eucalyptus Globlulus Leaf Oil	Nail polish and enamel	0.0001%
Eucalyptus Globlulus Leaf Oil	Other manicuring preparations	0.15%
Eucalyptus Globlulus Leaf Oil	Mouth washes and breath fresheners	0.74%
Eucalyptus Globlulus Leaf Oil	Bath soaps and detergents	0.00013-0.2%
Eucalyptus Globlulus Leaf Oil	Aftershave lotions	0.0005%
Eucalyptus Globlulus Leaf Oil	Preshave lotions	0.00015%
Eucalyptus Globlulus Leaf Oil	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.0001-0.1%
Eucalyptus Globlulus Leaf Oil	Face and neck products Not spray Spray	 0.098-0.27% 0.0008%
Eucalyptus Globlulus Leaf Oil	Body and hand products Not spray	 0.001-0.1%
Eucalyptus Globlulus Leaf Oil	Moisturizing products Not spray	 0.00071-0.2%
Eucalyptus Globlulus Leaf Oil	Night products Spray	 0.01%

Eucalyptus Globlulus Leaf Oil	Paste masks and mud packs	0.00091-0.025%
Eucalyptus Globlulus Leaf Oil	Skin fresheners	0.11%
Eucalyptus Globlulus Leaf Oil	Other skin care preparations	0.00001-0.2%
Eucalyptus Globlulus Leaf Oil	Suntan products Not spray Spray	 0.00016-0.001% 0.00056%
Eucalyptus Globlulus Leaf Oil	Indoor tanning preparations	0.00001%
Eucalyptus Globlulus Leaf Oil	Other suntan preparations	0.001%
Eucalyptus Globulus Leaf	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	1.2%
Eucalyptus Globlulus Leaf Extract	Hair conditioners	0.0087%
Eucalyptus Globlulus Leaf Extract	Hair sprays Aerosol	 0.000006-0.005%
Eucalyptus Globlulus Leaf Extract	Shampoos (noncoloring)	0.000008-0.005%
Eucalyptus Globlulus Leaf Extract	Tonics, dressings and other hair grooming aids	0.00021%
Eucalyptus Globlulus Leaf Extract	Foundations	0.001%
Eucalyptus Globlulus Leaf Extract	Dentifrices	0.41%
Eucalyptus Globlulus Leaf Extract	Mouth washes and breath fresheners	0.058%
Eucalyptus Globlulus Leaf Extract	Bath soaps and detergents	0.015-0.025%
Eucalyptus Globlulus Leaf Extract	Shaving cream	0.00048-0.00053%
Eucalyptus Globlulus Leaf Extract	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.0015%
Eucalyptus Globlulus Leaf Extract	Face and neck products Not spray	 0.005%
Eucalyptus Globlulus Leaf Extract	Paste masks and mud packs	0.01%
Eucalyptus Globlulus Leaf Extract	Other skin care preparations Rinse-off	 0.0003-0.01%
Eucalyptus Globlulus Leaf Extract	Indoor tanning preparations	0.00005%
Eucalyptus Globlulus Leaf Powder	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	1%
Eucalyptus Globlulus Leaf Water	Hair conditioners	0.02%
Eucalyptus Globlulus Leaf Water	Shampoos (coloring)	0.1%
Eucalyptus Globlulus Leaf Water	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.002%
Eucalyptus Globlulus Leaf Water	Face and neck products Not spray	 1.4%

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

Information collected in 2017

Table prepared: September 29, 2017

Correction February 20, 2018: maximum use concentration Eucalyptus Globulus Leaf Oil changed from 5.5% to 0.1%

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Memorandum

To: CIR Expert Panel Members and Liaisons
From: Wilbur Johnson, Jr.
Senior Scientific Analyst
Date: February 23, 2018
Subject: Wave 2 Data on Fluoropolymers

The data listed below are data that are summarized in a publication (Clayton, J. W., Jr. Fluorocarbon Toxicity and Biological Action. *Fluorine Chemistry Reviews*. 1967; 1(2):197-252.), unpublished data that were received from the Personal Care Products Council (*fluoro032018data4 file attachment)*, or current FDA use frequency data on PTFE (*fluoro032018fda* file attachment). A data summary document (*fluoro032018wave2studysummaries*) containing the new FDA data (summarized in Table 1) and the following study summaries is attached for the Panel's review:

data from Fluorocarbon Toxicity and Biological Action

- Acute oral toxicity study (rats) on a low molecular weight PTFE resin
- Short-term inhalation toxicity study (rats) on a low molecular weight PTFE resin (20% dispersion in $CCl_2F—CClF_2$)
- Subchronic oral toxicity study (rats) on 3 types of PTFE resin (including an unsintered PTFE resin)
- Dermal irritation and sensitization study (guinea pigs) on a low molecular weight PTFE resin (20% dispersion in $CCl_2F—CClF_2$)
- Ocular irritation study (rabbits) on a low molecular weight PTFE resin (20% dispersion in $CCl_2F—CClF_2$)

fluoro032018data4 file

- Skin and ocular irritation data on PTFE (rabbits)
- Skin sensitization data (maximization test, guinea pigs) on 75% Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether (challenge concentration)

fluoro032018fda file

- 2018 FDA VCRP data

These data will be added to the safety assessment after the Panel meeting.

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Wave 2 Data on Fluoropolymers

Use

Cosmetic

The Use section of the draft report on Fluoropolymers will be revised to include 2018 VCRP data, and these data are presented in Table1 in this document.[1] These use frequency data will replace the 2017 VCRP data that are included in the Use section of the draft report that was submitted to the Panel earlier this month. The number of product categories in the new VCRP data remains the same (i.e., no recent additions/deletions). However, the number of uses of PTFE in leave-on products has been reduced from 355 to 343. The number of uses of PTFE in rinse-off products remains the same (22 uses).

TOXICOLOGICAL STUDIES

Acute Toxicity Study

Dermal

PTFE

Results relating to the acute dermal toxicity of PTFE are presented in a study evaluating the skin irritation potential of this ingredient.[2] Skin irritation data from this study are summarized later in this report. The test substance (powder, 0.5 g) was applied to abraded and intact skin of the trunk (cm^2 area not stated) of 6 New Zealand White rabbits for 24 h. None of the animals died, and no clinical signs or behavioral alterations were observed during the study.

Oral

PTFE

A low molecular weight PTFE resin (fluorotelomer, chemical characterization data not included) was administered orally to rats (strain and dosing method not stated) at doses as high as 17 g/kg.[3] None of the animals died, and there were no clinical effects or organ changes that were related to test substance administration.

Short-Term Toxicity Study

Dermal

Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether

Results relating to the short-term dermal toxicity of Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether are presented in a guinea pig maximization test in which the test substance was injected/applied topically to 10 guinea pigs during a 7-day period.[4] Skin sensitization data from this study are summarized later in this report. No mortalities occurred and there were no signs of general toxicity in any of the animals tested.

Inhalation

PTFE

Spray inhalation experiments on a low molecular weight PTFE resin (fluorotelomer, chemical characterization data not included) were performed using 4 rats (strain not stated).[3] The rats were exposed for 9 days (3 times per day) to a 20% dispersion of the fluorotelomer in dichloro(fluoro)methyl (CCl_2F)—chlorodifluoromethyl radical ($CClF_2$) from a pressurized container. After spraying, the jars were sealed and exposure to the dispersion was continued for 15 minutes. A total of 26 exposures was performed. During exposure, incoordination, labored breathing, and irritation of the nose were observed. It was noted that these signs were primarily due to propellants and the dispersing agent (not stated). Recovery occurred immediately after exposure, and it was noted that there was no evidence of pathology that could have been attributed to exposure.

Subchronic Toxicity Study

Oral

PTFE

Three types of PTFE resin (chemical characterization data not included, 25% in the diet) were fed to male and female rats (strain and number per group not stated) for 90 days.[3] After feeding with each type of PTFE resin, there were no adverse effects on growth rate or behavior and there was no microscopic evidence of tissue changes. However, a slight shift in the distribution and number of white blood cells was observed. Also, feeding with 1 of the 3 types of resin (unsintered PTFE resin) caused an increase in the relative size of the liver (relative to body weight). This finding was not accompanied by any histological abnormality.

DERMAL IRRITATION AND SENSITIZATION STUDY

Irritation

PTFE

The skin irritation potential of PTFE (powder) was evaluated using 6 New Zealand White rabbits (3 males, 3 females).[2] Two areas on the trunk (cm^2 area not stated) were clipped free of hair and one area of skin was abraded. The test substance (0.5 g) was applied to occlusive patches that were applied to the skin for 24 h. The test sites were examined for reactions at 24 h and 72 h after patch application. Skin reactions were not observed at intact or abraded skin sites in any of the animals tested, and PTFE was classified as a non-irritant.

A 20% dispersion of the fluorotelomer in $CCl_2F—CClF_2$ (defined in Short-Term Inhalation toxicity section) was applied to the skin of 10 guinea pigs (strain not stated).[3] The method and duration of test substance application and dose per cm^2 were not stated. When the $CCl_2F—CClF_2$ evaporated, the material hardened and moderate mechanical irritation was observed. There was no evidence of sensitization in any of the animals tested.

Sensitization

Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether

The skin sensitization potential of Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether was evaluated in the maximization test using 15 male Dunkin Hartley albino guinea pigs (10 test animals and 5 controls).[4] On day 0, the 10 test animals received the following 3 pairs of intradermal injections: Freund's complete adjuvant (FCA) emulsion (0.1 ml), Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether (concentration not stated, 0.1 nml), and Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether in FCA (0.1 ml). Similarly, the 5 control animals received the following 3 pairs of intradermal injections: FCA emulsion (0.1 ml), vaseline oil vehicle (0.1 ml), and vehicle in FCA (0.1 ml). On day 6, the animals were treated topically with with 10% sodium lauryl sulfate in vaseline oil (0.5 ml). On day 7, the same area was treated with undiluted Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether, or the vehicle was applied to the skin for 48 h using an occlusive patch. The test sites were observed for signs of skin irritation 24 h after patch removal. At challenge on day 20, an occlusive patch containing 75% Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether or the vehicle was was applied for 24 h to animals of the 2 groups. Sites were observed for any reactions at 24 h after patch removal and at 24 h later.

The injection of the test substance (in vehicle) caused slight irritation (number of animals not stated). Reactions were not observed after injection of the vehicle alone. At 24 h post-removal of the 48-h occlusive patch, signs of slight irritation (erythema) were observed at sites treated with the test substance. None of the animals had a positive reaction after treatment with the test substance during the challenge phase. Also, no skin reactivity was observed in the negative control group. The authors concluded that Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether did not appear to possess sensitizing capacity in this study.[4]

OCULAR IRRITATION STUDY

PTFE

In a study involving 6 New Zealand White rabbits (3 males, 3 females), PTFE (powder, 0.1 g) was instilled into the conjunctival sac of the right eye.[2] The lids were held together for ~ 3 to 4 seconds in order to prevent loss of the test substance. The eyes were rinsed at 24 h post-instillation, and observations were made for up to 72 h post-instillation. No clinical signs or behavioral

alterations were observed. Conjunctival redness was observed in 4 rabbits. After 24 h, the reactions had cleared in 3 animals. The reaction had cleared after 48 h in the fourth animal. PTFE was classified as non-irritating to the eye in this study.

The ocular irritation potential of a 20% dispersion of the fluorotelomer in $CCl_2F—CClF_2$ was evaluated using rabbits (number and strain of animals and test protocol not stated).[3] The test substance caused mild conjunctival irritation, which was no longer observed in less than 72 h. Mild corneal injury was observed at 24 h, but not at 48 h. It was noted that the transient reactions observed in this study were no greater than those that were caused by $CCl_2F—CClF_2$ alone.

TABLES

Table 1. Frequency and Concentration of Use According to Duration and Type of Exposure.[1]

	PTFE	
	# of Uses	Conc. (%)
Totals/Conc. Range	365	0.11-13
Duration of Use		
Leave-On	343	0.11-13
Rinse off	22	0.15-2.4
Diluted for (bath) Use	NR	NR
Exposure Type		
Eye Area	229	0.11-13
Incidental Ingestion	4	0.44
Incidental Inhalation- Sprays	15*	NR
Incidental Inhalation- Powders	31	0.6-3
Dermal Contact	325	0.11-12
Deodorant (underarm)	NR	NR
Hair - Non-Coloring	NR	NR
Hair-Coloring	NR	2.4
Nail	NR	NR
Mucous Membrane	4	0.44
Baby Products	NR	NR

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

*It is possible that these products may be sprays, but it is not specified whether the reported uses are sprays.

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.

References

1. U.S. Food and Drug Administration Center for Food Safety & Applied Nutrition (CFSAN). Voluntary Cosmetic Registration Program - Frequency of Use of Cosmetic Ingredients. College Park, MD, 2018.

2. Anonymous. Summaries of dermal irritation and eye irritation studies of PTFE in rabbits. Unpublished data submitted by the Personal Care Products Council on 2-20-2018. 2018. pp.1-2.

3. Clayton, J. W., Jr. Fluorocarbon Toxicity and Biological Action. *Fluorine Chemistry Reviews*. 1967;1(2):197-252.

4. Anonymous. Summary of a skin sensitization test of polyperfluoroethoxymethoxy difluorohydroxyethyl ether in guinea pigs. Unpublished data submitted by the Personal Care Products Council on 2-20-2018. 2018. pp.1

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Memorandum

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

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

DATE: February 20, 2018

SUBJECT: lnformation on PTFE and Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether

Anonymous. 2018. Summaries of dermal irritation and eye irritation studies of PTFE in rabbits.

Anonymous. 1998. Summary of a skin sensitization test of Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether in guinea pigs.

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Feb. 2018

Two studies were conducted on Polytetrafluoroethylene (PTFE) and the reports were issued on October 30, 1989. Both studies were performed under OECD- GLP conditions. Both test methods were in accordance with the EU Community Guidelines EEC Directive 79/831 (VI Amendment), Annex V, EEC Directive 84/449 and the EEC Committee on Cosmetology (XI/424/80 rev. 8, CSC/109/80).

PRIMARY DERMAL IRRITATION STUDY IN RABBITS

A dermal irritation study was conducted on New Zealand White rabbits 3 males and 3 females. Two areas on the trunk were clipped and one of them was abraded by making four minor epidermal incisions (two perpendicular to the other and spaced 2 cm apart). The incisions were sufficiently deep to penetrate the stratum corneum but not to disturb the derma or to produce bleeding.

The test article in powder form (0.5 g/site) was applied directly onto the gauze patches which were held in close contact with the skin areas by a tape. Rabbit were exposed for 24 hours. At the end of exposure the patches were removed and the residual material wiped off using water. Animals were examined in the two areas of intact and abraded skin, signs of erythema and edema were scored at 24 and 72 hours after the beginning of the test. No animals died during the testing. No clinical signs or behavioral alternations were noted. At the application sities, no dermal reactions were detected in any rabbit at any observation time.Therefore the article is considered "non irritant" for the skin .

ERITHEMA and ESCHAR
(max score = 4)

	Rabbit#1	Rabbit#2	Rabbit#3	Rabbit#4	Rabbit#5	Rabbit#6
Intact skin						
24 hours	0	0	0	0	0	0
72 hours	0	0	0	0	0	0
Abraded skin						
24 hours	0	0	0	0	0	0
72 hours	0	0	0	0	0	0

EDEMA
(max score = 4)

	Rabbit#1	Rabbit#2	Rabbit#3	Rabbit#4	Rabbit#5	Rabbit#6
Intact skin						
24 hours	0	0	0	0	0	0
72 hours	0	0	0	0	0	0
Abraded skin						
24 hours	0	0	0	0	0	0
72 hours	0	0	0	0	0	0

ACUTE EYE IRRITATION STUDY IN RABBITS

An acute eye irritation study was conducted on New Zealand White rabbits using 3 males and 3 females at a dose of 0.1 g/animal. The test article which was in powder form was administered directly to the conjunctival sac of the right eye of each animal after gently pulling the lower lid away from the eyeball. The lids were then gently held together for about 3-4 seconds in order to prevent loss of the material. The left eye remained untreated and served as a control. They eyes of the test animals were washed out at 24 hours following the test article instillation. The eyes were observed at 1, 24, 48 and 72 hours after the

test article application. Eyes were scored for corneal opacity, Iritis, conjunctival redness and chemosis. After the 24 hour reading the cornea were examined after instillation of one drop of 1% sodium fluorescein and subsequent washing out with sterile saline. No clinical signs or behavioral alternations were observed. The following alternations of eye was observed: Conjunctival redness in four animals. The redness disappeared in all animals after 24 hours, except for one animal where it disappeared after 48 hours. The test article is considered to be "non irritant" for the eye.

CORNEA
(max score = 4)

	Rabbit#1	Rabbit#2	Rabbit#3	Rabbit#4	Rabbit#5	Rabbit#6
60 min	0	0	0	0	0	0
24 hours	0	0	0	0	0	0
48 hours	0	0	0	0	0	0
72 hours	0	0	0	0	0	0

IRITIS
(max score = 2)

	Rabbit#1	Rabbit#2	Rabbit#3	Rabbit#4	Rabbit#5	Rabbit#6
60 min	0	0	0	0	0	0
24 hours	0	0	0	0	0	0
48 hours	0	0	0	0	0	0
72 hours	0	0	0	0	0	0

CONJUCTIVAE
Redness

(max score = 3)

	Rabbit#1	Rabbit#2	Rabbit#3	Rabbit#4	Rabbit#5	Rabbit#6
60 min	1	1	1	1	1	1
24 hours	0	0	0	0	1	0
48 hours	0	0	0	0	0	0
72 hours	0	0	0	0	0	0

CHEMOSIS
(max score = 4)

	Rabbit#1	Rabbit#2	Rabbit#3	Rabbit#4	Rabbit#5	Rabbit#6
60 min	0	0	0	0	0	0
24 hours	0	0	0	0	0	0
48 hours	0	0	0	0	0	0
72 hours	0	0	0	0	0	0

SKIN SENSITIZATION TEST IN GUINEA PIGS
Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether
November 30, 1998

The sensitizing potential of the test article, Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether, was assessed in guinea pigs using the Magnusson maximization test. Seventeen male Dunkin Hartley albino guinea pigs were used(10 for the treated group, 5 for the control group and 2 animals for the preliminary test).
Basing on the observations in the preliminary test the test item was administered at 1% with the intradermal injection (induction phase), at 100% at the booster and at 75% in vaseline oil at the challenge application.
In the induction phase, on day 0 each animal was given three pairs of 0.1 ml intradermal injections in the skin area clipped the day before [Treatmend group: 1) 0.1 ml FCA emulsion; 2) 0.1 ml test article; 3) 0.1 ml test article in FCA; Control group: 1) 0.1 ml FCA emulsion; 2) 0.1 ml vehicle; 3) 0.1 ml vehicle in FCA].
On day 6 animals were topical treated with 0.5 ml of 10% sodium lauryl sulfate in vaseline oil, in order to create a local irritation, the same area were treated on day 7 with the undiluted test article or the vehicle applied to the skin areas for 48 hours with an occlusive patch (booster). Twenty-four hours after removal of the patches, the sites were observed for irritant effects.
At the challenge on day 20, an occlusive patch loaded with the 75% test article or vehicle was applied for 24 hours to the animals of the two groups.24 hours after patches removal the site was observed for any reaction. A second observation was made after further 24 hours.
No mortalities occurred and no signs of general toxicity were observed in any animal.The injection of the test article in the vehicle caused slight irritation. No reaction was seen after injection of the vehicle alone. Twenty-four hours after the removal of the 48-hours closed patch (booster), signs of slight irritation (erythema) were observed on the treatment sites of the test article treated animals. No animals treated with the test article showed a positive reaction at the challenge at any observation time.. No skin reactivity was observed in the negative control group. On the basis of this result and the experimental conditions applied the test article did not appear to possess sensitizing capacity.

2018 FDA VCRP Data

PTFE

03A - Eyebrow Pencil	3
03C - Eye Shadow	179
03D - Eye Lotion	6
03F - Mascara	36
03G - Other Eye Makeup Preparations	5
04C - Powders (dusting and talcum, excluding aftershave talc)	1
07A - Blushers (all types)	35
07B - Face Powders	30
07C - Foundations	6
07E - Lipstick	4
07G - Rouges	1
07H - Makeup Fixatives	1
07I - Other Makeup Preparations	2
11E - Shaving Cream	3
11G - Other Shaving Preparation Products	21
12A - Cleansing	1
12C - Face and Neck (exc shave)	4
12D - Body and Hand (exc shave)	11
12E - Foot Powders and Sprays	1
12F - Moisturizing	10
12G - Night	5
Total	**365**

Acrylates/Methoxy PEG-23 Methacrylate/Perfluorooctyl Ethyl Acrylate Copolymer - No Data

Acrylates/Perfluorohexylethyl Methacrylate Copolymer - No Data

Behenyl Methacrylate/Perfluorooctylethyl Methacrylate Copolymer - No Data

C6-14 Perfluoroalkylethyl Acrylate/HEMA Copolymer - No Data

Hexafluoropropylene/Tetrafluoroethylene Copolymer - No Data

PEG-10 Acrylate/Perfluorohexylethyl Acrylate Copolymer - No Data

Polychlorotrifluoroethylene - No Data

Polyperfluoroethoxymethoxy Difluoroethyl PEG Diisostearate - No Data

Polyperfluoroethoxymethoxy Difluoroethyl PEG Ether - No Data

Polyperfluoroethoxymethoxy Difluoroethyl PEG Diisostearate - No Data

Polyperfluoroethoxymethoxy Difluorohydroxyethyl Ether - No Data

Stearyl Methacrylate/Perfluorooctylethyl Methacrylate Copolymer - No Data

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Memorandum

To: CIR Expert Panel Members and Liaisons
From: Christina L. Burnett, Senior Scientific Writer/Analyst
Date: February 23, 2018
Subject: Wave 2 – *Ginkgo biloba*-Derived Ingredients

The Council has provided data on Ginkgo Biloba Leaf Extract and Ginkgo Biloba Nut Extract (*ginkgo032018wave2_data*). These data include information on method of manufacture and impurities data on Ginkgo Biloba Leaf Extract, and chemical specifications for Ginkgo Biloba Leaf Extract (in water) and Ginkgo Biloba Nut Extract (in glycerin).

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Memorandum

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

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

DATE: February 2, 2018

SUBJECT: Ginkgo Biloba Leaf Extract and Ginkgo Biloba Nut Extract

Anonymous. 2018. Ginkgo Biloba Leaf Extract and Ginkgo Biloba Nut Extract: Summary specification information.

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2018

- **Ginkgo Biloba Leaf Extract**
- **Ginkgo Biloba Nut Extract**

Manufacturing Process:

The fresh/dried leaf is extracted with specified eluent(s) under appropriate temperature conditions, to yield a concentrate. The concentrate containing the phytochemical constituents is then blended with the desired diluent(s) and preservation system to produce the final ingredient. The ingredient is evaluated for physiochemical properties according to the specification requirements for the batch to be released. In addition, the concentrate is also evaluated for contaminants and physiochemical properties as needed.

Heavy Metal & Pesticides/ Allergens/ Impurities: The following data are obtained based on the testing done on the leaf concentrate in an alcohol base. There is no test data available for nuts extract.

	Heavy Metal	Detection	Reporting Limit	Heavy Metal	Detection	Reporting Limit
Heavy metals:	Antimony	Not Detected	0.25 mg/L	Iron	Not Detected	5.0 mg/L
	Arsenic	Not Detected	0.050 mg/L	Lead	Not Detected	0.050 mg/L
	Cadmium	Not Detected	0.010 mg/L	Mercury	Not Detected	0.0040 mg/L
	Chromium	Not Detected	0.050 mg/L	Nickel	Not Detected	0.050 mg/L

Pesticides: There were no residual pesticides detected. (Parameters: 8081 GCS Pesticides and 8141 GCS, O/P Pesticides)

	Fragrance Ingredient	Threshold	Fragrance Ingredient	Threshold
Presence of the 26 allergens defined by the 7th amendment to the EU Cosmetic Directive:	Amyl Cinnamal	<10ppm-0.001%	Anise Alcohol	<10ppm-0.001%
	Benzyl Alcohol	<10ppm-0.001%	Benzyl Cinnamate	<10ppm-0.001%
	Cinnamyl Alcohol	<10ppm-0.001%	Farnesol	<10ppm-0.001%
	Citral	<10ppm-0.001%	Butylphenyl Methylpropional	<10ppm-0.001%
	Eugenol	<10ppm-0.001%	Linalool	<10ppm-0.001%
	Hydroxycitronellal	<10ppm-0.001%	Benzyl Benzoate	<10ppm-0.001%
	Isoeugenol	<10ppm-0.001%	Citronellol	<10ppm-0.001%
	Amylcinnamyl Alcohol	<10ppm-0.001%	Hexyl Cinnamal	<10ppm-0.001%
	Benzyl Salicylate	<10ppm-0.001%	Limonene	<10ppm-0.001%
	Cinnamal	<10ppm-0.001%	Methyl l2-octynoate	<10ppm-0.001%
	Hydroxyisohexyl 3-Cyclohexene Carboxaldehyde	<10ppm-0.001%	Alpha-Isomethyl Inone (Other Name: Methyl Lonone Gamma)	<10ppm-0.001%
	Coumarin	<10ppm-0.001%	Evernia Prunastri (Oak Moss) Extract	Not Tested
	Geraniol	<10ppm-0.001%	Evernia Furfuracea (Tree Moss) Extract	Not Tested

*The given values correspond to the limit of determination OR *Results have been calculated form highest reported values published.

Additional information:

- A typical product with the **Ginkgo Biloba Leaf Extract** prepared in water has the following specifications:

Analysis:

Specification	Range	Actual
APPEARANCE	Clear to slightly hazy liquid	PASS
COLOR	Light to medium yellow	PASS
MICROBIAL PLATE COUNT	Less than 100 organisms per gram	PASS
ODOR	Characteristic	PASS
PH	4.0 - 6.5 at 25° C	4.8
REFRACTIVE INDEX	1.3295 - 1.3395 at 25° C	1.3332
SOLUBILITY	Soluble in any proportion in water	PASS
SPECIFIC GRAVITY	0.99 - 1.02 at 25° C	1.00

- A typical product with the **Ginkgo Biloba Nut Extract** prepared in glycerin has the following specifications:

Analysis:

Specification	Range	Actual
APPEARANCE	Colorless to light amber liquid	PASS
MICROBIAL PLATE COUNT	Less than 100 organisms per gram	PASS
ODOR	Characteristic	PASS
PH	4.0 - 6.5 at 25° C	4.7
REFRACTIVE INDEX	1.3920 - 1.5000 at 25° C	1.3982
SOLUBILITY	Soluble in any proportion in water	PASS
SPECIFIC GRAVITY	1.05 - 1.15 at 25° C	1.12

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MEMORANDUM

To: CIR Expert Panel and Liaisons

From: Lillian C. Becker, M.S.
Scientific Analyst and Writer

Date: February 23, 2018

Subject: Additional Data for *Hamamelis virginiana* (Witch Hazel)-Derived Ingredients As Used In Cosmetics

The FDA's Voluntary Cosmetic Registration Program (VCRP) data for 2018 have been received (*HamVir032018FDA*). Below is the updated use table for *Hamamelis virginiana* (witch hazel)-derived ingredients.

Overall, there are no major changes in the numbers or types of formulations. The largest changes are an increase in the number of uses of Hamamelis Virginiana (Witch Hazel) Extract (from 359 to 393) and a reduction in uses in Hamamelis Virginiana (Witch Hazel) Water (from 386 to 376).

There is an entry for a single use for "Hamamelis Virginiana (Witch Hazel) Bark Extract" and 38 uses reported for "Witch Hazel". These are not INCI names in the web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI *Dictionary*), but are included to provide the Panel with complete information.

Table 8. Frequency of use according to duration and exposure of *Hamamelis virginiana* (witch hazel)-derived ingredients.[1,2]

Use type	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)	Uses	Maximum Concentration (%)
	Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract		Hamamelis Virginiana (Witch Hazel) Extract		Hamamelis Virginiana (Witch Hazel) Flower Water		Hamamelis Virginiana (Witch Hazel) Leaf Extract[f]	
Total/range	**125**	**0.00005-4.3**	**393**	**0.000013-1.8**	**39**	**NR**	**218**	**0.00018-0.011**
Duration of use								
Leave-on	89	0.00005-4.3	305	0.00003-1.8	18	NR	143	0.00018-0.011
Rinse-off	35	0.00005-0.072	86	0.000013-1.8	20	NR	68	0.00035-0.01
Diluted for (bath) use	1	NR	2	0.000013-0.0001	1	NR	7	NR
Exposure type								
Eye area	14	NR	18	0.1	3	NR	11	NR
Incidental ingestion	1	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-sprays	23[a]; 26[b]	0.18[a]	2; 95[a]; 138[b]	0.00003-0.03; 0.0013[a]	4[a]; 6[b]	NR	1; 43[a]; 64[b]	0.00035[a]
Incidental inhalation-powders	NR	0.004-4.3[c]	1; 138[b]	0.0001-1.8[c]	NR	NR	1; 64[b]	0.0018-0.011[c]
Dermal contact	121	0.00005-4.3	383	0.000013-1.8	39	NR	199	0.00018-0.011
Deodorant (underarm)	3[a]	NR	4[a]	0.0013[d]; 0.0013[e]	NR	NR	6[a]	0.00018[d]
Hair-noncoloring	1	NR	7	0.0001-0.3	NR	NR	19	0.00035-0.00042
Hair-coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	2	NR	2	NR	NR	NR	NR	NR
Mucous Membrane	6	NR	12	0.000013-1	7	NR	21	NR
Baby	1	NR	NR	NR	NR	NR	NR	NR

	Hamamelis Virginiana (Witch Hazel) Leaf Water		Hamamelis Virginiana (Witch Hazel) Water		Hamamelis Virginiana (Witch Hazel) Bark Extract[g]		Witch Hazel[g]	
Total/range	**NR**	**0.67-4.1**	**376**	**0.00008-43**	**1**	**NS**	**38**	**NS**
Duration of use								
Leave-on	NR	NR	244	0.00008-43	NR	NS	26	NS
Rinse-off	NR	0.67-4.1	122	0.00066-33.3	1	NS	10	NS
Diluted for (bath) use	NR	NR	10	0.43	NR	NS	2	NS
Exposure type								
Eye area	NR	NR	18	0.04-30.6	NR	NS	2	NS
Incidental ingestion	NR	NR	5	0.1-30.6	NR	NS	NR	NS
Incidental Inhalation-sprays	NR	NR	94[a]; 74[b]	0.00008-25.8; 0.00086-6.1[a]; 0.0086[b]	NR	NS	2; 8[a]; 5[b]	NS
Incidental inhalation-powders	NR	NR	2[c]; 74[b]	0.043-0.093; 0.00066-8.5[c]; 0.0086[b]	NR	NS	5[b]	NS
Dermal contact	NR	4.1-5	352	0.00008-43	1	NS	31	NS
Deodorant (underarm)	NR	NR	15[a]	0.086-5.2[d]	NR	NS	6[a]	NS
Hair-noncoloring	NR	NR	16	0.26-2.5	NR	NS	6	NS
Hair-coloring	NR	NR	NR	NR	NR	NS	NR	NS
Nail	NR	NR	1	4.3	NR	NS	1	NS
Mucous Membrane	NR	NR	45	0.0086-30.6	NR	NS	4	NS
Baby	NR	NR	4	NR	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.

Table 8. Frequency of use according to duration and exposure of *Hamamelis virginiana* (witch hazel)-derived ingredients.[1,2]

[d] Not spray.
[e] Spray.
[f] The VCRP had entries for "Witch Hazel Leaf Extract" and Hamamelis Virginiana (Witch Hazel) Leaf Extract, which are combined here.
[g] Listed in the VCRP but are not cosmetic ingredient names according to the wINCI *Dictionary*.

References

1. Personal Care Products Council. 10-16-2017. Updated Concentration of Use by FDA Product Category: Witch Hazel-Derived Ingredients.

2. U.S. Food and Drug Administration Center for Food Safety & Applied Nutrition (CFSAN). Voluntary Cosmetic Registration Program - Frequency of Use of Cosmetic Ingredients. College Park, MD, 2018.

2018 VCRP Data for *Hamamelis virginiana* (witch hazel)-Derived Ingredients

01A - Baby Shampoos	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	1
02B - Bubble Baths	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	1
03D - Eye Lotion	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	7
03E - Eye Makeup Remover	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	1
03G - Other Eye Makeup Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	6
07C - Foundations	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	1
07E - Lipstick	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	1
08B - Cuticle Softeners	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	1
08G - Other Manicuring Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	1
10B - Deodorants (underarm)	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	3
10E - Other Personal Cleanliness Products	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	4
11A - Aftershave Lotion	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	2
11E - Shaving Cream	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	4
11G - Other Shaving Preparation Products	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	1
12A - Cleansing	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	13
12B - Depilatories	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	1
12C - Face and Neck (exc shave)	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	24
12D - Body and Hand (exc shave)	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	2
12F - Moisturizing	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	12
12G - Night	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	1
12H - Paste Masks (mud packs)	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	10
12I - Skin Fresheners	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	7
12J - Other Skin Care Preps	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	18
13B - Indoor Tanning Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK/LEAF/TWIG EXTRACT	3
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02C - Bath Capsules	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	2
03D - Eye Lotion	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	6
03E - Eye Makeup Remover	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	1
03F - Mascara	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	1
03G - Other Eye Makeup Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	10
04C - Powders (dusting and talcum, excluding aftershave talc)	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	1
04E - Other Fragrance Preparation	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	1
05A - Hair Conditioner	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	1
05B - Hair Spray (aerosol fixatives)	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	1
05F - Shampoos (non-coloring)	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	3
05G - Tonics, Dressings, and Other Hair Grooming Aids	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	2
07C - Foundations	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	4
07F - Makeup Bases	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	1
07H - Makeup Fixatives	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	1
07I - Other Makeup Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	1
08G - Other Manicuring Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	2
10A - Bath Soaps and Detergents	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	7
10B - Deodorants (underarm)	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	4
10E - Other Personal Cleanliness Products	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	3
11A - Aftershave Lotion	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	7
11G - Other Shaving Preparation Products	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	4
12A - Cleansing	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	43
12B - Depilatories	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	8
12C - Face and Neck (exc shave)	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	129
12D - Body and Hand (exc shave)	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	9
12F - Moisturizing	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	71
12G - Night	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	5

12H - Paste Masks (mud packs)	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	16
12I - Skin Fresheners	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	12
12J - Other Skin Care Preps	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	32
13B - Indoor Tanning Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) EXTRACT	5
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02A - Bath Oils, Tablets, and Salts	HAMAMELIS VIRGINIANA (WITCH HAZEL) FLOWER WATER	1
03D - Eye Lotion	HAMAMELIS VIRGINIANA (WITCH HAZEL) FLOWER WATER	2
03G - Other Eye Makeup Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) FLOWER WATER	1
07A - Blushers (all types)	HAMAMELIS VIRGINIANA (WITCH HAZEL) FLOWER WATER	1
07C - Foundations	HAMAMELIS VIRGINIANA (WITCH HAZEL) FLOWER WATER	1
10A - Bath Soaps and Detergents	HAMAMELIS VIRGINIANA (WITCH HAZEL) FLOWER WATER	6
12A - Cleansing	HAMAMELIS VIRGINIANA (WITCH HAZEL) FLOWER WATER	11
12C - Face and Neck (exc shave)	HAMAMELIS VIRGINIANA (WITCH HAZEL) FLOWER WATER	3
12D - Body and Hand (exc shave)	HAMAMELIS VIRGINIANA (WITCH HAZEL) FLOWER WATER	3
12F - Moisturizing	HAMAMELIS VIRGINIANA (WITCH HAZEL) FLOWER WATER	4
12H - Paste Masks (mud packs)	HAMAMELIS VIRGINIANA (WITCH HAZEL) FLOWER WATER	3
12J - Other Skin Care Preps	HAMAMELIS VIRGINIANA (WITCH HAZEL) FLOWER WATER	3
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02B - Bubble Baths	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	5
02D - Other Bath Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	2
03D - Eye Lotion	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	6
03G - Other Eye Makeup Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	5
05A - Hair Conditioner	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	8
05B - Hair Spray (aerosol fixatives)	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	1
05F - Shampoos (non-coloring)	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	8
05I - Other Hair Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	1
07B - Face Powders	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	1
10A - Bath Soaps and Detergents	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	10
10B - Deodorants (underarm)	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	6
10E - Other Personal Cleanliness Products	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	4
11A - Aftershave Lotion	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	3
11E - Shaving Cream	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	4
12A - Cleansing	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	23
12C - Face and Neck (exc shave)	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	45
12D - Body and Hand (exc shave)	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	16
12F - Moisturizing	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	20
12G - Night	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	4
12H - Paste Masks (mud packs)	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	6
12I - Skin Fresheners	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	13
12J - Other Skin Care Preps	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	12
13B - Indoor Tanning Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT	3
NOTE: This was combined with WITCH HAZEL LEAF EXTRACT (not an INCI name)		**206**

05F - Shampoos (non-coloring)	WITCH HAZEL LEAF EXTRACT (Not an INCI name)	1
12A - Cleansing	WITCH HAZEL LEAF EXTRACT	1
12C - Face and Neck (exc shave)	WITCH HAZEL LEAF EXTRACT	2
12D - Body and Hand (exc shave)	WITCH HAZEL LEAF EXTRACT	1
12F - Moisturizing	WITCH HAZEL LEAF EXTRACT	1
12H - Paste Masks (mud packs)	WITCH HAZEL LEAF EXTRACT	3
12I - Skin Fresheners	WITCH HAZEL LEAF EXTRACT	2
12J - Other Skin Care Preps	WITCH HAZEL LEAF EXTRACT	1
Note: This was combined with HAMAMELIS VIRGINIANA (WITCH HAZEL) LEAF EXTRACT		**12**

01A - Baby Shampoos	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	1
01B - Baby Lotions, Oils, Powders, and Creams	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	2
01C - Other Baby Products	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	1
02A - Bath Oils, Tablets, and Salts	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	2
02B - Bubble Baths	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	5
02D - Other Bath Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	3
03D - Eye Lotion	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	7
03E - Eye Makeup Remover	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	1
03F - Mascara	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	2
03G - Other Eye Makeup Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	8
05A - Hair Conditioner	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	1
05C - Hair Straighteners	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	2
05D - Permanent Waves	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	2
05F - Shampoos (non-coloring)	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	4
05G - Tonics, Dressings, and Other Hair Grooming Aids	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	4
05I - Other Hair Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	2
07F - Makeup Bases	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	2

07H - Makeup Fixatives	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	1
07I - Other Makeup Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	2
08B - Cuticle Softeners	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	1
09B - Mouthwashes and Breath Fresheners	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	5
10A - Bath Soaps and Detergents	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	25
10B - Deodorants (underarm)	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	15
10E - Other Personal Cleanliness Products	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	5
11A - Aftershave Lotion	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	18
11G - Other Shaving Preparation Products	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	6
12A - Cleansing	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	48
12C - Face and Neck (exc shave)	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	59
12D - Body and Hand (exc shave)	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	15
12F - Moisturizing	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	38
12G - Night	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	7
12H - Paste Masks (mud packs)	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	22
12I - Skin Fresheners	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	29
12J - Other Skin Care Preps	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	20
13A - Suntan Gels, Creams, and Liquids	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	2
13B - Indoor Tanning Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	7
13C - Other Suntan Preparations	HAMAMELIS VIRGINIANA (WITCH HAZEL) WATER	2
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12A - Cleansing	HAMAMELIS VIRGINIANA (WITCH HAZEL) BARK EXTRACT (Not an INCI name)	1

02A - Bath Oils, Tablets, and Salts	WITCH HAZEL (Not an INCI name)	2
03D - Eye Lotion	WITCH HAZEL	1
03G - Other Eye Makeup Preparations	WITCH HAZEL	1
04A - Cologne and Toilet waters	WITCH HAZEL	1
04B - Perfumes	WITCH HAZEL	1
05A - Hair Conditioner	WITCH HAZEL	2
05F - Shampoos (non-coloring)	WITCH HAZEL	3
05G - Tonics, Dressings, and Other Hair Grooming Aids	WITCH HAZEL	1
08C - Nail Creams and Lotions	WITCH HAZEL	1
10A - Bath Soaps and Detergents	WITCH HAZEL	1
10B - Deodorants (underarm)	WITCH HAZEL	6
10E - Other Personal Cleanliness Products	WITCH HAZEL	1
12A - Cleansing	WITCH HAZEL	2
12B - Depilatories	WITCH HAZEL	1
12C - Face and Neck (exc shave)	WITCH HAZEL	2
12D - Body and Hand (exc shave)	WITCH HAZEL	3
12F - Moisturizing	WITCH HAZEL	2
12I - Skin Fresheners	WITCH HAZEL	5
12J - Other Skin Care Preps	WITCH HAZEL	2
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No reported uses in the 2018 VCRP:
Hamamelis Virginiana (Witch Hazel) Bark/Leaf Extract
Hamamelis Virginiana (Witch Hazel) Bark/Twig Extract
Hamamelis Virginiana (Witch Hazel) Leaf Water

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Memorandum

To: CIR Expert Panel Members and Liaisons
From: Christina L. Burnett, Senior Scientific Writer/Analyst
Date: February 23, 2018
Subject: Wave 2 – Malic Acid

CIR has received 2018 FDA VCRP data. Because the Safety Assessment on Malic Acid and Sodium Malate is in the Draft Final Report stage, we are submitting an updated Use Table along with the raw VCRP data (*maacid032018wave2_data*). Total reported uses for both ingredients have decreased since 2017. Malic Acid was used in 238 formulations last year; it is reported to be used in 228 formulations this year. Uses of Sodium Malate have decreased by 2 since 2017.

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Table 1. Current and historical frequency and concentration of use of Malic Acid and Sodium Malate according to duration and exposure.

	Malic Acid			
	# of Uses		*Max Conc of Use (%)*	
	2018	**1998**	**2016**	**1984** [#]
Totals*	**228**	**47**	**0.000012-50**	**< 0.1-1**
Leave-On	*114*	*31*	*0.000012-2.1*	*< 0.1-1*
Rinse-Off	*112*	*16*	*0.00013-4*	*<0.1-1*
Diluted for (Bath) Use	*2*	*NR*	*0.006-50*	*NR*
Eye Area	4	NR	0.000012	NR
Incidental Ingestion	4	NR	0.0006-0.55	NR
Incidental Inhalation-Spray	1; 26[a]; 26[b]	2; 3[a]; 3[b]	0.0011-2.1; 0.00013-1.9[a]	NR
Incidental Inhalation-Powder	26[b]	3[b]	0.0004-1[c]	NR
Dermal Contact	109	7	0.000012-50	NR
Deodorant (underarm)	NR	NR	NR	NR
Hair - Non-Coloring	86	18	0.00013-4	0.1-1
Hair-Coloring	14	NR	0.00015-0.05	< 0.1-1
Nail	15	22	0.3	< 0.1-1
Mucous Membrane	15	NR	0.0006-50	NR
Baby Products	9	1	NR	NR
	Sodium Malate			
	# of Uses		*Max Conc of Use (%)*	
	2018	**1998**	**2017 (disodium)**	**1984** [#]
Totals*	**3**	**1**	**0.02**	**NR**
Leave-On	*2*	*1*	*0.02*	*NR*
Rinse-Off	*1*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*
Eye Area	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR
Incidental Inhalation-Spray	1[a]	1[b]	NR	NR
Incidental Inhalation-Powder	NR	1[b]	NR	NR
Dermal Contact	3	1	0.02	NR
Deodorant (underarm)	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR
Nail	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR

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

[#] At the time of the original safety assessment, concentration of use data were not reported by the FDA; however, the FDA provided historic data

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

[b] Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories

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

NR – no reported use

2018 FDA VCRP RAW DATA

01C - Other Baby Products	MALIC ACID	9
02A - Bath Oils, Tablets, and Salts	MALIC ACID	2
03B - Eyeliner	MALIC ACID	3
03E - Eye Makeup Remover	MALIC ACID	1
04E - Other Fragrance Preparation	MALIC ACID	1
05A - Hair Conditioner	MALIC ACID	38
05E - Rinses (non-coloring)	MALIC ACID	1
05F - Shampoos (non-coloring)	MALIC ACID	31
05G - Tonics, Dressings, and Other Hair Grooming Aids	MALIC ACID	3
05I - Other Hair Preparations	MALIC ACID	13
06C - Hair Rinses (coloring)	MALIC ACID	10
06D - Hair Shampoos (coloring)	MALIC ACID	4
07E - Lipstick	MALIC ACID	4
08A - Basecoats and Undercoats	MALIC ACID	1
08B - Cuticle Softeners	MALIC ACID	2
08E - Nail Polish and Enamel	MALIC ACID	9
08G - Other Manicuring Preparations	MALIC ACID	3
10A - Bath Soaps and Detergents	MALIC ACID	5
10E - Other Personal Cleanliness Products	MALIC ACID	4
12A - Cleansing	MALIC ACID	13
12C - Face and Neck (exc shave)	MALIC ACID	14
12D - Body and Hand (exc shave)	MALIC ACID	12
12F - Moisturizing	MALIC ACID	19
12G - Night	MALIC ACID	4
12H - Paste Masks (mud packs)	MALIC ACID	5
12J - Other Skin Care Preps	MALIC ACID	17
12A - Cleansing	SODIUM MALATE	1
12F - Moisturizing	SODIUM MALATE	1
12J - Other Skin Care Preps	SODIUM MALATE	1

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Memorandum

To: CIR Expert Panel Members and Liaisons
From: Wilbur Johnson, Jr.
Senior Scientific Analyst
Date: February 23, 2018
Subject: Wave 2 Data on *Mentha piperita* (Peppermint)-Derived Ingredients

The 2018 VCRP data on *Mentha piperita* (peppermint)-derived ingredients that were received from the FDA are being submitted as an attachment (*pepper032018fda file*) to this memorandum. A data summary document (*pepper032018wave2studysummaries*) is also attached for the Panel's review.

These data will be added to the safety assessment after the Panel meeting.

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Wave 2 Data on Mentha Piperita (Peppermint)-Derived Ingredients

Use

Cosmetic

The Use section of the draft report on Mentha Piperita-Derived Ingredients will be revised to include 2018 VCRP data, and these data are presented in Table 1 on the following page.[1] These use frequency data will replace the 2017 VCRP data that are included in the Use section of the draft final report that was submitted to the Panel earlier this month. The following information relates to changes (product category additions/deletions) in the VCRP data that should be noted:

- Mentha Piperita (Peppermint) Extract is being used in the Hair Straighteners (5C) product category (1 rinse-off product).
- Mentha Piperita (Peppermint) Leaf Extract is being used in the Other Eye Makeup Preparations (3G) product category (1 leave-on product).
- Mentha Piperita (Peppermint) Leaf Extract is no longer being used in the Nail Polish and Enamel Removers (8F, rinse-off products) product category.
- Mentha Piperita (Peppermint) Leaf Water is being used in the Rinses (non-coloring) (5E) product category (1 rinse-off product)
- Mentha Piperita (Peppermint) Oil is no longer being used in the Wave Sets (5H, rinse-off products) product category.
- Mentha Piperita (Peppermint) Oil is no longer being used in the Night Skin Care Preparations (12G, leave-on products) product category

The new VCRP data indicate that the greatest use frequency is being reported for Mentha Piperita (Peppermint) Oil (815 uses: 432 leave-on, 349 rinse-off, and 34 diluted for (bath) use).

Table 1. Frequency and Concentration of Use of *Mentha piperita* (peppermint)-derived Ingredients According to Duration and Exposure.[1]

	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	Mentha Piperita (Peppermint) Oil				**Mentha Piperita (Peppermint) Leaf Extract**			
	2018	**1998**	**2017**	**1997**	**2018**	**1998**	**2017**	**1997**
Totals*	**815**	**102**	**0.0001-5**	**0.1-3**	**205**	**35**	**0.000075-0.5**	**NR**
Duration of Use								
Leave-On	*432*	*52*	*0.0006-5*	*0.2-2*	*126*	*10*	*0.000075-0.5*	*NR*
Rinse-Off	*349*	*44*	*0.0001-1.9*	*0.1-3*	*78*	*24*	*0.0001-0.2*	*NR*
Diluted for (Bath) Use	*34*	*6*	*0.018-3.9*	*NR*	*1*	*1*	*NR*	*NR*
Exposure Type								
Eye Area	4	NR	0.00094	NR	5	NR	0.0018	NR
Incidental Ingestion	207	24	0.05-2.9	0.2-1.2	8	NR	0.00075-0.5	NR
Incidental Inhalation-Spray	22;114[a]	NR;23[a]	0.017-1;0.002-1.1[a]	NR	5;36[a]	NR;2[a]	0.00041-0.0046;0.00057-0.026[a]	NR
Incidental Inhalation-Powder	1	NR	0.01-1	NR	3	NR	0.0018	NR
Dermal Contact	457	75	0.0006-5	0.1-2	147	22	0.000075-0.2	NR
Deodorant (underarm)	4	NR	NR	NR	NR	NR	0.0018	NR
Hair - Non-Coloring	144	1	0.0001-0.96	3	48	13	0.00018-0.2	NR
Hair-Coloring	NR	NR	0.0024	NR	NR	NR	0.032	NR
Nail	7	2	0.00064-1.5	NR	1	NR	NR	NR
Mucous Membrane	310	30	0.0025-3.9	0.2-1.2	7	6	0.00075-0.5	NR
Baby Products	1	NR	0.2	NR	NR	NR	NR	NR
	Mentha Piperita (Peppermint) Leaf				**Mentha Piperita (Peppermint) Leaf Water**			
	2018	**1998**	**2017**	**1997**	**2018**	**1998**	**2017**	**1997**
Totals*	**NR**	**NR**	**0.0002-1.6**	**NR**	**16**	**NR**	**0.00013-40**	**NR**
Duration of Use								
Leave-On	*NR*	*NR*	*0.001*	*NR*	*9*	*NR*	*0.00013-40*	*NR*
Rinse-Off	*NR*	*NR*	*0.0002-1.6*	*NR*	*7*	*NR*	*0.00021-0.00067*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	***NR***	*NR*
Exposure Type								
Eye Area	NR	NR	NR	NR	2	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	NR	NR;0.001[a]	NR	NR;4[a]	NR	NR;0.00043-10[a]	NR
Incidental Inhalation-Powder	NR	NR	NR	NR	NR	NR	NR	NR
Dermal Contact	NR	NR	0.001-1.6	NR	13	NR	0.00013-40	NR
Deodorant (underarm)	NR	NR	NR	NR	1	NR	15	NR
Hair - Non-Coloring	NR	NR	0.0002-0.023	NR	1	NR	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	0.001-0.16	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR
	Mentha Piperita (Peppermint) Extract							
	2018		**2017**					
Totals*	**82**		**0.00006-7.9**					
Duration of Use								
Leave-On	*49*		*0.00006-7.9*					
Rinse-Off	*32*		*0.0001-1*					
Diluted for (Bath) Use	*1*		*1*					
Exposure Type								
Eye Area	NR		NR					
Incidental Ingestion	4		0.0099-3.4					
Incidental Inhalation-Spray	10; 22[a]		1.3; 0.005-1[a]					
Incidental Inhalation-Powder	NR		NR					
Dermal Contact	73		0.00006-7.9					
Deodorant (underarm)	2		1					
Hair - Non-Coloring	5		0.0004-1					
Hair-Coloring	NR		NR					
Nail	NR		NR					
Mucous Membrane	7		0.0099-3.4					
Baby Products	NR		NR					

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

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

NR - no reported use

References

1. U.S. Food and Drug Administration Center for Food Safety & Applied Nutrition (CFSAN). Voluntary Cosmetic Registration Program - Frequency of Use of Cosmetic Ingredients. College Park, MD, 2018.

2018 FDA VCRP Data

Mentha Piperita (Peppermint) Oil

01B - Baby Lotions, Oils, Powders, and Creams	1
02A - Bath Oils, Tablets, and Salts	24
02B - Bubble Baths	2
02D - Other Bath Preparations	8
03G - Other Eye Makeup Preparations	4
04B - Perfumes	2
04E - Other Fragrance Preparation	19
05A - Hair Conditioner	40
05B - Hair Spray (aerosol fixatives)	1
05F - Shampoos (non-coloring)	59
05G - Tonics, Dressings, and Other Hair Grooming Aids	27
05I - Other Hair Preparations	17
07E - Lipstick	89
07I - Other Makeup Preparations	34
08B - Cuticle Softeners	2
08E - Nail Polish and Enamel	2
08G - Other Manicuring Preparations	3
09A - Dentifrices	28
09B - Mouthwashes and Breath Fresheners	17
09C - Other Oral Hygiene Products	73
10A - Bath Soaps and Detergents	45
10B - Deodorants (underarm)	4
10E - Other Personal Cleanliness Products	24
11A - Aftershave Lotion	3
11B - Beard Softeners	2
11D - Preshave Lotions (all types)	2
11E - Shaving Cream	10
11G - Other Shaving Preparation Products	2
12A - Cleansing	33
12C - Face and Neck (exc shave)	30
12D - Body and Hand (exc shave)	42
12E - Foot Powders and Sprays	8
12F - Moisturizing	61
12H - Paste Masks (mud packs)	16
12I - Skin Fresheners	9
12J - Other Skin Care Preps	72
Total	**815**

Mentha Piperita (Peppermint) Leaf (No Posting)

Mentha Piperita (Peppermint) Leaf Extract

02D - Other Bath Preparations	1
03D - Eye Lotion	4
03G - Other Eye Makeup Preparations	1

04C - Powders (dusting and talcum, excluding aftershave talc)	1
04E - Other Fragrance Preparation	4
05A - Hair Conditioner	22
05B - Hair Spray (aerosol fixatives)	1
05F - Shampoos (non-coloring)	17
05G - Tonics, Dressings, and Other Hair Grooming Aids	3
05I - Other Hair Preparations	5
07B - Face Powders	2
07C - Foundations	2
07D - Leg and Body Paints	1
07E - Lipstick	5
07I - Other Makeup Preparations	2
08G - Other Manicuring Preparations	1
09A - Dentifrices	2
09B - Mouthwashes and Breath Freshners	1
10A - Bath Soaps and Detergents	4
10E - Other Personal Cleanliness Products	6
11A - Aftershave Lotion	3
11G - Other Shaving Preparation Products	1
12A - Cleansing	16
12C - Face and Neck (exc shave)	26
12D - Body and Hand (exc shave)	6
12E - Foot Powders and Sprays	1
12F - Moisturizing	18
12G - Night	2
12H - Paste Masks (mud packs)	8
12I - Skin Fresheners	11
12J - Other Skin Care Preps	27
13A - Suntan Gels, Creams, and Liquids	1
Total	**205**

Mentha Piperita (Peppermint) Leaf Water

03G - Other Eye Makeup Preparations	2
05E - Rinses (non-coloring)	1
10A - Bath Soaps and Detergents	1
10B - Deodorants (underarm)	1
11G - Other Shaving Preparation Products	1
12A - Cleansing	3
12C - Face and Neck (exc shave)	1
12F - Moisturizing	3
12H - Paste Masks (mud packs)	1
12I - Skin Fresheners	1
12J - Other Skin Care Preps	1
Total	**16**

Mentha Piperita (Peppermint) Extract

02A - Bath Oils, Tablets, and Salts	1
05A - Hair Conditioner	1
05C - Hair Straighteners	1
05E - Rinses (non-coloring)	1
05F - Shampoos (non-coloring)	1
05G - Tonics, Dressings, and Other Hair Grooming Aids	1
07E - Lipstick	2
07I - Other Makeup Preparations	1
09B - Mouthwashes and Breath Fresheners	2
10A - Bath Soaps and Detergents	5
10B - Deodorants (underarm)	2
10E - Other Personal Cleanliness Products	4
11A - Aftershave Lotion	1
11E - Shaving Cream	3
12A - Cleansing	4
12C - Face and Neck (exc shave)	13
12D - Body and Hand (exc shave)	2
12E - Foot Powders and Sprays	3
12F - Moisturizing	18
12H - Paste Masks (mud packs)	10
12I - Skin Fresheners	1
12J - Other Skin Care Preps	5
Total	**82**

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Memorandum

To: CIR Expert Panel Members and Liaisons
From: Wilbur Johnson, Jr.
Senior Scientific Analyst
Date: February 23, 2018
Subject: Wave 2 Data on Polyol Phosphates

The data listed below (in *phytic032018data5 file*) on Sodium Phytate were received from the Council and are being submitted as an attachment to this memorandum. Other data mentioned below (see attachment) include 2018 FDAVCRP data on polyol phosphates (*phytic032018fda file).* A data summary document (*phytic032018wave2studysummaries*) is also attached for the Panel's review. The data that were received include:

phytic032018data5 file:

- *in vitro* genotoxicity data on a Sodium Phytate trade name material consisting of 50% water and 1% ethanol
- *in vitro* irritation and sensitization data on this trade name material (dried material)
- *in vitro* ocular irritation data on this trade name material (as is and dried material)

phytic032018fda file:

- 2018 FDA VCRP data

These data will be added to the safety assessment after the Panel meeting.

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Wave 2 Data on Polyol Phosphates

Use

Cosmetic

The Use section of the draft report on Polyol Phosphates will be revised to include 2018 VCRP data, and these data are presented in Table1 in this document.[1] These use frequency data will replace the 2017 VCRP data that are included in the Use section of the draft report that was submitted to the Panel earlier this month. The following information relates to changes (product category additions/deletions) in the VCRP data that should be noted:

- Sodium Phytate is now being used in the Other Fragrance Preparation (4E) product category (3 leave-on products) and in the Other Oral Hygiene Products (9C) product category (1 rinse-off product).
- Phytic Acid is now being used in the Other Makeup Preparations (7I) product category (1 leave-on product)
- Phytic Acid is no longer being used in the following product categories: Bath Soaps and Detergents (10A, rinse-off products), Other Personal Cleanliness Products (10E, rinse-off products), and Skin Fresheners (12I, leave-on products).

The new VCRP indicate that the greatest use frequency is being reported for Sodium Phytate (412 uses: 259 leave-on, 146 rinse-off, and 7 diluted for (bath) use.

GENOTOXICITY STUDIES

In Vitro

Sodium Phytate

The genotoxicity of a Sodium Phytate (concentration not stated) trade name material consisting of 50% water and 1% ethanol was evaluated in the Ames test using the following *Salmonella typh*imurium strains: TA 97a, TA 98, TA 100, TA 102, and TA 1535.[2] The test material, in deionized water, was evaluated at doses up to 4995 µg/plate with and without metabolic activation. Results were negative for genotoxicity, with and without metabolic activation, throughout the range of doses tested. There also was no evidence of bacterial toxicity. All positive controls (not stated) were genotoxic with and without metabolic activation. A second experiment (pre-incubation method, modification of Ames test) was performed to confirm the results of the first. The test material was evaluated at doses up to 5013 µg/plate, with and without metabolic activation. There were no signs of genotoxicity or bacterial toxicity with and without metabolic activation. All positive controls (not stated) were genotoxic with and without metabolic activation.

DERMAL IRRITATION AND SENSITIZATION STUDIES

Irritation

In Vitro

Sodium Phytate

The skin corrosion potential of a Sodium Phytate trade name material consisting of 50% water and 1% ethanol was evaluated in an *in vitro* skin model (reconstructed human epidermis) test for skin corrosion.[2] The concentration of Sodium Phytate in the trade name material was not stated. Prior to testing, the trade name material was dried, yielding 0.1% to 10% residual water. The test was performed in accordance with the Organization for Economic Co-operation and Development (OECD) 431 protocol. Two tissues of the human skin model were treated with the dried test material (applied and spread to match the tissue size [not stated]). One tissue was treated with 26.2 mg (3-minute incubation) and 25.8 mg (1-h incubation). The second tissue was treated with 26 mg (3-minute incubation) and 26.2 mg (1-h incubation). Each dose was applied to tissue with 25 µl demineralized water (mean concentration = 1.042 g/ml). Dimineralized water served as the negative control, and 8M potassium hydroxide served as the positive control. Tissues were rinsed at the end of the incubation period, and cell viability was evaluated by the addition of 3-(4,5-dimethylthiazole-2-yl)-2,5-diphenyl tetrazolium bromide (MTT), which can be reduced to a blue fomazan. The production of formazan was evaluated by measuring the optical density of the resulting solution. After 3 minutes of treatment with the test material, the mean value of relative tissue viability was reduced to 80.6%. This value was above the threshold for corrosion potential (50%). After 1 h of treatment, the mean value of relative tissue viability was reduced to 86.9% (above the threshold for corrosion potential [15%]). The dried test material was classified as non-corrosive to the skin. The positive control was classified as corrosive.

The skin irritation potential of a dried Sodium Phytate trade name material (See preceding test) was also evaluated *in vitro* using the reconstructed human epidermis test method (OECD 439 protocol).[2] The tissues were moistened with 25 µl of Dulbecco's phosphate-buffered saline (DPBS) prior to application of the test material (doses range: 25.3 to 26.3 mg) and spreading it to match the tissue size (0.63 cm^2). DPBS served as the negative control, and 5% sodium dodecyl sulfate solution served as the positive control. At the end of the 60-minute application period for the test material, the mean value of relative tissue viability was reduced to 84.7%. This value is above the threshold for skin irritation potential (50%). The dried test material was classified as non-irritating to the skin. The positive control caused skin irritation.

Sensitization

In Vitro

Sodium Phytate

The skin sensitization potential of a dried Sodium Phytate trade name material (described in preceding section) was evaluated in the *in vitro* ArE-Nrf2 Luciferase test (OECD 442d protocol, 2 experiments) for skin sensitization.[2] This test evaluates the potential for the test material to activate the Nrf2 transcription factor (sensitizing potential) using the LuSens cell line. The dried test material was tested at concentrations ranging from 54 µg/ml to 333 µg/ml in the first experiment, and at concentrations ranging from 54 µg/ml to 278 µg/ml in the second experiment. The authors noted that these test concentrations were associated with a viability of ≥ 70%, meaning that it was possible for the test material to be evaluated for luciferase induction. Lactic acid (5000 µM) served as the negative control, and p-Phenylenediamine served as the positive control. No substantial and reproducible dose-dependent increase in luciferase induction above 1.5-fold was observed in both experiments up to the maximum test concentration. It was concluded that the dried test material was negative in the LuSens assay, and, therefore, was considered as not having the potential to activate the Nrf2 transcription factor (no sensitizing potential). Results for the positive control were not included.

OCULAR IRRITATION STUDIES

In Vitro

Sodium Phytate

The ocular irritation potential of a dried Sodium Phytate trade name material (See Skin Irritation section above) was evaluated in the bovine corneal opacity and permeability test (OECD 437 protocol, 3 experiments).[2] The dried test material (750 µl), at a concentration of 20% in Hank's Balanced Salt Solution (HBSS), was applied for 4 h to the corneas of eyes that had been incubated (with cMEM [not defined] without phenol red) for 1 h. HBSS served as the negative control, and 20% imidazole solution served as the positive control. Opacity and permeability were measured at the end of the incubation period. The calculated *in vitro* irritancy scores (IVIS) were: 5.39 (1st experiment), 2.33 (2nd experiment), and 2.91 (3rd experiment). It was noted that a score of ≤ 3 requires no classification for eye irritation or serious eye damage. The first experiment was considered insufficient for assessment because 2 of the 3 replicates yielded discordant predictions from the mean value. The authors concluded that no effects on corneas from bovine eyes treated with the dried test material were observed. The positive control caused serious eye damage.

A dried Sodium Phytate trade name material was evaluated in the bovine corneal opacity and permeability test (similar procedure, stated above) at a concentration of 2% w/w in water.[2] The incubation period was not stated. However, opacity and permeability were measured at the end of the incubation period and at 2 h post-incubation. Physiological sodium chloride served as the negative control, and 10% sodium hydroxide solution served as the positive control. No effects on the cornea were observed, and an IVIS of -0.532 (IVIS ≥ 55.1 = corrosive or severe irritant) was reported. The test substance was classified as non-corrosive and/or non-severe irritant. The positive control caused severe corneal irritation.

In another study, the ocular irritation potential of a dried Sodium Phytate trade name material (same as above) was evaluated using the reconstructed human cornea-like epithelium (RhCE) test (OECD 492 protocol, 2 experiments).[2] The tissues were moistened with 25 µl of DPBS buffer and incubated for 30 minutes. The test material was then applied (doses of 50.1 mg and 52.3 mg) for 6 h to a 3-dimensional human cornea tissue model in duplicate. Tissues were rinsed at the end of the incubation period, and cell viability was evaluated by addition of MTT, which can be reduced to formazan. Demineralized water served as the negative control, and methyl acetate served as the positive control. The first experiment was determined to be invalid because the variation between the tissue replicates of the negative control was too high, and, therefore, outside of the range of validity. Thus, only the results from the second experiment were considered valid. After treatment with the dried test material, the mean value of relative tissue viability was 66.9%. This value is above the threshold for eye irritation potential (≤ 60%). It was concluded that the dried test material was non-irritating to the eye in this test. The positive control caused eye irritation, i.e., the mean value of the relative tissue viability was 42.2% (< 50%).

The *in vitro* hen's egg chorioallantoic membrane test (HET-CAM) was used to evaluate the ocular irritation potential of a Sodium Phytate trade name material consisting of 50% water and 1% ethanol.[3] The concentration of Sodium Phytate in the trade name material was not stated. The trade name material (2% in 0.9% sodium chloride) was applied to the CAM of fertilized and incubated hen's eggs at a dose of 300 µl. An irritation value of 0 was determined, and, based on this value, it was determined that the test material can be classified as slightly irritating *in vivo*. The reference material (5% concentration) was classified as moderately irritating, demonstrating the validity of the test procedure.

TABLES

Table 1. Frequency and Concentration of Use According to Duration and Type of Exposure.[1]

	Sodium Phytate		Phytic Acid		Sodium Mannose Phosphate	
	# of Uses	Conc. (%)	# of Uses	Conc. (%)	# of Uses	Conc. (%)
Totals/Conc. Range	412	0.0099-0.5	115	0.003-2	33	0.1
Duration of Use						
Leave-On	259	0.0099-0.5	88	0.003-2	30	0.1
Rinse off	146	0.025-0.3	27	0.005-0.3	3	NR
Diluted for (bath) Use	7	NR	NR	NR	NR	NR
Exposure Type						
Eye Area	18	0.025-0.05	5	0.025-0.05	3	NR
Incidental Ingestion	2	0.5	NR	0.3	NR	NR
Incidental Inhalation- Sprays	4;121*	0.05-0.3*	27*	0.005-0.05*	12*	NR
Incidental Inhalation- Powders	1**	NR	NR	NR	NR	0.1**
Dermal Contact	352	0.0099-0.3	75	0.003-2	33	0.1
Deodorant (underarm)	NR	NR	1	NR	NR	NR
Hair - Non-Coloring	58	0.05-0.3	22	0.005	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous Membrane	43	0.3-0.5	NR	0.3	NR	NR
Baby Products	2	NR	NR	NR	NR	NR

NR = Not Reported; Totals = Rinse-off + Leave-on + Diluted for Use Product Uses
*It is possible that these products may be sprays, but it is not specified whether the reported uses are sprays.
**It is possible that these products may be powders, but it is not specified whether the reported uses are powders.
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 of total uses.

References

1. U.S. Food and Drug Administration Center for Food Safety & Applied Nutrition (CFSAN). Voluntary Cosmetic Registration Program - Frequency of Use of Cosmetic Ingredients. College Park, MD, 2018.

2. Laus GmbH. Summaries of studies of sodium phytate. Unpublished data submitted by the Personal Care Products Council on 2-8-2018. 2018.

3. Labor L + S AG. Hen's egg chorioallantoic membrane test (HET-CAM) on sodium phytate. Unpublished data submitted by the Personal Care Products Council on 2-8-2018. 2018.

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: February 8, 2018

SUBJECT: Sodium Phytate

Anonymous. 2018. Summaries of Studies of Sodium Phytate.

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February 2018

Summaries of Studies of Sodium Phytate

trade name:	dermofeel® PA-3
INCI:	Sodium Phytate, Aqua, Alcohol
Composition:	ca. 50% water and 1% Ethanol
chemical name:	Esters of sodium hydrogen phosphate with myo-Inositol, plant-derived
EC number:	238-242-6
CAS:	14306-25-3

All studies described below, with the exception of the last study (HET-CAM), were completed at Laus GmbH under GLP conditions.

In Vitro Skin Corrosion: Human Skin Model Test (OECD 431)

Test Item: dermofeel PA-3 (dried) (= dried dermofeel® PA-3 in freeze drier (Alpha 2-4 LSCplus) => 0.1-10% residual water)"

Appearance of Test Item: white solid powder

Amounts/Concentrations Applied: Tissue No.1: 26.2 mg (3 minutes incubation); 25.8 mg (1 hour incubation)

Tissue No.2: 26.0 mg (3 minutes incubation); 26.2 mg (1 hour incubation)

Test item was applied to tissue with 25 µl demineralised water (mean conc.: 1.042 g/mL)

Experimental Period of the Study: 07.08.2017 - 10.08.2017

Study report – Date of Release: 12.04.2017

Result: non-corrosive to skin

Executive Summary: One valid experiment was performed. Two tissues of the human skin model EpiDermTM were treated with the test item dermofeel PA-3 (dried) for 3 minutes and 1 hour, respectively. The test item was applied to each tissue and spread to match the tissue size. Demineralised water was used as negative control and 8M KOH was used as positive control. After treatment, the respective substance was rinsed from the tissues. Then, cell viability of the tissues was evaluated by addition of MTT, which can be reduced to a blue formazan. Formazan production was evaluated by measuring the optical density (OD) of the resulting solution.

After treatment with the negative control, the absorbance values were within the required acceptability criterion of mean OD ≥ 0.8 and ≤ 2.8 for both treatment intervals thus showing the quality of the tissues. The OD was 1.7 (3 minutes experiment) and 1.6 (1 hour experiment).

The positive control showed clear corrosive effects for both treatment intervals. The mean relative tissue viability value was reduced to 4.8 % for the 1 hour treatment. After 3 minutes treatment with the test item, the mean value of relative tissue viability was reduced to 80.6 %. This value is above the threshold for corrosion potential (50%). After 1 hour treatment, mean value of relative tissue viability was reduced to 86.9%. This value, too, is above the threshold for corrosion potential (15%).

Therefore, dermofeel PA-3 (dried) is considered non-corrosive to skin in the Reconstructed Human Epidermis (RHE) Test Method.

In Vitro Skin Irritation: Reconstructed Human Epidermis Test Method (OECD 439)

Test Item: dermofeel PA-3 (dried) (= dried dermofeel® PA-3 in freeze drier (Alpha 2-4 LSCplus) => 0.1-10% residual water)

Appearance of Test Item: white solid powder

Amounts/Concentrations Applied: 26.1 mg (Tissue No. 1)
26.3 mg (Tissue No. 2)
25.3 mg (Tissue No. 3)

The tissues were wetted with 25 µL DPBS buffer before applying the test item and spreading it to match the tissue size (0.63 cm^2).

Experimental Period of the Study: 11.09.2017 - 15.09.2017

Study Report – Date of Release: 12/11/2017

Result: non-irritant to skin

Executive Summary: One valid experiment was performed.
Three tissues of the human skin model EpiDermTM were treated with the test item dermofeel PA-3 (dried) for 60 minutes. The test item was applied directly to each tissue and spread to match the tissue size (0.63 cm^2; as indicated by the supplier). DPBS-buffer was used as negative control and 5% SDS

solution was used as positive control. After treatment with the negative control, the absorbance values were within the required acceptability criterion of 0.8 ≤ mean OD ≤ 2.8, OD was 2.0. The positive control showed clear irritating effects. The mean value of relative tissue viability was reduced to 2.5% (required: ≤ 20%). The variation within the tissue replicates of negative, control, positive control and test item was acceptable (required: ≤ 18%). For these reasons, the experiment was considered to be valid.

After the treatment with the test item, the mean value of relative tissue viability was reduced to 84.7 %. This value is above the threshold for skin irritation potential (50%). Test items that induce values above the threshold of 50% are considered non-irritant to skin.

Therefore, dermofeel PA-3 (dried) is considered non-irritant to skin in the Reconstructed human Epidermis (RhE) Test Method.

Bovine Corneal Opacity and Permeability Test Method for Identifying Ocular Corrosives and Severe Irritants (OECD 437)

Test Item: dermofeel PA-3 (dried) (=> freeze dried dermofeel® PA-3 in freeze drier (Alpha 2-4 L5Cplus)) => 0.1-10% residual water"

Appearance of Test Item: white solid powder

Amounts/Concentrations Applied: 750 µL of the test item (dermofeel PA-3 (dried)) was tested as solution at 20% concentration in HBSS.

Experimental Period of the Study: 14.09.2017 / 21. 09.2017 / 28.09.2017

Study Report – Date of Release: 12.12.2017

Result: no effects on the cornea of the bovine eye

Executive Summary: Three experiments were performed.
The first experiment was considered as insufficient for assessment, because two of the three replicates gave discordant predictions from the mean value. Therefore, the experiment was repeated and the second experiment was sufficient for assessment, but the results showed a non-concordant prediction from the mean result of the first experiment. Based on these results, a third experiment was performed; this experiment confirmed the results of the second experiment.

All experiments are listed in this report. For all experiments, bovine corneas were used. They were collected from slaughtered cattle which were between 12 and 60 months old. The test item dermofeel PA-3 (dried), tested as 20 % solution in HBSS, was brought onto the cornea of a bovine eye which had

been incubated with cMEM without phenol red at 32 ± 1 °C for 1 hour and whose opacity had been measured. The test item was incubated on the cornea for 4 hours at 32 ± 1 °C. After removal of the test item, opacity and permeability values were measured. HBSS was used as negative control. The negative control showed no irritating effect on the cornea and the calculated IVIS (in vitro irritancy score) is 0.90 in the first experiment, 2.65 in the second experiment and 2.27 in the third experiment. 20% imidazole solution was used as positive control. The positive control induced serious eye damage on the cornea and was within two standard deviations of the current historical mean. The calculated IVIS (in vitro irritancy score) is 92.36 in the first experiment, 127.02 in the second experiment and 113.65 in the third experiment.

Under the conditions of this study, based on all three experiments, the test item dermofeel PA-3 (dried), tested as 20% solution in HBSS, showed no effects on the cornea of the bovine eye. The calculated IVIS (in vitro irritancy score) is 5.39 in the first experiment, 2.33 in the second experiment and 2.91 in the third experiment. According to OECD Guideline no. 437 (Jul. 2013), a substance with an IVIS ≤ 3 requires no classification for eye irritation or serious eye damage.

Reconstructed human Cornea-like Epithelium (RhCE) test method for identifying chemicals not requiring classification and labelling for eye irritation or serious eye damage (OECD 492)

Test Item: dermofeel PA-3 (dried) (= dried dermofeel® PA-3 in freeze drier (Alpha 2-4 LSCplus) => 0.1-10% residual water)

Appearance of Test Item: white solid powder

Amounts/Concentrations Applied: 50.1 mg test item (Tissue No. 1)
52.3 mg test item (Tissue No. 2)

The tissues were pre-wetted with 20 µL DPBS buffer and were then incubated at 37 ± 1 °C (5 ± 1 % CO2; 80-100 % relative humidity) for 30 minutes.
After that the test item was applied in duplicate.

Experimental Period of the Study: 11.09.2017 - 28.09.2017

Study Report – Date of Release: 12.16.2017

Result: non-eye irritant

Executive Summary: Two experiments were performed.

The first experiment was not valid, because the variation between the tissue replicates of the negative control was too high and therefore outside the range of validity. This experiment is not reported in this report, but the raw data are kept in the test facility in the GLParchive.

The second experiment was valid and the results are reported here.

The test item dermofeel PA-3 (dried) was applied to a three-dimensional human cornea tissue model in duplicate for an exposure time of 6 hours. The solid test item was applied to two tissue replicates. After treatment, the respective substance was rinsed from the tissue; then, cell viability of the tissues was evaluated by addition of MTT, which can be reduced to formazan. The formazan production was evaluated by measuring the optical density (OD) of the resulting solution. Demineralised water was used as negative control and methyl acetate was used as positive control. The controls showed the following results: After treatment with the negative control, the absorbance values were within the required acceptability criterion of mean OD > 0.8 and < 2.5, OD was 1.6. The positive control showed clear eye irritating effects, mean value of the relative tissue viability was 42.2 % (< 50%). Variation within tissue replicates was acceptable (< 20%). After treatment with the test item, the mean value of relative tissue viability was 66.9 %.

This value is above the threshold for eye irritation potential (≤ 60%).

Under the conditions of the test, dermofeel PA-3 (dried) is considered non-eye irritant in the EpiOcularTM Eye Irritation Test.

In Vitro Skin Sensitisation: ARE-Nrf2 Luciferase Test Method (OECD 442d)

Test Item: dermofeel PA-3 (dried)(= dried dermofeel® PA-3 in freeze drier (Alpha 2-4 L5Cplus) => 0.1-10% residual water)

Appearance of Test Item: white solid powder

Amounts/Concentrations Applied: The following test item concentrations showed a viability ≥ 70 % and could therefore be evaluated for luciferase induction:

Experiment I:
54 µg/mL, 65 µg/mL, 78 µg/mL, 93 µg/mL, 112 µg/mL, 134 µg/mL, 161 µg/mL, 193 µg/mL, 231 µg/mL, 278 µg/mL, 333 µg/mL

Experiment II:
54 µg/mL, 65 µg/mL, 78 µg/mL, 93 µg/mL, 112 µg/mL, 134 µg/mL, 161 µg/mL, 193 µg/mL, 231 µg/mL, 278 µg/mL"

Experimental Period of the Study: 18.09.2017 - 13.10.2017

Study Report – Date of Release: 01.19.2018

Result: no skin sensitization potential

Executive Summary: This in vitro study evaluates the potential of the test item dermofeel PA-3 (dried) to activate the Nrf2 transcription factor (sensitizing potential) by using the Lu5ens cell line. This test is part of a tiered strategy for the evaluation of skin sensitization potential. Thus, data generated with the present Test Guideline should be used to support the discrimination between skin sensitizers and non-sensitizers in the context of an integrated approach to testing and assessment. The Lu5ens test is an ARE Reporter Gene Assay that was developed by the BASF SE (Ludwigshafen, Germany) and is based on the OECD 442D Guideline (KeratinoSens Assay).

The assay differs in some points from the OECD guideline.
The assay included a cytotoxicity range finder test (CRFT) and two independent experiments (experiment I and II) with a treatment period of 48 h. The CRFT was performed to detect a potential cytotoxic effect of the test item. Based on the results of this test the concentrations for the two experiments were determined. In the experiments, the highest nominal applied concentration (400 µg/mL) was chosen based on the results obtained in the CRFT. A geometric series (factor 1.21) of eleven dilutions thereof was prepared. Precipitation of the test item was not visible in any of the experiments. Medium no. 3 was used as solvent control and as growth control. Lactic acid (5000 µM) was used as negative control and p-Phenylenediamine (80 µM) as positive control. No substantial and reproducible dose dependent increase in luciferase induction above 1.5 fold was observed in both experiments up to the maximal tested concentration of the test item.

Conclusion:
Under the experimental conditions of this study, the test item, dermofeel PA-3 (dried), was negative in the Lu5ens assay and is therefore considered not having the potential to activate the Nrf2 transcription factor (no sensitizing potential).

Bacterial Reverse Mutation Test (OECD 471)

Test Item: dermofeel PA-3

Appearance of Test Item: colorless to brownish liquid

Amounts/Concentrations Applied: Experiment 1: 4995 / 1499 / 500 / 150 / 50 µg/plate
Experiment 2: 5013 / 2507 / 1254 / 627 / 314 µg/plate"

Experimental Period of the Study: 15.11.2011 - 25.11.2011

Study Report – Date of Release: 01.06.2012

Result: not mutagenic

Executive Summary: "Two valid experiments were performed.

First Experiment: Five concentrations of the test item, dissolved in deionised water (ranging from 4995 to 50 µg / plate) were used. Five genetically manipulated strains of *Salmonella typhimurium* (TA 97a, TA 98, TA 100, TA 102 and TA 1535) were exposed to the test item both in the presence and in the absence of a metabolic activation system (S9) for 48 hours, using the plate incorporation method. None of the concentrations caused a significant increase in the number of revertant colonies in the tested strains. The test item didn't show any mutagenic effects in the first experiment. No signs of toxicity towards the bacteria could be observed.
The sterility control and the determination of the titre didn't show any inconsistencies. The determined values for the spontaneous revertants of the negative controls were in the normal range. All positive controls showed mutagenic effects with and without metabolic activation.

Second Experiment:
To verify the results of the first experiment, a second experiment was performed, using five concentrations of the test item (ranging from 5013 to 314 µg / plate) and a modification in study performance (pre-incubation method). The test item didn't show mutagenic effects in the second experiment, either. No signs of toxicity towards the bacteria could be observed. The sterility control and the determination of the titre didn't show any inconsistencies. The determined values for the spontaneous revertants of the negative controls were in the normal range. All positive controls showed mutagenic effects with and without metabolic activation.

Under the conditions of the test, the test item didn't show mutagenic effects towards *Salmonella typhimurium*, strains TA 97a, TA 98, TA 100, TA 102 and TA 1535. Therefore, no concentration-effect relationship could be determined.

The test item dermofeel® PA-3 is considered as "not mutagenic under the conditions of the test".

Bovine Corneal Opacity and Permeability Test Method for Identifying Ocular Corrosives and Severe Irritants (OECD 437)

Test Item: dermofeel PA-3

Appearance of Test Item: colorless to brownish liquid

Amounts/Concentrations Applied: 750 µL of the test item (dermofeel PA-3 (dried)) was tested as solution at 2% concentration in Aqua demin..

Experimental Period of the Study: 11.17.2011

Study Report – Date of Release: 01.10.2012

Result: non-corrosive and/or no severe irritant

Executive Summary: One valid experiment was performed.

Bovine corneas were used. They were collected from slaughtered cattle which were between 12 and 60 months old.
The test item dermofeel PA-3 diluted in Aqua demin. to obtain a 2% (w/w) solution was brought onto the cornea of a bovine eye which had been incubated with cMEM without Phenol red at 32 ± 1°C. After removal of the test item and two hours post-incubation, opacity and permeability values were measured.

Physiological sodium chloride solution was used as negative control. The negative control showed no irritation effect on the cornea.

10% sodium hydroxide solution was used as positive control. The positive control induced a severe irritation on the cornea.

The test item dermofeel PA-3 diluted in Aqua demin. to obtain a 2% (w/w) solution showed no effects on the cornea of the bovine eye.

The calculated IVIS (in vitro irritancy score) is - 0.352.

In conclusion, it can be stated that in this study and under the experimental conditions reported, the test item dermofeel PA-3 diluted in Aqua demin to obtain a 2% (w/w) solution possesses no eye irritation potential (according to ICCVAM).

According to OECD Guideline no. 437 (2009), a substance that induces an IVIS ≥ 55.1 is defined as a corrosive or severe irritant.

Therefore, according to OECD, dermofeel PA-3 diluted in Aqua demin. to obtain a 2% (w/w) solution is classified as "non-corrosive"and/or "no severe irritant".

Hen´s egg chorioallantoic membrane test (HET-CAM); according to Steiling et al. 1999 (non-GLP study completed at Labor L+S AG)

Test Item: dermofeel PA-3

Appearance of Test Item: colorless to brownish liquid

Amounts/Concentrations Applied: 2.0% (solvent 0.9% NaCl); applied to the CAM in a dose of 300 µl

Experimental Period of the Study: 04.11.2011 - 14.11.2011

Study Report – Date of Release: 11.16.2011

Result: Slightly irritating (Score:0) ("slightly irritating" is the best possible outcome in this scoring system)

Executive Summary: Object of this assay is to assess the acute irritation potential of a test item to mucous membranes in analogy to the Draize Eye Test. For this purpose a definite dose of the test item is applied to chlorioallantoic membrane (CAM) of fertilized and incubated hen's eggs. An item can be classified as irritating if at least one reaction type is assessed at least as moderate (sum of all scores [S] > 12 < 16) after 30 seconds. Severe in vivo effects are expected if one type is classified as strong (sum of all scores ≥ 16). In all other cases the expected irritation property of the test item in vivo is low.
For the test item (2.0%) dermofeel PA-3 an irritation value of 0 was determined. On this account the test item can be classified in vivo as "slightly irritating".

The reference item Texapon ASV 5% was assessed as "moderately irritating" (irritation value of 6) which demonstarted the validity of the test procedure."

2018 FDA VCRP Data

Sodium Phytate

01B - Baby Lotions, Oils, Powders, and Creams	1
01C - Other Baby Products	1
02B - Bubble Baths	6
02D - Other Bath Preparations	1
03B - Eyeliner	1
03C - Eye Shadow	1
03D - Eye Lotion	9
03E - Eye Makeup Remover	1
03G - Other Eye Makeup Preparations	6
04B - Perfumes	1
4E - Other Fragrance Preparation	3
05A - Hair Conditioner	21
05E - Rinses (non-coloring)	1
05F - Shampoos (non-coloring)	25
05G - Tonics, Dressings, and Other Hair Grooming Aids	10
05I - Other Hair Preparations	1
07A - Blushers (all types)	2
07C - Foundations	6
07I - Other Makeup Preparations	1
09A - Dentifrices	1
9C - Other Oral Hygiene Products	1
10A - Bath Soaps and Detergents	27
10E - Other Personal Cleanliness Products	8
11A - Aftershave Lotion	3
11E - Shaving Cream	6
11F - Shaving Soap	3
11G - Other Shaving Preparation Products	1
12A - Cleansing	42
12C - Face and Neck (exc shave)	57
12D - Body and Hand (exc shave)	29
12F - Moisturizing	90
12G - Night	12
12H - Paste Masks (mud packs)	9
12I - Skin Fresheners	6
12J - Other Skin Care Preps	16
13B - Indoor Tanning Preparations	3
Total	**412**

Phytic Acid

03D - Eye Lotion	5
05A - Hair Conditioner	6
05F - Shampoos (non-coloring)	6
05G - Tonics, Dressings, and Other Hair Grooming Aids	1
05I - Other Hair Preparations	9
07F - Makeup Bases	1

07I - Other Makeup Preparations	1
10B - Deodorants (underarm)	1
12A - Cleansing	16
12C - Face and Neck (exc shave)	30
12D - Body and Hand (exc shave)	16
12F - Moisturizing	13
12G - Night	1
12H - Paste Masks (mud packs)	2
12J - Other Skin Care Preps	7
Total	**115**

Disodium Glucose Phosphate (No FDA data)

Manganese Fructose Diphosphate (No FDA data)

Phytin (No FDA data)

Sodium Mannose Phosphate

03D - Eye Lotion	3
07C - Foundations	1
11A - Aftershave Lotion	3
12A - Cleansing	2
12C - Face and Neck (exc shave)	3
12D - Body and Hand (exc shave)	4
12F - Moisturizing	9
12G - Night	3
12H - Paste Masks (mud packs)	1
12J - Other Skin Care Preps	4
Total	**33**

Trisodium Fructose Diphosphate (No FDA data)

Trisodium Inositol Triphosphate (No FDA data)

Xylityl Phosphate (No FDA data)

Zinc Fructose Diphosphate (No FDA data)

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Memorandum

To: CIR Expert Panel Members and Liaisons
From: Christina L. Burnett, Senior Scientific Writer/Analyst
Date: February 23, 2018
Subject: Wave 2 – Sultaines

CIR has received 2018 FDA VCRP data. Because the Safety Assessment on Sultaines is in the Draft Final Report stage, we are submitting an updated Use Table along with the raw VCRP data (*sultan032018wave2_data*). Total reported uses for Cocamidopropyl Hydroxysultaine and Lauryl Hydroxysultaine have decreased since 2017. Cocamidopropyl Hydroxysultaine was used in 310 formulations last year; it is reported to be used in 280 formulations this year. Uses of Lauryl Hydroxysultaine have decreased by 4 since 2017. Reported uses for Erucamidopropyl Hydroxysultaine, Capryl Sultaine, and Lauryl Sultaine have not changed since last year.

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Table 1. Frequency (2018) and concentration of use (2017) according to duration and type of exposure for alkyl sultaines.

	# of Uses	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*
	Capryl Sultaine		**Cocamidopropyl Hydroxysultaine**		**Erucamidopropyl Hydroxysultaine**		**Lauryl Hydroxysultaine**	
Totals†	**2**	**0.25**	**280**	**0.05-11.5**	**1**	**NR**	**4**	**0.013-5**
Duration of Use								
Leave-On	2	0.25	15	0.05-2.5	NR	NR	NR	NR
Rinse Off	NR	0.25	242	0.1-11.5	1	NR	4	0.013-5
Diluted for (Bath) Use	NR	NR	23	0.97-6	NR	NR	NR	NR
Exposure Type								
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	0.25[a]	10[a]; 3[b]	0.05; 0.18-0.58[a]	NR	NR	NR	NR
Incidental Inhalation-Powder	NR	0.25[c]	3[b]	2.5[c]	NR	NR	NR	NR
Dermal Contact	2	0.25	180	0.1-11.5	1	NR	2	4.5
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	98	0.05-5	NR	NR	2	5
Hair-Coloring	NR	NR	2	1.5	NR	NR	NR	0.013
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	119	0.13-6.8	1	NR	NR	NR
Baby Products	NR	NR	3	2.2	NR	NR	NR	NR

	Lauryl Sultaine	
Totals†	**2**	**NR**
Duration of Use		
Leave-On	NR	NR
Rinse Off	2	NR
Diluted for (Bath) Use	NR	NR
Exposure Type		
Eye Area	NR	NR
Incidental Ingestion	NR	NR
Incidental Inhalation-Spray	NR	NR
Incidental Inhalation-Powder	NR	NR
Dermal Contact	2	NR
Deodorant (underarm)	NR	NR
Hair - Non-Coloring	NR	NR
Hair-Coloring	NR	NR
Nail	NR	NR
Mucous Membrane	2	NR
Baby Products	NR	NR

NR = Not reported.

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

[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.

2018 FDA VCRP RAW DATA

12J - Other Skin Care Preps	CAPRYL SULTAINE	2
01A - Baby Shampoos	COCAMIDOPROPYL HYDROXYSULTAINE	2
01C - Other Baby Products	COCAMIDOPROPYL HYDROXYSULTAINE	1
02A - Bath Oils, Tablets, and Salts	COCAMIDOPROPYL HYDROXYSULTAINE	5
02B - Bubble Baths	COCAMIDOPROPYL HYDROXYSULTAINE	16
02D - Other Bath Preparations	COCAMIDOPROPYL HYDROXYSULTAINE	2
05A - Hair Conditioner	COCAMIDOPROPYL HYDROXYSULTAINE	1
05F - Shampoos (non-coloring)	COCAMIDOPROPYL HYDROXYSULTAINE	86
05G - Tonics, Dressings, and Other Hair Grooming Aids	COCAMIDOPROPYL HYDROXYSULTAINE	9
06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	COCAMIDOPROPYL HYDROXYSULTAINE	2
07I - Other Makeup Preparations	COCAMIDOPROPYL HYDROXYSULTAINE	1
10A - Bath Soaps and Detergents	COCAMIDOPROPYL HYDROXYSULTAINE	58
10E - Other Personal Cleanliness Products	COCAMIDOPROPYL HYDROXYSULTAINE	38
11E - Shaving Cream	COCAMIDOPROPYL HYDROXYSULTAINE	3
11F - Shaving Soap	COCAMIDOPROPYL HYDROXYSULTAINE	3
12A - Cleansing	COCAMIDOPROPYL HYDROXYSULTAINE	48
12C - Face and Neck (exc shave)	COCAMIDOPROPYL HYDROXYSULTAINE	3
12F - Moisturizing	COCAMIDOPROPYL HYDROXYSULTAINE	1
12H - Paste Masks (mud packs)	COCAMIDOPROPYL HYDROXYSULTAINE	1
10E - Other Personal Cleanliness Products	ERUCAMIDOPROPYL HYDROXYSULTAINE	1
05F - Shampoos (non-coloring)	LAURYL HYDROXYSULTAINE	2
12A - Cleansing	LAURYL HYDROXYSULTAINE	2
10A - Bath Soaps and Detergents	LAURYL SULTAINE	2

Cosmetic Ingredient Review

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Memorandum

To: CIR Expert Panel Members and Liaisons
From: Monice M. Fiume MMF
Senior Director, CIR
Date: February 23, 2018
Subject: Wave 2 –Zinc Salts

As stated in the original transmittal memo for the Zinc Salts report, several sets of comments were received on the Tentative Report, and that the comments regarding the association between zinc uptake and prostate cancer needed more time for processing. The comments received on February 1 from the CIR Science and Support Committee addressed the need to further look at this issue, and referenced several citations. These and others have been obtained, and a table that briefly summarizes that information is attached. [*zincst032018w2_rep*] Please let me know if you would like to see any of these papers.

Guidance is needed as to what extent this information should be included in the report. Additionally, please provide language for use in the Discussion to address this issue.

Also included in this Wave 2 submission is updated frequency of use information. VCRP data were received after the March Panel materials were distributed. Because Zinc Salts is a draft Final Report, this updated information is being provided to the Panel to inform you of any frequency of use changes. Many (but not) all of the total number of uses per ingredient decreased, but nothing significant was noted. The greatest number of uses (Zinc Stearate) decreased from 2321 to 2204.

An updated use table is included with this submission, and it contains track changes so that the changes in frequencies of use are obvious (*zincst032018w2_use table*). Also included are the 2018 FDA raw data (*zincst032018w2_FDA 2018*).

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Zinc and Prostate Cancer

Study Details	Results	Reference
the association between self-reported zinc intake and prostate cancer in a hospital-based case-control study of African Americans was compared with results of previous studies by performing a meta-analysis to summarize the evidence regarding the association between zinc and prostate cancer n=127 Newly diagnosed African American men with histologically confirmed prostate cancan; 81 controls controls had higher zinc intake, with a mean of 14 mg/day vs. 11 mg/day for cases	- researchers reported a non-significant, non-linear increase in prostate cancer when comparing tertiles of zinc intake (OR $_{<6.5 \text{ vs } 6.5 \pm 12.5 \text{ mg/day}}$ 1.8, 95% CI: 0.6, 5.6; OR $_{<6.5 \text{ vs} >12.5 \text{ mg/day}}$ 1.3, 95% CI: 0.2, 6.5). - pooled estimate from 17 studies (3 cohorts, 2 nested case-control, 11 case-control studies, and 1 randomized clinical trial, with a total of 111,199 participants and 11,689 cases of prostate cancer) was 1.07 $_{\text{hi vs lo}}$ 95% CI: 0.98±1.16 - a dose-response meta-analysis reported a non-linear trend in the relationship between zinc intake and prostate cancer (p for nonlinearity = 0.0022) - meta-analysis indicated no evidence for an association between zinc intake and prostate cancer	1
disagreement exists regarding the correlation of the concentration of zinc in prostate cancer	one group of researchers reported that zinc levels are increased in prostate cancer	2,3
	separate researchers state that there is years of evidence that a marked decrease in zinc levels is involved in the development and progression of prostate cancer	4
a multicenter hospital- based case-control study on prostate cancer in Italy (1991-2002) 1294 men with incident, histologically confirmed prostate cancer; controls included 1451 patients admitted to the same hospitals as cases for a wide spectrum of acute non-neoplastic, non–hormone-related diseases	- compared with the lowest quintile, the OR for the highest quintile was 1.56 (95% CI, 1.07–2.26), with a significant trend in risk (p = 0.04); the trend in risk was significant for advanced cancers only, the OR being 2.02 (95% CI, 1.14–3.59) for prostate cancers with a high Gleason score - researchers reported a a direct association between high zinc intake and prostate cancer risk, particularly for advanced cancers	5
response to above study outlined several reasons for disagreement with the above results	- no conclusive evidence is presented that the zinc component is responsible for anything in the report, or that an increase, rather than decrease, in bioavailable zinc is the associated factor - .stated that there is 50 yrs of clinical studies that consistently establish that zinc is markedly decreased in malignant prostate glands in situ. - questioned the estimations of dietary intake, zinc levels, and subgroupings of <2 mg/d; large populations that consume multivitamin supplements usually containing 15–20 mg zinc would exceed their high-zinc high-risk group, and the incidence of advanced cancer would be much greater than actually occurs. - was the of the opinion that the results are inconsistent with virtually all other epidemiologic - was of the opinion that supporting citation did not support their findings - “Epidemiologic studies have been conflicting, inconsistent, and inconclusive.”	6
original researcher response	- the original researchers rebutted that “cases were more frequently consumers of diets rich in zinc than controls; even after allowance for several covariates, including total energy intake, subjects in the highest quintile of zinc intake had a >50% increase in the risk of prostate cancer and twice the risk of advanced cancers compared with subjects in the first quintile of intake. The trend in risk was statistically significant for advanced and all cancers” - the researchers also agreed “that inconsistent results on zinc and prostate cancer do not allow the provision of definite evidence of an association between (dietary and supplemental) zinc and prostate cancer risk. However, our findings from a large case-control study exclude a favorable effect of dietary zinc on prostate carcinogenesis.”	7
currently in text: a Health Professionals Follow-Up Study evaluated the association of supplemental zinc consumption and risk of prostate cancer in 46,974 men in the United States (1986 – 2000) - there were 2901 new cases of prostate cancer. Of the new cases, 434 were advanced cancer	- study researchers observed that there was no association with prostate cancer risk in those who consumed supplements of 100 mg zinc (usually in the form of Zinc Gluconate) or less per day. - compared to men who did not consume zinc supplements, those who supplemented with more than 100 mg/day zinc showed a 2.29 (95% CI of 1.06 to 4.95, p = 0.003) RR in advanced prostate cancer. - the risk increased to 2.37 (95% CI of 1.42 to 3.95, p = 0.001) for men who supplemented with zinc for ≥10 yrs - the study researchers noted that there could be confounding factors such as calcium intake supplementation or another unmeasured correlation related to zinc supplementation	8

Study Details	Results	Reference
response to above study population-based study (Sweden); n = 1499 prostate cancer case patients, 1130 control subjects - use of supplemental zinc at least 1 year prior to completion of the questionnaire was reported by 3.4% (n = 51) of case patients and 2.5% (n = 28) of control subjects	- after adjusting for age, there was no statistically significant difference in the prevalence of supplemental zinc use between case patients and control subjects (OR = 1.3, 95% CI = 0.8 - 2.1). - further multivariate adjustment for possible confounders, including height, body mass index, family history of prostate cancer, smoking status, alcohol intake, and use of other nutritional supplements, did not appreciably affect the results. - the researchers stated the association did not vary for risk of localized versus advanced disease or for risk of sporadic versus familial or hereditary disease - researchers noted that the study had limited power to detect any association with risk of prostate cancer or to analyze a dose–response relationship in detail because of the low prevalence of supplemental zinc use among the case patients and the control subjects	[9]
original researcher response	Potential reasons for discrepancies: - proportion of subjects in our study with zinc supplement exposure was greater than that in the Swedish study, 2.5% vs. 25% - it is likely that the doses of zinc consumed by subjects in the Swedish study were largely compatible with the RDA of 11 mg/day of zinc for men; original study included 4374 men whose zinc intake exceeded the RDA by at least twofold - it is possible that the duration of zinc supplement use is critical for an increase in prostate cancer risk; original study included 6177 men with consistent use of zinc supplements for ≥10 yrs - the apparent adverse effect of zinc supplement use observed by the original researches was restricted to cases of advanced prostate cancer.	[10]
response to above study	suggested that cadmium content of the zinc supplements could be the reason for the increased prostate cancer risk	[11]
original researcher response	data were not available to determine that cadmium was the cause	[12]

Abbreviations: CI – confidence interval; OR – odds ratio; RDA – recommended daily allowance; RR – relative risk

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Table 1. Frequency and concentration of use according to duration and type of exposure for zinc salts[2-5,7,65,66]

	# of Uses	*Max Conc Use (%)*	*# of Uses*	*Max Conc Use (%)*	*# of Uses*	*Max Conc Use (%)*
	Zinc Acetate		**Zinc Acetate**		**Zinc Ascorbate**	
	2009	***2010***	**2017**	**2016**	**2017**	**2016**
Totals*	***1***	***0.4***	**2**	**NR**	**NR**	**0.01-5**
Duration of Use						
Leave-On	*NR*	*NR*	*NR*	*NR*	*NR*	*0.047-0.3*
Rinse-Off	*1*	*0.4*	*2*	*NR*	*NR*	*0.01-5*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Eye Area	*NR*	*NR*	NR	NR	NR	0.047
Incidental Ingestion	*1*	*0.4*	2	NR	NR	NR
Incidental Inhalation-Spray	*spray: NR possible: 1*[a]	*spray: NR possible: 0.4*[a]	spray: NR possible: 2[a]	NR	NR	spray: 0.05 possible: NR
Incidental Inhalation-Powder	*NR*	*NR*	powder: NR possible: NR	NR	NR	powder: 0.095 possible: 0.05-0.1[c]
Dermal Contact	*NR*	*NR*	NR	NR	NR	0.047-0.3
Deodorant (underarm)	*NR*	*NR*	NR	NR	NR	not spray: 0.3
Hair - Non-Coloring	*NR*	*NR*	NR	NR	NR	0.01-5
Hair-Coloring	*NR*	*NR*	NR	NR	NR	NR
Nail	*NR*	*NR*	NR	NR	NR	NR
Mucous Membrane	*1*	*0.4*	2	NR	NR	not oral: 0.05
Baby Products	*NR*	*NR*	NR	NR	NR	0.01

	Zinc Aspartate		**Zinc Carbonate**		**Zinc Chloride**	
	2017	**2016**	**2017**	**2016**	**2017**	**2016**
Totals*	**25**	**NR**	~~2~~1	**1.6**	~~76~~70	**0.000095-0.47**
Duration of Use						
Leave-On	*8*	*NR*	~~*2*~~*1*	*NR*	~~*62*~~*61*	*0.0001-0.47*
Rinse-Off	*17*	*NR*	*NR*	*1.6*	~~*14*~~*9*	*0.000095-0.21*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Eye Area	1	NR	1	NR	8	0.039-0.064
Incidental Ingestion	NR	NR	NR	NR	~~9~~5	oral care: 0.088 (0.041% Zn)
Incidental Inhalation-Spray	spray: NR possible: 5[a], 2[b]	NR	spray: NR possible: 1[b]	NR	spray: 1 possible: ~~15~~[a]11[a], 3[b]	spray: NR possible: 0.003-0.088[a]
Incidental Inhalation-Powder	powder: NR possible: 2[b]	NR	powder: NR possible: 1[b]	NR	powder: NR possible: 3[b]	powder: 0.04-0.47 possible: NR
Dermal Contact	9	NR	~~2~~1	NR	~~64~~62	0.00075-0.47
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	16	NR	NR	1.6	3	0.000095-0.21
Hair-Coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous Membrane	1	NR	NR	NR	~~9~~5	oral care: 0.088 (0.041% Zn)
Baby Products	NR	NR	NR	NR	NR	NR

Table 1. Frequency and concentration of use according to duration and type of exposure for zinc salts[2-5,7,65,66]

	# of Uses	Max Conc Use (%)	# of Uses	Max Conc Use (%)	# of Uses	Max Conc Use (%)
	Zinc Citrate		**Zinc Citrate**		**Zinc Gluconate**	
	2011	***2011***	**2017**	**2016**		
Totals*	***9***	***0.05-2***	~~13~~12	**0.05-2**	~~318~~321	**0.000005-3**
Duration of Use						
Leave-On	*5*	*0.05*	~~5~~6	*NR*	~~243~~255	*0.00024-3*
Rinse-Off	*4*	*0.3-2*	~~8~~6	*0.05-2*	~~73~~66	*0.00005-0.5*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	~~2~~*NR*	*0.000005*
Exposure Type						
Eye Area	*NR*	*NR*	NR	NR	35	0.0048-3
Incidental Ingestion	*4*	*0.3-2*	~~8~~5	oral care: 0.28-2 (0.031 - 0.22% Zn)	~~10~~9	lipstick: 0.1 (0.031% Zn)
Incidental Inhalation-Spray	*NR*	*NR*	~~NR~~ possible: 2[a]	spray: NR possible: 0.28[a]	spray: NR possible: ~~76~~[a]81[a], ~~65~~[b]–71[b]	spray: NR possible: 0.001[a]
Incidental Inhalation-Powder	*NR*	*powder: 0.05*	NR	NR	powder: NR possible: ~~65~~[b]–71[b]	powder: NR possible: 0.001-1[c]
Dermal Contact	*5*	*0.05*	~~5~~6	0.05	~~282~~286	0.000005-3
Deodorant (underarm)	*4*[a]	*NR*	~~3~~[a]2[a]	NR	14[a]	NR
Hair - Non-Coloring	*NR*	*NR*	~~NR~~1	NR	22	0.00005-0.5
Hair-Coloring	*NR*	*NR*	NR	NR	4	NR
Nail	*NR*	*NR*	NR	NR	NR	NR
Mucous Membrane	*4*	*0.3-2*	~~8~~6	oral care: 0.28-2 (0.031-0.22% Zn) not oral: 0.05	~~19~~17	lipstick: 0.1 (0.031% Zn) not oral: 0.000005
Baby Products	*NR*	*NR*	NR	NR	NR	NR

	Zinc Glycinate		**Zinc Hydroxide**		**Zinc Lactate**	
	2017	**2016**	**2017**	**2016**	**2017**	**2016**
Totals*	**NR**	**0.009**	**2**	**NR**	~~1~~NR	**0.25-1.8**
Duration of Use						
Leave-On	*NR*	*0.009*	*2*	*NR*	*NR*	*NR*
Rinse-Off	*NR*	*NR*	*NR*	*NR*	~~1~~*NR*	*0.25-1.8*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Eye Area	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	~~1~~NR	oral care: 0.25-0.44 (0.065-0.12% Zn)
Incidental Inhalation-Spray	NR	NR	spray: NR possible: 1[a], 1[b]	NR	~~spray: NR possible: 1~~[a]	spray: NR possible: 0.25[a]
Incidental Inhalation-Powder	NR	NR	powder: NR possible: 1[b]	NR	NR	NR
Dermal Contact	NR	0.009	2	NR	NR	1.8
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	~~1~~NR	oral care: 0.25-0.44 (0.065-0.12% Zn)
Baby Products	NR	NR	NR	NR	NR	NR

Table 1. Frequency and concentration of use according to duration and type of exposure for zinc salts[2-5,7,65,66]

	# of Uses	Max Conc Use (%)	# of Uses	Max Conc Use (%)	# of Uses	Max Conc Use (%)
	Zinc Laurate		***Zinc Myristate***		**Zinc Myristate**	
	2017	**2016**	***2007***	***2006***	**2017**	**2016**
Totals*	**~~11~~560**	**1-7**	***122***	***0.00005-20***	**~~59~~33**	**0.005-20**
Duration of Use						
Leave-On	*~~97~~45*	*1-7*	*122*	*0.00005-20*	*~~59~~33*	*0.005-20*
Rinse-Off	*~~17~~15*	*1.2*	*NR*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*~~1~~NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Eye Area	~~56~~6	NR	*60*	*0.05-6*	~~25~~14	0.51-20
Incidental Ingestion	NR	NR	*NR*	*5*	NR	lipstick: 0.063-5 (0.0077-0.61% Zn)
Incidental Inhalation-Spray	spray: NR possible: 2[b]	NR	*NR*	*spray: NR possible: 0.1[a], 5[b]*	NR	NR
Incidental Inhalation-Powder	powder: 8 possible: 2[b]	powder: 3-7	*powder: 18*	*powder: 20 possible: 5[b]*	powder: ~~18~~ 14 possible: NR	powder: 2-20 possible: 5-15[c]
Dermal Contact	~~105~~50	1-7	*117*	*0.001-20*	~~59~~33	0.51-20
Deodorant (underarm)	NR	NR	*NR*	*NR*	NR	NR
Hair - Non-Coloring	10	NR	*NR*	*NR*	NR	NR
Hair-Coloring	NR	NR	*NR*	*NR*	NR	NR
Nail	NR	NR	*5*	*0.00005*	NR	0.005-0.035
Mucous Membrane	~~5~~3	NR	*NR*	*5*	NR	lipstick: 0.063-5 (0.0077-0.61% Zn)
Baby Products	NR	NR	*NR*	*NR*	NR	NR

	Zinc Phosphate		***Zinc Ricinoleate***		**Zinc Ricinoleate**	
	2017	**2016**	***2002***	***2004***	**2017**	**2016**
Totals*	**NR**	**1**	***3***	***1-2***	**~~27~~21**	**0.15-2.3**
Duration of Use						
Leave-On	*NR*	*NR*	*2*	*1-2*	*~~25~~20*	*0.15-2.3*
Rinse-Off	*NR*	*1*	*1*	*NR*	*~~2~~1*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Eye Area	NR	NR	*NR*	*NR*	NR	NR
Incidental Ingestion	NR	oral care: 1 (0.17% Zn)	*NR*	*NR*	2	lipstick: 1.1 (0.11% Zn)
Incidental Inhalation-Spray	NR	NR	*NR*	*spray: 1 possible: 1[b]*	spray: NR possible: 1[a]	NR
Incidental Inhalation-Powder	NR	NR	*NR*	*powder: NR possible: 1[b]*	NR	powder: NR possible: 0.15[c]
Dermal Contact	NR	NR	*3*	*1-2*	~~23~~17	0.15-2.3
Deodorant (underarm)	NR	NR	*2[a]*	*2[a]*	~~21~~[a]16[a]	spray: 0.82-2.3 not spray: 0.82-2
Hair - Non-Coloring	NR	NR	*NR*	*1*	~~NR~~1	NR
Hair-Coloring	NR	NR	*NR*	*NR*	NR	NR
Nail	NR	NR	*NR*	*NR*	1	NR
Mucous Membrane	NR	oral care: 1 (0.17% Zn)	*NR*	*NR*	~~3~~2	lipstick: 1.1 (0.11% Zn)
Baby Products	NR	NR	*NR*	*NR*	NR	NR

Table 1. Frequency and concentration of use according to duration and type of exposure for zinc salts[2-5,7,65,66]

	# of Uses	Max Conc Use (%)	# of Uses	Max Conc Use (%)	# of Uses	Max Conc Use (%)
	Zinc Salicylate		***Zinc Stearate***		**Zinc Stearate**	
	2017	**2016**	***2001***	***2001***	**2017**	**2016**
Totals*	**NR**	**0.47**	***746***	***0.5-51***	~~2321~~2204	**0.2-32**
Duration of Use						
Leave-On	*NR*	*0.47*	*742*	*0.5-51*	~~2312~~*2198*	*0.2-32*
Rinse-Off	*NR*	*NR*	*2*	*1*	~~7~~6	*0.28-3.3*
Diluted for (Bath) Use	*NR*	*NR*	*2*	*3*	~~2~~*NR*	*NR*
Exposure Type						
Eye Area	NR	NR	*346*	*1-16*	~~139~~71369	1-32
Incidental Ingestion	NR	NR	*2*	*3*	~~5~~3	oral care: 2 (0.2% Zn) lipstick: 0.5 (0.05% Zn)
Incidental Inhalation-Spray	NR	NR	*spray: NR possible: 2[a], 5[b]*	*spray: 2 possible: 1-2[a], 1-2[b]*	spray: NR possible: ~~10~~[a]7[a], ~~8~~[b] 7[b]	spray: 0.3 possible: NR
Incidental Inhalation-Powder	NR	NR	*powder: 236 possible: 5[b], 2[c]*	*powder: 2-24 possible: 1-2[b], 0.5[c]*	powder: ~~456~~–416 possible: ~~8~~[b]7[b], 1[c]	powder: 1.1-14 possible: 0.2-1[c]
Dermal Contact	NR	0.47	*738*	*0.5-51*	~~230~~82193	0.2-32
Deodorant (underarm)	NR	not spray: 0.47	*NR*	*2[a]*	NR	NR
Hair - Non-Coloring	NR	NR	*1*	*NR*	NR	NR
Hair-Coloring	NR	NR	*NR*	*NR*	6	3.3
Nail	NR	NR	*NR*	*NR*	NR	NR
Mucous Membrane	NR	NR	*4*	*3*	~~7~~3	oral care: 2 (0.2% Zn) lipstick: 0.5 (0.05% Zn)
Baby Products	NR	NR	*2*	*0.5*	1	NR

	Zinc Sulfate* **		**Zinc Undecylenate**	
	2017	**2016**	**2017**	**2016**
Totals*	~~134~~149	**0.0001-1**	**NR**	**0.25**
Duration of Use				
Leave-On	~~75~~86	*0.0001-1*	*NR*	*0.25*
Rinse-Off	~~59~~63	*0.0003-0.15*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*
Exposure Type				
Eye Area	11	0.02	NR	NR
Incidental Ingestion	1	NR	NR	NR
Incidental Inhalation-Spray	spray: NR possible: ~~14~~[a]15[a], ~~20~~[b]–19[b]	spray: NR possible: 0.003[a]	NR	spray: NR possible: 0.25[b]
Incidental Inhalation-Powder	powder: 5 possible: ~~20~~[b]–19[b]	powder: 0.02 possible: 0.0008-0.12[c]	NR	powder: NR possible: 0.25[b]
Dermal Contact	~~101~~103	0.0003-1	NR	0.25
Deodorant (underarm)	NR	0.0015	NR	NR
Hair - Non-Coloring	~~32~~37	0.003-0.15	NR	NR
Hair-Coloring	NR	NR	NR	NR
Nail	~~NR~~8	0.0001-0.001	NR	NR
Mucous Membrane	~~13~~15	not oral: 0.0003-0.057	NR	NR
Baby Products	NR	NR	NR	NR

* Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.
** Ingredient was reviewed previously; current use and use from previous report are included for comparison.
*** Frequency of use data from the VCRP was reported separately for Zinc Sulfate and zinc sulfate anhydrous, but the above frequency of use totals for Zinc Sulfate are the sum of uses for both forms of the ingredient.
[a] Includes products that can be sprays, but it is not known whether the reported uses are sprays.
[b] Not specified whether this product is a spray or a powder or neither, but it is possible it may be a spray or a powder, so this information is captured for both categories of incidental inhalation.
[c] Includes products that can be powders, but it is not known whether the reported uses are powders.
NR – no reported use.

ZINC SALTS - 2018 VCRP

Zinc Acetate	
09B - Mouthwashes and Breath Fresheners	2
Zinc Aspartate	
03G - Other Eye Makeup Preparations	1
05A - Hair Conditioner	1
05F - Shampoos (non-coloring)	12
05G - Tonics, Dressings, and Other Hair Grooming Aids	3
10A - Bath Soaps and Detergents	1
12A - Cleansing	2
12D - Body and Hand (exc shave)	2
12F - Moisturizing	2
12H - Paste Masks (mud packs)	1
Zinc Carbonate	
12C - Face and Neck (exc shave)	1
Zinc Chloride	
03B - Eyeliner	1
03C - Eye Shadow	7
04E - Other Fragrance Preparation	1
05A - Hair Conditioner	1
05G - Tonics, Dressings, and Other Hair Grooming Aids	1
05I - Other Hair Preparations	1
07A - Blushers (all types)	1
07B - Face Powders	1
07C - Foundations	3
07G - Rouges	30
07I - Other Makeup Preparations	2
09A - Dentifrices	2
09B - Mouthwashes and Breath Fresheners	1
09C - Other Oral Hygiene Products	2
12A - Cleansing	1
12C - Face and Neck (exc shave)	3
12F - Moisturizing	8
12H - Paste Masks (mud packs)	2
12I - Skin Fresheners	1
12J - Other Skin Care Preps	1
Zinc Citrate	
05G - Tonics, Dressings, and Other Hair Grooming Aids	1
07I - Other Makeup Preparations	1
09A - Dentifrices	4
09C - Other Oral Hygiene Products	1
10B - Deodorants (underarm)	2
10E - Other Personal Cleanliness Products	1
11A - Aftershave Lotion	1
12F - Moisturizing	1
Zinc Gluconate	
03B - Eyeliner	15
03D - Eye Lotion	6
03E - Eye Makeup Remover	1
03G - Other Eye Makeup Preparations	13
05A - Hair Conditioner	1
05E - Rinses (non-coloring)	2
05F - Shampoos (non-coloring)	6

05G - Tonics, Dressings, and Other Hair Grooming Aids	6
05I - Other Hair Preparations	7
06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	4
07B - Face Powders	1
07C - Foundations	9
07E - Lipstick	9
07F - Makeup Bases	1
10A - Bath Soaps and Detergents	4
10B - Deodorants (underarm)	14
10E - Other Personal Cleanliness Products	4
11A - Aftershave Lotion	4
11G - Other Shaving Preparation Products	3
12A - Cleansing	29
12C - Face and Neck (exc shave)	64
12D - Body and Hand (exc shave)	7
12F - Moisturizing	53
12G - Night	14
12H - Paste Masks (mud packs)	12
12I - Skin Fresheners	7
12J - Other Skin Care Preps	24
13B - Indoor Tanning Preparations	1

Zinc Hydroxide

12D - Body and Hand (exc shave)	1
12F - Moisturizing	1

Zinc Laurate

03A - Eyebrow Pencil	1
03B - Eyeliner	1
03C - Eye Shadow	4
05F - Shampoos (non-coloring)	10
07A - Blushers (all types)	5
07B - Face Powders	8
07C - Foundations	22
07G - Rouges	1
07I - Other Makeup Preparations	1
10A - Bath Soaps and Detergents	2
10E - Other Personal Cleanliness Products	1
12A - Cleansing	2
12D - Body and Hand (exc shave)	2

Zinc Myristate

03C - Eye Shadow	12
03G - Other Eye Makeup Preparations	2
07A - Blushers (all types)	4
07B - Face Powders	14
07C - Foundations	1

Zinc Ricinoleate

05C - Hair Straighteners	1
07E - Lipstick	2
08G - Other Manicuring Preparations	1
10B - Deodorants (underarm)	16
12F - Moisturizing	1

Zinc Stearate

01B - Baby Lotions, Oils, Powders, and Creams	1
03A - Eyebrow Pencil	27
03B - Eyeliner	45

03C - Eye Shadow	1264
03F - Mascara	2
03G - Other Eye Makeup Preparations	31
04C - Powders (dusting and talcum, excluding aftershave talc)	11
06H - Other Hair Coloring Preparation	6
07A - Blushers (all types)	271
07B - Face Powders	405
07C - Foundations	79
07D - Leg and Body Paints	2
07E - Lipstick	3
07F - Makeup Bases	3
07G - Rouges	6
07H - Makeup Fixatives	5
07I - Other Makeup Preparations	28
12C - Face and Neck (exc shave)	6
12E - Foot Powders and Sprays	1
12F - Moisturizing	1
12G - Night	1
12J - Other Skin Care Preps	1
13B - Indoor Tanning Preparations	3
13C - Other Suntan Preparations	2

Zinc Sulfate and Zinc Sulfate, Anhydrous

03C - Eye Shadow	8
03D - Eye Lotion	2
03G - Other Eye Makeup Preparations	1
05A - Hair Conditioner	14
05F - Shampoos (non-coloring)	15
05G - Tonics, Dressings, and Other Hair Grooming Aids	1
05I - Other Hair Preparations	4
07A - Blushers (all types)	6
07B - Face Powders	5
07C - Foundations	8
07E - Lipstick	1
08A - Basecoats and Undercoats	1
08E - Nail Polish and Enamel	7
10A - Bath Soaps and Detergents	13
10E - Other Personal Cleanliness Products	1
11G - Other Shaving Preparation Products	2
12A - Cleansing	14
12C - Face and Neck (exc shave)	19
12F - Moisturizing	12
12G - Night	2
12H - Paste Masks (mud packs)	3
12J - Other Skin Care Preps	7
05F - Shampoos (non-coloring)	1
05I - Other Hair Preparations	2