ADMIN

Memo

Agenda

Minutes

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CIR EXPERT PANEL MEETING
APRIL 8-9, 2019

Cosmetic Ingredient Review

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MEMORANDM

To: CIR Expert Panel Members and Liaisons
From: Bart Heldreth, Ph.D., Executive Director, Cosmetic Ingredient Review
Subject: 150th Meeting of the CIR Expert Panel — Monday and Tuesday, April 8-9, 2019
Date: March 15, 2019

Welcome to the April 2019 CIR Expert Panel Meeting. Enclosed are the agenda and accompanying materials for the 150th CIR Expert Panel Meeting to be held on April 8-9, 2019. The location is different from the last meeting – The Westin Hotel, Washington, D.C. City Center, 1400 M St NW, Washington, District of Columbia, 20005. Phone: (202) 429-1700.

The meeting agenda includes the consideration of 13 reports advancing in the review process, including 6 final reports, 1 tentative report, 4 draft reports, and 2 re-reviews. Also on the agenda are the Draft 2020 Priorities.

Schedule and hotel accommodations

We have reserved rooms for the nights of Sunday, April 7th and Monday, April 8th at the Westin Hotel. If you encounter travel problems, please contact Monice on her cell phone at 703-801-8156.

Team Meetings

Draft Reports - there are 4 draft reports for review.

1. Hexa/Penta-hydric Alcohols – This is the first time that the Panel is seeing this report on 3 sugar alcohols. On January 25, 2019, a Scientific Literature Review (SLR) was issued with an invitation for submission of data on these ingredients.

   The Personal Care Products Council (Council) provided maximum concentration of use data and comments on the SLR. The data have been incorporated into the report and the comments on the SLR have been addressed.

   According to data received in 2019 from the Food and Drug Administration's (FDA's) Voluntary Cosmetic Registration Program (VCRP), Sorbitol has the highest frequency of use, with a total of 1976 formulations. Sorbitol is most commonly used in moisturizing products (269 formulations), face and neck products (217 formulations), and bath soaps and detergents (205 formulations). Xylitol is reported to have 472 uses, 290 of which are leave-on formulations. Mannitol has a frequency of use of 404 formulations, 104 of which are face and neck products. The results of the concentration of use survey conducted by the Personal Care Products Council (Council) indicate Sorbitol also has the highest concentration of use; it is used at up to 70% in dentifrices. The highest concentration of use reported for products resulting in leave-on dermal exposure is 60.5% Mannitol in other skin care preparations.

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

specifying the data needs therein.

2. Palm – This is the first time that the Panel is seeing this report on 8 palm tree-derived (*Euterpe oleracea* and *Euterpe edulis*) ingredients. On January 22, 2019, CIR issued the SLR for these ingredients. According to the *Dictionary*, these ingredients are reported to function mostly as skin conditioning agents in cosmetic products. Euterpe Oleracea Pulp Powder and Euterpe Oleracea Seed Powder also are reported to function as abrasives and exfoliants in cosmetics.

   According to 2019 VCRP data, Euterpe Oleracea Fruit Extract is reported to be used at the highest FOU, in 430 cosmetic products (297 leave-on products, 129 rinse-off products, 4 products that are diluted for (bath) use). The results of a concentration of use survey conducted by the Council in 2017 indicate that Euterpe Oleracea Pulp Powder is being used at maximum use concentrations up to 3% in leave-on products (the highest reported concentration of any of these ingredients) and maximum use concentrations up to 0.6% in rinse-off products. Expect to find HRIPT data at 3% in the Wave 2 supplement

   In addition to maximum concentration of use data, Council provided compositional breakdown data on organic Euterpe Oleracea Juice, method of manufacturing data on Euterpe Oleracea Juice, compositional breakdown data on a Euterpe Oleracea Fruit Extract trade name material, properties data on a Euterpe Oleracea Fruit Extract trade name material, method of manufacturing data on a Euterpe Oleracea Fruit Extract trade name material, in vitro dermal and ocular irritation data on a Euterpe Oleracea Fruit Extract trade name material, *in chemico* skin sensitization data on a Euterpe Oleracea Fruit Extract trade name material, in vitro skin sensitization data on a Euterpe Oleracea Fruit Extract trade name material, and in vitro genotoxicity data on a Euterpe Oleracea Fruit Extract trade name material. Comments have also been received and addressed.

   If no further data are needed, the Panel should formulate a Discussion and issue a Tentative Report. However, if additional data are required, the Panel should be prepared to identify those needs and issue an IDA.

3. Pomegranate – This is the first time the Panel is seeing this safety assessment of 18 pomegranate-derived (*Punica granatum*) ingredients as used in cosmetics. The SLR of these botanical ingredients was issued by CIR on January 24, 2019. According to the *Dictionary*, most of these ingredients are reported to function in cosmetics as skin conditioning agents, while some are reported to have other functions, such as abrasives and antioxidants.

   According to 2019 VCRP data, Punica Granatum Extract has the most reported uses in cosmetic products, with a total of 312; the majority of the uses are in leave-on skin care products. The results of the concentration of use survey conducted in 2018 by the Council indicated that Punica Granatum Seed Extract is used at up to 0.3% in leave-on cuticle softeners (the highest reported concentration of use for any of these ingredients).

   The Council provided concentration of use survey data as well as composition, physical properties, genotoxicity, dermal and ocular irritation, and dermal sensitization data on Punica Granatum Pericarp Extract and Punica Granatum Fruit Extract. Comments on the SLR were received from the Council and addressed. In the comments, the Council notes that Punica Granatum Extract has been incorrectly defined as an extract of “the whole plant.” Companies that reported concentration of use for this safety assessment have been asked to clarify the source of the ingredient with this INCI name.

   If no further data are needed, the Panel should formulate an updated Discussion and issue a Tentative Report. However, if additional data are required, the Panel should be prepared to identify those needs and issue an IDA.

4. Alkyl Amide MIPA – This is the first time the Panel is seeing this safety assessment of 14 alkyl amide MIPA ingredients. On January 28, 2019, CIR issued the SLR for these ingredients. According to the *Dictionary*, all but a few of these ingredients are reported to function in cosmetics as a surfactant or viscosity increasing agent.

   According to 2019 VCRP survey data, Lauramide MIPA has the highest frequency of use, with a

total of 485 formulations. The results of the concentration of use survey conducted in 2017 by the Council indicate that Cocamide MIPA has the highest maximum concentration of use, and is used at up to 12% in hair bleaches. The next highest reported maximum concentration of use is 4.8% Lauramide MIPA in bath soaps and detergents. The highest concentration of use reported for products resulting in leave-on dermal exposure is 1% Cocamide MIPA in body and hand preparations.

In addition to maximum concentration of use data, the Council provided comments on the SLR. These comments on the SLR have been addressed.

If no further data are needed, the Panel should formulate an updated Discussion and issue a Tentative Amended Report. However, if additional data are required, the Panel should be prepared to identify those needs and issue an IDA.

Draft Tentative Report – there is 1 draft tentative report.

1. Silicates – At the December 2018 meeting, the Panel issued an IDA for the 40 silica and silicate ingredients. The additional data needs were:

    - The range of particle sizes for all silica and silicate ingredients that are used in spray and powder formulations
    - Chemical characterization, composition, and impurities data for all ingredients, except Silica
    - Method of manufacturing and/or source data for all ingredients, except Silica and Hydrated Silica.

    Since the December Panel meeting, CIR has received a process flow chart and particle analyses on Bentonite. VCRP data were updated. No other unpublished data were received in time for inclusion in the initial report package.

    Comments provided by the Council prior to the December meeting on the Draft Amended Report have been addressed. CIR has also received comments from the Synthetic Amorphous Silica and Silicate Industry Association (SASSI) in response to the letter CIR received from Women's Voices for the Earth (WVE) in late November 2018; although the WVE memo was discussed at the December meeting, it is being provided again because SASSI addresses issues raised in the letter. In addition to the feedback and clarification provided in response to the WVE letter, SASSI indicate that they will be providing data on the silica and silicate products used in cosmetics. Expect to find these data in the Wave 2 supplement.

    The Panel should carefully consider the data presented in this report, and issue a Tentative Amended Report with a safe, safe with qualifications, unsafe, insufficient data, or split conclusion.

Draft Final Reports - there are 6 draft final reports for consideration (including two amended reports). After reviewing these drafts, especially the rationales provided in the Discussion sections, the Panel should issue them as Final Reports, as appropriate.

1. Fatty Acids – At the December 2018 meeting, the Panel issued a Tentative Report with the conclusion that these 102 fatty acid and fatty acid salt ingredients are safe in the present practices of use and concentration described in the safety assessment when formulated to be non-irritating and non-sensitizing, which may be based on a QRA.

    Council comments regarding the Tentative Report were received and addressed. VCRP data have been updated. Additional data from the published literature, including short-term toxicity, chronic toxicity, and genotoxicity studies on Isomerized Safflower Acid, a phototoxicity study on damaged skin following exposure to Linoleic Acid, and genotoxicity studies on Magnesium Stearate, have also been incorporated into the report.

The Panel should carefully review the Abstract, Discussion, and Conclusion of this safety assessment. If these are satisfactory, the Panel should issue a Final Report.

2. Salicylates – At the December 2018 meeting, the Panel issued a revised tentative amended report with the conclusion that Salicylic Acid and the 18 salicylate ingredients reviewed in this safety assessment are safe in cosmetics in the present practices of use and concentration described in the safety assessment, when formulated to be non-irritating and non-sensitizing, which may be based on a QRA.

   However, it has come to our attention that Capryloyl Salicylic Acid appears to have been seriously mischaracterized. This ingredient has thus been removed from this report and is proposed for a separate and individual safety assessment. Accordingly, the draft final amended report for Panel review is actually on Salicylic Acid and the ***17*** salicylate ingredients.

   The safety assessment has been revised to include comments that were received from the Council and 2019 FDA VCRP data. The Panel should carefully review the Abstract, Discussion, and Conclusion of this safety assessment. If these are satisfactory, the Panel should issue a Final Amended Report.

3. Parabens – At the September 2018 meeting, the Panel issued a tentative amended report with the conclusion that 20 of the 21 paraben ingredients are safe in cosmetics in the present practices of use and concentration described in the safety assessment. The Panel also determined that the available data are insufficient to determine the safety of Benzylparaben. The data needed to determine safety of this ingredient comprise a no-observed-adverse-effect-level (NOAEL) derived from developmental and reproductive toxicity (DART) studies. This ingredient is not reported to be in use.

   The Panel's previous deliberations comprised extensive revisions to better identify, and explain the rationale for, the values utilized in conducting the risk assessment therein. The Panel further requested that the margin of safety (MOS) be re-calculated, weighing the different use concentrations and exposures of Butylparaben in various cosmetic product categories. The report was revised accordingly.

   Since the September meeting, additional data on biomonitoring, endocrine activity, dermal sensitization, and epidemiological studies have been incorporated into the report. The input of new studies as well as discussions regarding bioaccumulation, dermal absorption rate, and Physiologically Based Pharmacokinetic (PBPK) Model for the estimating the internal exposure of parabens, are highlighted within the text of this report.

   The Panel should carefully review the Abstract, Discussion, and Conclusion of this safety assessment. If these are satisfactory, a Final Amended Report should be issued.

4. Titanium Complexes – At the September 2018 meeting, the Panel issued a tentative report with a split conclusion: Isopropyl Titanium Triisostearate is safe in cosmetics in the present practices of use and concentration described in the safety assessment, when used as a surface modifier. The data are insufficient to determine the safety of the following 4 ingredients: Titanium Citrate, Titanium Ethoxide, Titanium Isostearates, and Titanium Salicylate.

   The Panel determined that the following data are needed to assess the safety of these 4 ingredients:
   - Maximum use concentrations
   - Methods of manufacture
   - Impurities
   - 28-day dermal toxicity data
   - Depending on the results of these studies, various systemic toxicity data may also be needed
   - Genotoxicity data
   - Skin irritation and sensitization data at maximum cosmetic use concentrations, except for Titanium Citrate

Furthermore, the Panel noted that if data indicate the presence of significant levels of residual Isopropyl Titanium Triisostearate result with use as a surface modifier, 28-day dermal toxicity data and genotoxicity data would then be needed to evaluate the safety of this ingredient. The same would apply to any other identified use(s) of this ingredient that would yield free Isopropyl Titanium Triisostearate in the product formulation.

The Panel requested clarification of the following:

1) Isopropyl Titanium Triisostearate is only being used as a surface modifier,
2) the other titanium complex ingredients are not being used as surface modifiers, and
3) surface modification does not result in any appreciable residual Isopropyl Titanium Triisostearate in the final product.

The identification of whether or not Isopropyl Titanium Triisostearate was used as a surface modifier in product formulations tested, text added to the report discussion, and the following unpublished data, received in response to the Panel's data requests, are highlighted in the report text:

- Use concentration data on Isopropyl Titanium Triisostearate (with confirmation that all relate to use as a surface modifier)
- HRIPT on a foundation containing 0.433% Isopropyl Titanium Triisostearate (used as a surface modifier)
- HRIPT on a foundation containing 0.348% Isopropyl Titanium Triisostearate (used as a surface modifier)
- Summaries of HRIPTs on products containing Isopropyl Titanium Triisostearate (0.276%, 0.281%, and 0.337%) (used as a surface modifier)
- Memorandum from the Council stating whether or not Isopropyl Titanium Triisostearate was used as a surface modifier in HRIPT data previously submitted

However, data relating to the presence of residual, unreacted Isopropyl Titanium Triisostearate in products in which this ingredient is being used as a surface modifier were not provided. Until these data are provided, whether or not the use concentration data represent the bound ingredient or the bound + unreacted ingredient remains unknown. Information on whether or not the remaining ingredients in this safety assessment function as surface modifiers also has not been provided, and the same is true for the safety test and other data on these ingredients that were requested by the Panel.

If the Conclusion is unchanged, the Panel should carefully review the Abstract and Discussion of this safety assessment. If these are satisfactory, a Final Report should be issued.

5. Brown Algae – At the December 2018 meeting, the Panel concluded that the following 6, of the 82, brown algae-derived ingredients are safe in cosmetics in the present practices of use and concentration described in the safety assessment: Alaria Esculenta Extract, Laminaria Digitata Extract, Laminaria Saccharina Extract, Macrocystis Pyrifera (Kelp) Extract, Undaria Pinnatifida Extract, and Undaria Pinnatifida Cell Culture Extract. The Panel came to this conclusion by assessing the systemic toxicity potential (either in repeated dose studies or GRAS status/use in food) and sensitization data of the ingredients. However, the Panel concluded that the data are insufficient to determine the safety of the remaining ingredients and requested the following data:

   - Systemic toxicity data
   - Sensitization data

   Although this safety assessment includes 82 brown algae-derived ingredients, it should be noted that several of these ingredients appear to be equivalent based on the accepted taxonomic names. Accordingly, the total number of distinct cosmetic ingredients is 74. Table 1 in the report has been updated to include all 82 ingredients, along with their respective synonyms.

   Since the December Panel meeting, CIR has received the following data, which have been incorporated into the report:

- summary of edible seaweeds and French regulations
- dermal toxicity, sensitization, solvent information, and arsenic/iodine impurities data on several brown algae-derived ingredients
- human sensitization data on a cream containing Cystoseira Amentacea/Caespitosa/Branchycarpa Extract and a cream containing Himanthalia Elongata Extract
- specifications, method of manufacturing information, heavy metal impurities, ocular irritation data, and dermal irritation data for a mixture containing water, Himanthalia Elongata Extract, Fucus Vesiculosus Extract, and saccharomyces cerevisiae extract
- specifications, method of manufacturing information, heavy metal impurities, ocular irritation data, and dermal irritation data for a mixture containing caprylic/capric triglyceride, Laminaria Ochroleuca Extract, and tocopherol
- specifications, method of manufacturing information, heavy metal impurities, ocular irritation data, and dermal irritation data for a mixture containing water, Ascophyllum Nodosum Extract, and Halopteris Scoparia Extract
- specifications, method of manufacturing information, heavy metal impurities, ocular irritation data, and dermal irritation data for a mixture containing water and Fucus Serratus Extract
- specifications, method of manufacturing information, heavy metal impurities, ocular irritation data, and dermal irritation data for a mixture containing water, butylene glycol, and Lessonia Nigrescens Extract
- specifications, method of manufacturing information, heavy metal impurities, ocular irritation data, dermal irritation data, a bacterial reverse mutation assay, and sensitization data for a mixture containing water, Fucus Spiralis Extract, and tetraselmis chi extract
- specifications, method of manufacturing information, heavy metal impurities, ocular irritation data, and dermal irritation data for a mixture containing water and Sargassum Muticum Extract
- specifications, method of manufacturing information, heavy metal impurities, ocular irritation data, dermal irritation data, and sensitization data for a mixture containing water and Pelvetia Canaliculata Extract
- sensitization data of a trade name mixture containing Fucus Vesiculosus Extract
- composition data and sensitization data of a trade name mixture containing Sargassum Filipendula Extract
- updated use information for Halidrys Siliquosa Extract

A table is included in the report package presenting each ingredient, as well as a notation of the presence or absence of systemic toxicity data (repeated dose studies or the ingredients' use in food/as a GRAS substance) and sensitization data.

Comments provided by the Council after the December meeting on the draft tentative report have been addressed. If the Conclusion is unchanged, the Panel should carefully consider the Abstract, Discussion, and data presented in this report, and issue a Final Report with a safe, safe with qualifications, insufficient data, or split conclusion.

6. Benzyl Salicylate – At the December 2018 meeting, the Panel issued a tentative report with the conclusion that Benzyl Salicylate is safe in cosmetics in the present practices of use and concentration when formulated to be non-irritating and non-sensitizing, which may be based on a QRA.

   FOU data has been updated accordingly to 2019 VCRP information. Benzyl Salicylate is reported to be used in 3079 formulations, 2419 of which are leave-on products. Also, it should be noted that use concentration survey data provided by the Council on Benzyl Salicylate were reported for its functions only as a light stabilizer; however, the VCRP does not indicate the function of ingredients in cosmetic formulations, so it is not known what the intended function of Benzyl Salicylate is in any of the reported ingredient categories.

   Council comments received prior to the December 2018 meeting are included in the packet and have been addressed. In addition, Council comments regarding the Tentative Report were

received also addressed.

The Panel should carefully review the Abstract, Discussion, and Conclusion of this safety assessment. If these are satisfactory, the Panel should issue a Final Report.

Re-Reviews – there are 2 Re-Reviews

1. MCI/MI – Since the original report on the combination use of Methylchloroisothiazolinone/ Methylisothiazolinone (MCI/MI) in 1992, the Panel has reviewed the stand-alone ingredient, MI, twice and issued a final amended report in 2014 with the conclusion that MI is safe for use in rinse-off cosmetic products at concentrations up to 100 ppm and safe in leave-on cosmetic products when they are formulated to be non-sensitizing, which may be determined based on a quantitative risk assessment (QRA).

   Since 1992, numerous case reports and sensitization studies have been published. This re-review document contains a sampling of these data. If the Panel chooses to re-open this assessment, all the relevant studies will be included in the amended report. Also, as is typical in all of our re-review documents, summary information from the original report will also be included.

   According to 2019 VCRP data, MCI and MI are surveyed separately and not as a mixture. The total number of uses reported for MCI are 5137; 480 of these are in leave-on products. MI has 6037 reported uses; 1042 of these are in leave-on products. The Council is currently conducting a concentration of use survey.

   At the September 2018 meeting, a strategy memo was issued in advance to obtain Panel input and direct the CIR staff towards information sought in that re-review document. The Panel considered changes in report conclusion procedures and evaluated the relevance of a recent risk assessment (Towle et al 2018). The Panel also commented that it may be helpful, after choosing a no expected sensitization induction level (NESIL), for industry stakeholders to provide a second-generation quantitative risk assessment (QRA 2.0) calculation. Comments and any data or risk assessments, have yet to be received.

   In the absence of these pivotal data, the Panel may want to table this assessment until such time as that information is available. However, in the meantime, the Panel should review the available data in this re-review package and move to re-open this safety assessment if the conclusion is likely to be amended.

2. Squalane & Squalene – The Panel first reviewed the safety of Squalane and Squalene in 1982. The Panel concluded that "both Squalane and Squalene are safe as cosmetic ingredients in the present practices of use and concentration." In 2001, after considering new studies and updated use data on these two ingredients, the Panel determined to not re-open the safety assessment.

   Because it has been at least 15 years since the first re-review summary was published, in accord with CIR Procedures, the Panel should again consider whether the safety assessment of Squalane and Squalene should be re-opened. An exhaustive search of the world's literature was performed for studies dated 1995 forward.

   The frequency of use has increased significantly for both ingredients since the initial re-review was considered. According to VCRP data, Squalane and Squalene were reported to be used in 595 and 29 formulations, respectively, in 2001. In 2019, the VCRP indicates that Squalane is used in 2785 formulations, and Squalene is used in 527 formulations. For Squalane, the current maximum concentration of use (96.8%) is the same as that reported in 2001 (97%); however, the maximum concentrations of use by exposure type (e.g., eye area, nails) have increased for some categories. The opposite is true for Squalene; the maximum concentration of use has decreased since the previous re-review. In 2001, Squalene was used at up to 10%; data received in 2018 report that the maximum concentration of use is 1.2%.

   If, upon review of the new studies and updated use data, the Panel determines that a re-review is warranted, a full draft amended report will be presented at an upcoming meeting.

Administrative Items - there is 1 priorities document

1. Priorities – The Draft 2020 Priority List is being issued for comment earlier in the process (CIR Procedures require this by June 1st) to allow more time for the acquisition of data. The list is based on stakeholder requests; frequency of use data (FOU) from FDA's VCRP received on February 5, 2018; and on CIR staff and Panel workflow. While this list has been updated with 2019 frequency of use data, and a report in progress has been removed from the list, the Draft Priorities for 2020 are the same as those finalized for 2019. Most of the ingredients herein have increased in FOU. Of those that decreased, Calcium Sulfate decreased the most and may be considered for deletion. While no new ingredients are being proposed for addition to the CIR docket, submissions of ingredients for cause are welcome, as always.

Full Panel Meeting

Remember, the breakfast buffet will open at 8:00 am and the meeting starts at 8:30 am on day 1 and on day 2.

The Panel will consider the 6 reports to be issued as final safety assessments, followed by the remaining reports advancing in the process (including the tentative reports, draft reports, and re-reviews), and priorities. It is likely that the full Panel session will conclude before lunch on day 2, so plan your travel accordingly.

Have a safe journey!

Agenda
150th Cosmetic Ingredient Review Expert Panel Meeting
April 8th - 9th, 2019

The Westin Hotel
1400 M Street, NW,
Washington, District of Columbia, 20005

Monday, April 8th

8:00 am	**CONTINENTAL BREAKFAST**	
8:30 am	**WELCOME TO THE 150th EXPERT PANEL TEAM MEETINGS**	**Drs. Bergfeld/Heldreth**
8:45 am	**TEAM MEETINGS**	**Drs. Marks/Belsito**

Dr. Marks' Team		**Dr. Belsito's Team***	
RR (MF)	Squalene & Squalane	Admin (BH)	Priorities
FR (CB)	Fatty Acids	FAR (PC)	Parabens
TAR (CB)	Silicates	FR (PC)	Brown Algae
DR (CB)	Pomegranate	DR (PC)	Hexa/Penta-hydric Alcohols
RR (CB)	MI/MCI	FR (WJ)	Titanium Complexes
FR (AA)	Benzyl Salicylate	FAR (WJ)	Salicylates
DR (AA)	Alkyl Amide MIPA	DR (WJ)	Palm
FAR (PC)	Parabens	FR (AA)	Benzyl Salicylate
FR (PC)	Brown Algae	DR (AA)	Alkyl Amide MIPA
DR (PC)	Hexa/Penta-hydric Alcohols	FR (CB)	Fatty Acids
FR (WJ)	Titanium Complexes	TAR (CB)	Silicates
FAR (WJ)	Salicylates	DR (CB)	Pomegranate
DR (WJ)	Palm	RR (CB)	MI/MCI
Admin (BH)	Priorities	RR (MF)	Squalene & Squalane

The purpose of the Cosmetic Ingredient Review is to determine those cosmetic ingredients for which there is a reasonable certainty in the judgment of competent scientists that the ingredients are safe under intended conditions of use.

FR: Final Report // FAR: Final Amended Report // TR: Tentative Report // TAR: Tentative Amended Report // DR: Draft Report // DAR: Draft Amended Report // RR: Re-Review // RRsum: Re-Review Summary // SM: Strategy Memo // Admin: Administrative item

(AA): Alice Akinsulie || (CB): Christina Burnett || (BH) Bart Heldreth || (MF): Monice Fiume || (PC): Priya Cherian || (WJ): Wilbur Johnson

*Team moves to breakout room.

Tuesday, April 9th			
8:00 am	**CONTINENTAL BREAKFAST**		
8:30 am	**WELCOME TO THE 150th FULL CIR EXPERT PANEL MEETING**		**Dr. Bergfeld**
8:45 am	Admin	**MINUTES OF THE DECEMBER 2018 EXPERT PANEL MEETING**	**Dr. Bergfeld**
9:00 am	**DIRECTOR'S REPORT**		**Dr. Heldreth**
9:10 am	**FINAL REPORTS, REPORTS ADVANCING TO THE NEXT LEVEL, OTHER ITEMS**		

Final Reports

FAR (PC)	Parabens – *Dr. Marks Reports*
FR (PC)	Brown Algae – *Dr. Belsito Reports*
FR (WJ)	Titanium Complexes – *Dr. Marks Reports*
FAR (WJ)	Salicylates – *Dr. Belsito Reports*
FR (AA)	Benzyl Salicylate – *Dr. Marks Reports*
FR (CB)	Fatty Acids – *Dr. Belsito Reports*

Reports Advancing

TAR (CB)	Silicates – *Dr. Marks Reports*
DR (CB)	Pomegranate – *Dr. Belsito Reports*
RR (CB)	MI/MCI – *Dr. Marks Reports*
DR (AA)	Alkyl Amide MIPA – *Dr. Belsito Reports*
RR (MF)	Squalene & Squalane – *Dr. Marks Reports*
DR (PC)	Hexa/Penta-hydric Alcohols – *Dr. Belsito Reports*
DR (WJ)	Palm – *Dr. Marks Reports*

Other Items

Admin (BH)	Priorities – *Dr. Belsito Reports*

ADJOURN - *Next meeting **Thursday** and **Friday**, June 6-7, 2019, at The Westin Washington, D.C. City Center, 1400 M St NW, Washington, District of Columbia, 20005*

On the basis of all data and information submitted, and after following all of the Procedures (https://www.cir-safety.org/supplementaldoc/cir-procedures), the Expert Panel shall determine whether each ingredient, under each relevant condition of use, is safe, safe with qualifications, unsafe, or there are insufficient data or information to make a determination of safety. Upon making such a determination, the Expert Panel shall issue a conclusion and/or announcement.

FR: Final Report // FAR: Final Amended Report // TR: Tentative Report // TAR: Tentative Amended Report // DR: Draft Report // DAR: Draft Amended Report // RR: Re-Review // RRsum: Re-Review Summary // SM: Strategy Memo // Admin: Administrative item

(AA): Alice Akinsulie || (CB): Christina Burnett || (BH) Bart Heldreth || (MF): Monice Fiume || (PC): Priya Cherian || (WJ): Wilbur Johnson

Commitment & Credibility since 1976

ONE HUNDRED FORTY-NINTH MEETING

OF THE

EXPERT PANEL

December 3-4, 2018

Darcy Hotel

Washington, D.C.

Expert Panel Members

Wilma F. Bergfeld, M.D., Chair

Donald V. Belsito, M.D.

Ronald A. Hill, Ph.D.

Curtis D. Klaassen, Ph.D.

Daniel C. Liebler, Ph.D.

James G. Marks, Jr., M.D.

Ronald C. Shank, Ph.D.

Thomas J. Slaga, Ph.D.

Paul W. Snyder, D.V.M., Ph.D.

Liaison Representatives

Consumer

Thomas Gremillion, J.D.

Industry

Alexandra Kowcz, M.B.A.

Government

Linda Katz, MD., M.P.H.

Adopted (Date)

Wilma F. Bergfeld, M.D.

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Others Present at the Meeting

Alice Akinsulie	CIR
Nan An	FDA
Jay Ansell	PCPC
Don Bjerke	P & G
Roshil Budhram	Mast
Christina Burnett	CIR
Catherine Casey	Vanderbilt Minerals
H. Chen	J & J
Priya Cherian	CIR
Sylvia Cho	Amorepacific
Mark Choo	Amorepacific
Shawn Deadwiler	Govt
Carol Eisenmann	PCPC
Monice Fiume	CIR
Frank Flynn	Vanderbilt Minerals
Eileen Francis	Rose Sheet
Kevin Fries	CIR
Thomas Gremillion	CFA
Tracy Guerrero	ACC/SGHSC
Bart Heldreth	CIR
Carla Jackson	CIR
Wilbur Johnson, Jr.	CIR
Jon Lalko	Estee Lauder
Julia Linthicum	CIR
Linda Loretz	PCPC
Sun Hong mei	Infinitive
Wan Xianghong	Mary Kay
Liu Yang	CAFFCI
Liang Yanhui	CAFFCI
Shi Yue	CAFFCI
Wang Zemin	FDA
Jinqiu Zhu	CIR

MINUTES FROM THE 149th CIR EXPERT PANEL MEETING

CHAIRMAN'S OPENING REMARKS

Dr. Bergfeld welcomed the attendees to the 149th meeting of the Cosmetic Ingredient Review (CIR) Expert Panel. She noted that the 12 ingredient reports reviewed in Teams on the preceding day are being reviewed at today's meeting. The reports that are being reviewed by the Panel include 5 final reports and 7 reports that are advancing to the next level of review, one of which is a re-review summary. Additionally, unpublished data relating to some of these documents were received from the Council on the preceding day. Dr. Bergfeld also stated that the Panel would also be reviewing 2 administrative documents, the aerosol inhalation document and the hair dye epidemiology document, and a strategy document on Polyaminopropyl Biguanide at today's meeting.

APPROVAL OF MINUTES

The minutes of the September 24-25, 2018 (148th) CIR Expert Panel meeting were approved.

DIRECTOR'S REPORT

Dr. Heldreth expressed gratitude for the Panel's and other stakeholders' continued support of the Cosmetic Ingredient Review program. He wrote to FDA Commissioner Scott Gottlieb, updating him on the work of this Panel over the last year, and received a thank you for CIR's commitment to ingredient safety.

Dr. Heldreth recalled that over the last few years, Dr. Bergfeld, Ms. Fiume, and he had visited Beijing a number of times to discuss the work of this Panel. While there, they enjoyed in-depth discussions with members of the industry association there and the Chinese FDA on multiple safety assessment aspects. With this regard, he welcomed the delegation visiting from the China Association of Fragrance Flavor and Cosmetic Industries (CAFFCI), who were in attendance to see the Panel in action at this meeting.

Since the September meeting, CIR had the fortune of participating in a special forum arranged in part by the US Department Commerce to inform other parts of the world, specifically Brazil in this case, about the great work of this Panel. Specifically, Dr. Heldreth presented the Brazilian Health Regulatory Agency and the Brazilian Ministry of Industry, Foreign Trade and Services with an overview of the CIR process and the significant utility of this Panel's reports.

Very recently, there have been some positive points with regard to the visibility of CIR. At the end of November, USA Today featured, on their front page a column about cosmetics and chemophobia. Dr. Klaassen is featured significantly therein, dispelling some of the myths about chemical safety. Also, Dr. Heldreth published a column, that is out this month in Cosmetics & Toiletries Magazine, showcasing the work of this Panel on the safety assessment of Parabens (https://www.cosmeticsandtoiletries.com/regulatory/region/northamerica/CIR-Conclusion-Parabens-Are-Safe-500174801.html).

Final Safety Assessments

Hydroxyethyl Urea

The Panel issued a final safety assessment with the conclusion that Hydroxyethyl Urea is safe in cosmetics in the present practices of use and concentration described in the safety assessment when formulated to be non-irritating.

The Panel made note that Hydroxyethyl Urea was slight irritating, and thus specified that products containing Hydroxyethyl Urea should be formulated to be non-irritating. The Panel found that the systemic toxicity carcinogenicity, genotoxicity, and developmental and reproductive toxicity data in this report were sufficient. The Panel did note that carcinogenicity data are lacking; however, because the genotoxicity studies were negative and there are no structural alerts, the Panel was not concerned that Hydroxyethyl Urea had carcinogenic potential. Finally, the Panel discussed the similarities between hydroxyurea (a DNA synthesis inhibitor that acts by inhibiting ribonucleotide reductase) and Hydroxyethyl Urea; despite the similarity in structure, Hydroxyethyl Urea lacks the key structural features required for this inhibition.

Methylxanthines

The Panel issued a final report with the conclusion that the methylxanthines, Caffeine, Theobromine, and Theophylline, are safe in cosmetics in the present practices of use and concentration described in the safety assessment.

All three ingredients are reported to be in use. According to 2018 US FDA Voluntary Cosmetic Registration Program (VCRP) data, Caffeine is used in 1033 formulations, at a maximum concentration of 6%. Theobromine and Theophylline were reported to be used in 5 formulations, each.

The Panel found that the systemic toxicity, developmental and reproductive toxicity, carcinogenicity, and irritation data in this report were sufficient. The Panel recognized the positive genotoxicity studies but considered them potentially misleading due to the fact that positive results were only observed in in vitro studies without metabolic activation. Studies performed with metabolic activation, as well as all in vivo mammalian studies, yielded negative results. Positive results for developmental and reproductive studies were also noted, but were considered irrelevant to intended use exposure, considering effects were only seen at concentrations much higher than what would be used in cosmetics.

Acrylates Copolymers

The Panel issued a final amended report with the conclusion that the 126 ingredients named below are safe in cosmetics in the present practices of use and concentration described in the safety assessment when formulated to be non-irritating.

Acrylates Copolymer
Acrylates Crosspolymer
Acrylates Crosspolymer-3
Acrylates Crosspolymer-4
Acrylates Crosspolymer-5*
Acrylates/Ammonium Methacrylate Copolymer
Acrylates/Beheneth-25 Methacrylate Copolymer
Acrylates/Beheneth-25 Methacrylate/Steareth-30 Methacrylate Copolymer*
Acrylates/C10-30 Alkyl Methacrylate Copolymer
Acrylates/C10-30Alkyl Acrylate Crosspolymer
Acrylates/C12-13 Alkyl Methacrylates/Methoxyethyl Acrylate Crosspolymer*
Acrylates/C12-22 Alkyl Methacrylate Copolymer
Acrylates/C26-28 Olefin Copolymer*
Acrylates/C5-8 Alkyl Acrylate Copolymer*
Acrylates/Ceteareth-20 Methacrylate Crosspolymer*
Acrylates/Ceteareth-20 Methacrylate Crosspolymer-2*
Acrylates/Ceteth-20 Methacrylate Copolymer*
Acrylates/Ethylhexyl Acrylate Copolymer
Acrylates/Ethylhexyl Acrylate Crosspolymer
Acrylates/Ethylhexyl Acrylate/Glycidyl Methacrylate Crosspolymer*
Acrylates/Hydroxyesters Acrylates Copolymer
Acrylates/Hydroxyethyl Acrylate/Lauryl Acrylate Copolymer*
Acrylates/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer*
Acrylates/Laureth-25 Methacrylate Copolymer*
Acrylates/Lauryl Methacrylate Copolymer*
Acrylates/Lauryl Methacrylate/Tridecyl Methacrylate Crosspolymer*
Acrylates/Methoxy PEG-4 Methacrylate Copolymer*
Acrylates/Methoxy PEG-15 Methacrylate Copolymer*
Acrylates/Methoxy PEG-23 Methacrylate Copolymer
Acrylates/Methoxy PEG-90 Methacrylate Crosspolymer*
Acrylates/Palmeth-25 Acrylate Copolymer
Acrylates/PEG-4 Dimethacrylate Crosspolymer*
Acrylates/Steareth-20 Methacrylate Copolymer
Acrylates/Steareth-20 Methacrylate Crosspolymer
Acrylates/Steareth-30 Methacrylate Copolymer
Acrylates/Steareth-50 Acrylate Copolymer*
Acrylates/Stearyl Methacrylate Copolymer
Acrylates/VA Copolymer
Acrylates/VA Crosspolymer
Acrylates/Vinyl Isodecanoate Crosspolymer
Acrylates/Vinyl Neodecanoate Crosspolymer
Acrylic Acid/C12-22 Alkyl Acrylate Copolymer*
Acrylic Acid/Stearyl Acrylate Copolymer
Allyl Methacrylate/Glycol Dimethacrylate Crosspolymer*
Allyl Methacrylates Crosspolymer
Ammonium Acrylates Copolymer
Ammonium Acrylates/Ethylhexyl Acrylate Copolymer*
Ammonium Acrylates/Methyl Styrene/Styrene Copolymer
Ammonium Polyacrylate
Ammonium Styrene/Acrylates Copolymer
Ammonium Styrene/Acrylates/Ethylhexyl Acrylate/Lauryl Acrylate Copolymer*
Ammonium VA/Acrylates Copolymer*
AMP-Acrylates Copolymer
Behenyl Methacrylate/t-Butyl Methacrylate Copolymer
Butyl Acrylate/Cyclohexyl Methacrylate Copolymer*
Butyl Acrylate/Ethylhexyl Methacrylate Copolymer*
Butyl Acrylate/Glycol Dimethacrylate Crosspolymer
Butyl Acrylate/Hydroxyethyl Methacrylate Copolymer*
Butyl Methacrylate/Acryoyloxy PG Methacrylate Copolymer*
C12-22 Alkyl Acrylate/Hydroxyethylacrylate Copolymer
C8-22 Alkyl Acrylates/Methacrylic Acid Crosspolymer*
Calcium Potassium Carbomer*
Carbomer

Cyclohexyl Methacrylate/Ethylhexyl Methacrylate Copolymer*
Ethylene/Acrylic Acid Copolymer
Ethylene/Acrylic Acid/VA Copolymer*
Ethylene/Calcium Acrylate Copolymer*
Ethylene/Magnesium Acrylate Copolymer*
Ethylene/Methacrylate Copolymer
Ethylene/Sodium Acrylate Copolymer
Ethylene/Zinc Acrylate Copolymer*
Ethylhexyl Acrylate/Methoxy PEG-23 Methacrylate/Vinyl Acetate Copolymer*
Ethylhexyl Acrylate/Methyl Methacrylate Copolymer
Glycol Dimethacrylate Crosspolymer*
Glycol Dimethacrylate/Vinyl Alcohol Crosspolymer*
Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer*
Lauryl Acrylate Crosspolymer
Lauryl Acrylate/VA Copolymer*
Lauryl Acrylate/VA Crosspolymer*
Lauryl Methacrylate/Glycol Dimethacrylate Crosspolymer
Lauryl Methacrylate/Sodium Methacrylate Crosspolymer
Methacrylic Acid/PEG-6 Methacrylate/PEG-6 Dimethacrylate Crosspolymer*
Methacryloyl Ethyl Betaine/Acrylates Copolymer
Methoxy PEG-23 Methacrylate/Glyceryl Diisostearate Methacrylate Copolymer
Methyl Methacrylate Crosspolymer
Methyl Methacrylate/Glycol Dimethacrylate Crosspolymer
Methyl Methacrylate/PEG/PPG-4/3 Methacrylate Crosspolymer
PEG/PPG-5/2 Methacrylate/Methacrylic Acid Crosspolymer*
Poly C10-30 Alkyl Acrylate
Poly(Methoxy PEG-9 Methacrylate)*
Polyacrylate-14
Polyacrylate-29*
Polyacrylate-34*
Polyacrylate-1 Crosspolymer
Polyacrylic Acid
Polybutyl Acrylate*
Polybutyl Methacrylate*
Polyethylacrylate
Polyhydroxyethylmethacrylate*
Polyisobutyl Methacrylate*
Polymethyl Acrylate
Polymethyl Methacrylate
Polypropyl Methacrylate*
Polystearyl Methacrylate*
Potassium Acrylate Crosspolymer*
Potassium Acrylates Copolymer
Potassium Acrylates/C10-30 Alkyl Acrylate Crosspolymer
Potassium Acrylates/Ethylhexyl Acrylate Copolymer*
Potassium Aluminum Polyacrylate*
Potassium Carbomer
Potassium Polyacrylate*
Sodium Acrylate/Acrolein Copolymer*
Sodium Acrylate/Vinyl Alcohol Copolymer
Sodium Acrylates Copolymer
Sodium Acrylates Crosspolymer-2
Sodium Acrylates/Beheneth-25 Methacrylate Crosspolymer*
Sodium Acrylates/C10-30 Alkyl Acrylate Crosspolymer
Sodium Acrylates/Ethylhexyl Acrylate Copolymer*
Sodium Acrylates/Vinyl Isodecanoate Crosspolymer
Sodium Carbomer
Sodium Polyacrylate
Sodium Polymethacrylate
Steareth-10 Allyl Ether/Acrylates Copolymer
Stearyl/Lauryl Methacrylate Crosspolymer*
Styrene/Acrylates/Ammonium Methacrylate Copolymer
VA/Butyl Maleate/Isobornyl Acrylate Copolymer

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

Ingredients from the 2011 report on Polymethyl Methacrylate are included in this ingredient family. At the time of that report, Polymethyl Methacrylate was reported to be used in "microbeads." To acknowledge that Polymethyl Methacrylate is no longer used in microbeads, the Panel has added the following statement to the Cosmetic Use section of the report.

> *Based on environmental concerns, the use of microbeads in cosmetics is being phased out in many jurisdictions, including the US. Microbeads includes the Polymethyl Methacrylate beads described in the 2011 CIR report.*

However, in the Discussion, the Panel also acknowledges that environmental issues are not under the purview of the Panel, and the clarification was added to the Cosmetic Use section to inform the reader that the use as microbeads that was described in the 2011 CIR report is no longer accurate.

The Panel noted these polymers are generally large molecules, and significant dermal absorption is not expected. Therefore, topically applied cosmetics are not expected to result in systemic toxicity from these ingredients. Additionally, the existing data support a lack of sensitization potential. However, the Panel was concerned that the potential exists for dermal irritation with the use of products formulated using the ingredients named in this assessment. Therefore, the Panel specified that products containing the ingredients listed above must be formulated to be non-irritating.

The Panel also addressed the concern for residual monomer that might be present in the copolymers; manufacturers should continue to use good manufacturing processes to ensure the amount of residual monomer is kept to a minimum.

Additionally, the Panel discussed the issue of residual solvent that might be present. The amount of residual solvent should be minimized; however, the Panel was particularly concerned with polymerization in benzene. It cannot be predicted with certainty what quantity of benzene would be volatilized/leached from a polymer during manufacture, formulation, or use; while some benzene is inevitably volatilized during manufacture, some may be trapped in the polymer matrix and may leach out during formulation and use. Because of this uncertainty, the Panel stipulated that these ingredients should not be polymerized in benzene.

Vinylpyrrolidone Polymers

The Panel issued a final report with a split conclusion. The Panel determined that the following 27 vinylpyrrolidone polymers are safe in cosmetics in the present practices of use and concentration described in the safety assessment:

VP Copolymers
Acrylic Acid/VP Crosspolymer
Maltodextrin/VP Copolymer
PVP/Decene Copolymer*
PVP/VA/Itaconic Acid Copolymer*
PVP/VA/Vinyl Propionate Copolymer*
Styrene/VP Copolymer
Triacontene/VP Copolymer*
VP/Eicosene Copolymer
VP/Hexadecene Copolymer
VP/VA Copolymer
VP/Vinyl Alcohol Copolymer*

Polyvinylpyrrolidone (PVP) and Modified PVP Polymers
Butylated PVP
PVP
Triacontanyl PVP

VP Crosspolymers
Hydrolyzed Wheat Protein/PVP Crosspolymer
Sodium Acryloyldimethyltaurate/VP Crosspolymer

VP Acrylate Copolymers
Acrylates/Stearyl Methacrylate/VP Copolymer*
Acrylates/VP Copolymer
Ammonium Acryloyldimethyltaurate/VP Copolymer
Ethylhexyl Acrylate/VP/Dimethicone Methacrylate Copolymer*
Ethylhexyl Methacrylate/Methyl Methacrylate/VP Copolymer*
Methacrylic Acid/Styrene/VP Copolymer*
Vinyl Caprolactam/VP/Dimethylaminoethyl Methacrylate Copolymer
VP/Acrylates/Lauryl Methacrylate Copolymer
VP/Dimethylaminoethylmethacrylate Copolymer
VP/DMAPA Acrylates Copolymer
VP/Vinyl Caprolactam/DMAPA Acrylates Copolymer

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

For these 27 vinylpyrrolidone polymers deemed safe, concern over the lack of dermal absorption data was mitigated by large ingredient molecular weights, low residual monomer content, and related compositional characteristics and physical properties, despite differences in monomer identities. However, for the following urethanes subgroup, the Panel concluded that the data are insufficient to determine safety:

Urethanes
VP/Dimethiconylacrylate/Polycarbamyl/Polyglycol Ester
VP/Dimethylaminoethylmethacrylate/Polycarbamyl Polyglycol Ester
VP/Polycarbamyl Polyglycol Ester

The Panel determined that the following data are needed to assess the safety of these 3 ingredients:

- Residual monomer concentration for at least a representative ingredient from this subgroup

Additionally, the Panel requested data on the average molecular weight range for the three urethanes, if available.

The Panel also agreed that the Discussion be revised to include a statement on using current good manufacturing practices (cGMPs) to limit impurities, including acrylate-type monomers. Because of the sensitizing potential of certain methacrylates, nail enhancement products containing Methacrylic Acid/Styrene/VP Copolymer and VP/Acrylates/Lauryl Methacrylate Copolymer should be accompanied with directions to avoid skin contact.

Tentative Safety Assessments

Salicylic Acid & Salicylates

The Panel issued a revised tentative amended report for public comment with the conclusion that Salicylic Acid and the 18 salicylate ingredients listed below are safe in cosmetics in the present practices of use and concentration described in the safety assessment, when formulated to be non-irritating and non-sensitizing, which may be based on a quantitative risk assessment (QRA).

Butyloctyl Salicylate
Calcium Salicylate*
C12-15 Alkyl Salicylate*
Capryloyl Salicylic Acid
Ethylhexyl Salicylate
Hexyldodecyl Salicylate*
Isocetyl Salicylate*
Isodecyl Salicylate
Magnesium Salicylate
Methyl Salicylate
Myristyl Salicylate*
Potassium Salicylate*
Salicylic Acid
Sodium Salicylate
TEA-Salicylate
Tridecyl Salicylate
Amyl Salicylate
Hexyl Salicylate
Isotridecyl Salicylate*

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

Ingredients identified by blue text were not included in the original safety assessment.

The Panel originally published a Safety Assessment of Salicylic Acid and 16 salicylates in 2003 with the conclusion that Salicylic Acid; the salts, Calcium Salicylate, Magnesium Salicylate, MEA-Salicylate, Potassium Salicylate, Sodium Salicylate, and TEA-Salicylate; the esters, Capryloyl Salicylic Acid, C12-15 Alkyl Salicylate, Isocetyl Salicylate, Isodecyl Salicylate, Methyl Salicylate, Myristyl Salicylate, Ethylhexyl Salicylate, and Tridecyl Salicylate; and the compounds, Butyloctyl Salicylate and Hexyldodecyl Salicylate, are safe as used when formulated to avoid skin irritation and when formulated to avoid increasing the skin's sun sensitivity, or, when increased sun sensitivity would be expected, directions for use include the daily use of sun protection. The complete report is available on the CIR website (https://www.cir-safety.org/ingredients).

According to 2018 VCRP data, the ingredient with the greatest use frequency of is Ethylhexyl Salicylate (3474 uses), followed by Salicylic Acid (1300 uses). The results of a concentration of use survey conducted by the Personal Care Products Council (Council) in 2018 indicate that Butyloctyl Salicylate is being used at concentrations up to 35.9% in leave-on products (lipstick), which is the highest maximum use concentration that is being reported for ingredients being reviewed in this safety assessment.

The qualification relating to formulating products to avoid increasing the skin's sun sensitivity that was included in the original conclusion is now omitted, based on results from a National Toxicology Program (NTP) photocarcinogenicity study indicating that Salicylic Acid has some protective effect at lower light intensities. In the NTP study, the effects of synthetic solar light on the skin of hairless mice treated with creams containing 2% or 4% Salicylic Acid, were evaluated. Creams containing Salicylic Acid decreased the incidence of skin tumors in mice receiving the lower of two light intensities.

At its June 2018 meeting, the Panel issued a tentative amended report with a conclusion that these ingredients are safe when formulated to be non-irritating. However, upon further review at this meeting, in addition to concern for irritation potential, the Panel acknowledged positive sensitization data on salicylates. The Panel noted that the potential for induction of skin sensitization varies depending on a number of factors, including the area of product application; thus, formulators should assess the potential for final formulations to induce sensitization using a QRA or other accepted methodologies. Therefore, the Panel issued a revised tentative amended report with qualifications addressing sensitization as well as irritation, as stated above.

Alkyl Lactyl Lactate Salts

The Panel issued a tentative report for public comment with the conclusion that the 10 alkyl lactyl lactate salts listed below are safe in cosmetics in the present practices of use and concentration described in the safety assessment, when formulated to be non-irritating and non-sensitizing, which may be based on a QRA.

Calcium Stearoyl Lactylate
Sodium Behenoyl Lactylate
Sodium Caproyl Lactylate
Sodium Caproyl/Lauroyl Lactylate
Sodium Cocoyl Lactylate*
Sodium Cupheoyl Lactylate*
Sodium Isostearoyl Lactylate
Sodium Lauroyl Lactylate
Sodium Oleoyl Lactylate*
Sodium Stearoyl Lactylate

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

Alkyl lactyl lactate salts are the carboxylic acid salts of diesters that are formed between a fatty acid group and two equivalents of lactic acid. Acknowledging positive sensitization data on alkyl lactyl lactate salts, the Panel noted that the potential for induction of skin sensitization varies depending on a number of factors, including the area of product application; thus, formulators should assess the potential for final formulations to induce sensitization using a QRA or other accepted methodologies. The Panel was also concerned that the potential exists for dermal irritation with the use of products formulated using alkyl lactyl lactate salts. The Panel also specified that products containing alkyl lactyl lactate salts must be formulated to be nonirritating.

Fatty Acids & Fatty Acid Salts

The Panel issued a tentative report with the conclusion that the following 102 ingredients are safe in the present practices of use and concentration described in the safety assessment when formulated to be non-irritating and non-sensitizing, which may be based on a QRA.

Aluminum Dilinoleate*
Aluminum Distearate
Aluminum Isostearate*
Aluminum Isostearates/Palmitates*
Aluminum Isostearates/Stearates*
Aluminum Isostearates/Laurates/Palmitates*
Aluminum Isostearates/Laurates/Stearates*
Aluminum Lanolate*
Aluminum Stearate
Aluminum Stearates
Aluminum Tristearate
Ammonium Isostearate*
Ammonium Oleate*
Ammonium Stearate*
Arachidic Acid
Beeswax Acid*
Behenic Acid
C14-28 Alkyl Acid
C10-40 Isoalkyl Acid
C14-28 Isoalkyl Acid
C32-36 Isoalkyl Acid*
Calcium Behenate
Calcium Laurate*
Calcium Stearate
Calcium Undecylenate*
Capric Acid
Caproic Acid
Caprylic Acid
Dilinoleic Acid
Dierucic Acid*
Eicosatrienoic Acid*
Erucic Acid*
Hydroxycapric Acid
Hydroxycaprylic Acid
10-Hydroxydecanoic Acid
Hydroxylauric Acid*
Hydroxystearic Acid
10-Hydroxystearic Acid*
Isomerized Linoleic Acid
Isomerized Safflower Acid*
Isostearic Acid
Lauric Acid
Linoleic Acid
Linolenic Acid
Lithium Stearate
Magnesium Lanolate*
Magnesium Laurate
Magnesium Palmitate*
Magnesium Stearate
Magnesium Tallowate*
Myristic Acid
Methyl Myristic Acid*
Oleic Acid
Palmitic Acid
Potassium Behenate
Potassium Borageate*
Potassium Camelliate*
Potassium Caprate*
Potassium Caprylate*
Potassium Caprylate/Caprate*
Potassium Castorate
Potassium Hydrogenated Tallowate

Potassium Hydroxystearate*
Potassium Isostearate
Potassium Lanolate*
Potassium Laurate
Potassium Linoleate*
Potassium Linseedate*
Potassium Oleate
Potassium Olivate/Sunflowerseedate*
Potassium Palmitate
Potassium Stearate
Potassium Sunflowerseedate*
Potassium Tallate
Potassium Tallowate
Potassium Undecylenate*
Sodium Arganate*
Sodium Beeswax*
Sodium Behenate
Sodium Camellia Japonica Seedate*
Sodium Caprate*
Sodium Caprylate*
Sodium Castorate
Sodium Dilinoleate*
Sodium Hydrogenated Tallowate*
Sodium Hydroxystearate*
Sodium Isostearate
Sodium Lanolate*
Sodium Lardate*
Sodium Laurate
Sodium Laurate/Linoleate/Oleate/Palmitate
Sodium Linoleate*
Sodium Oleate
Sodium Palmitate
Sodium Stearate
Sodium Tallowate
Sodium Tamanuseedate*
Sodium Undecylenate*
Stearic Acid
Trilinoleic Acid
Undecanoic Acid
Undecylenic Acid

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

Ingredients denoted in blue were previously reviewed by the Panel.

The Expert Panel recognized that these ingredients, particularly Myristic Acid, Oleic Acid, and Sodium Caprate, can enhance the penetration of other ingredients through the skin. The Panel cautioned that care should be taken in formulating cosmetic products that may contain these ingredients in combination with any ingredients whose safety was based on their lack of dermal absorption data, or when dermal absorption was otherwise a concern.

The Panel was concerned that the potential exists for dermal irritation with the use of products formulated using fatty acids and fatty acid salts. The Panel specified that products containing fatty acids and fatty acid salts must be formulated to be non-irritating. The Panel was also concerned about the potential for polyunsaturated fatty acids to undergo oxidation during the formulation, or storage of cosmetic products, that may produce compounds that are dermal sensitizers. The Panel advises industry to limit oxidative products in formulations containing fatty acids and fatty acid salts, and to utilize accepted methodologies, such as a QRA, to ensure formulations are non-sensitizing.

Brown Algae

The Panel issued a tentative report for public comment with the conclusion that the following 6 of the 82 reviewed brown algae-derived ingredients are safe in the present practices of use and concentration described in the safety assessment.

Alaria Esculenta Extract
Laminaria Digitata Extract
Laminaria Saccharina Extract
Macrocystis Pyrifera (Kelp) Extract
Undaria Pinnatifida Extract
Undaria Pinnatifida Cell Culture Extract*

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

The Panel determined that there was insufficient data to determine the safety of the remaining 76 ingredients. The insufficiencies include a lack of systemic toxicity data and/or sensitization data. In addition to either systemic and/or sensitization data, the Panel requested information regarding the organic constituents and compositions of these ingredients.

Agarum Cribrosum Extract
Ascophyllum Nodosum**
Ascophyllum Nodosum Extract
Ascophyllum Nodosum Powder
Cladosiphon Novae-Caledoniae Extract**
Cladosiphon Okamuranus Extract
Cystoseira Amentacea/Caespitosa/Branchycarpa Extract**
Cystoseira Baccata Extract**
Cystoseira Balearica Extract*

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

***Not reported to be in current use.*

Ingredients in green type were considered sufficient in systemic toxicity data, however, sensitization data is insufficient to determine safety.
Ingredients in blue type were considered sufficient in sensitization data, however, systemic toxicity data is insufficient to determine safety.
Ingredients in black type were considered insufficient in both systemic toxicity and sensitization data.

Clinical studies suggesting the toxic potential of iodine via brown algae consumption as a dietary supplement were noted. However, the exposure to iodine via the use of brown algae ingredients in cosmetics would be far less than oral exposure. The Panel also expressed concern about heavy metals, and arsenic that may be present in these ingredients. They stressed that the cosmetics industry should continue to use cGMPs to limit impurities.

In addition to the requested systemic toxicity data and sensitization data for all ingredients that are lacking this data, the Panel has requested data regarding the possible constituents of concern of these brown-algae derived ingredients (e.g., specific terpenoids and flavonoids, and concentrations of such). As an alternative, the Panel suggested obtaining representative data for each genus, which may be used to formulate decisions regarding other ingredients of the same genus.

Basic Red 76

The Panel issued a tentative report for public comment with the conclusion that Basic Red 76 is safe in cosmetics in the present practices of use and concentration described in the safety assessment. According to 2018 US FDA VCRP data, Basic Red 76 is used in 46 hair- coloring formulations; and according to a survey conducted by the Council, at a maximum use concentration of 0.35%.

The Panel found that the systemic toxicity, developmental and reproductive toxicity, genotoxicity, and irritation data in this report were sufficient. The Panel recognized the positive genotoxicity studies, but considered these irrelevant due to the fact that such results were only obtained at concentrations much higher than what would be used in cosmetics. The Panel also noted the carcinogenic potential of certain aromatic amines metabolites of Basic Red 76. The concern regarding

these metabolites was mitigated considering Basic Red 76 is poorly absorbed, used in rinse-off products only, and formulated at very low concentrations.

Benzyl Salicylate

The Panel issued a tentative report for public comment with a conclusion of safe in cosmetics in the present practices of use and concentration described in the safety assessment when formulated to be non-irritating and non-sensitizing, which may be based on a QRA.

According to 2018 VCRP data, Benzyl Salicylate is reported to be used in 2908 formulations. Based on the results of a survey conducted by the Council on the concentration of use of Benzyl Salicylate as a light stabilizer, it is used at a maximum concentration of up to 0.5% in skin cleansing preparations. The greatest leave-on use concentration for this function is up to 0.15% in "other" makeup preparations.

Acknowledging the positive sensitization data on Benzyl Salicylate, the Panel noted that the potential for induction of skin sensitization varies depending on a number of factors, including the area of product application; thus, formulators should assess the potential for final formulations to induce sensitization using a QRA or other accepted methodologies. The Panel was also concerned that the potential exists for dermal irritation with the use of products formulated using Benzyl Salicylate; thus, products containing Benzyl Salicylate must be formulated to be non-irritating.

Alkoxylated Fatty Amides

The Panel issued a tentative report for public comment with the conclusion that the 40 ingredients listed below are safe in cosmetics in the present practices of use and concentration described in the safety assessment when formulated to be non-irritating.

PEG-2 Cocamide
PEG-3 Cocamide
PEG-4 Cocamide*
PEG-5 Cocamide
PEG-6 Cocamide
PEG-7 Cocamide*
PEG-11 Cocamide*
PEG-20 Cocamide*
PEG-3 Cocamide DEA*
PEG-20 Cocamide MEA*
PEG-6 Hydrogenated Palmamide*
PEG-50 Hydrogenated Palmamide
PEG-13 Hydrogenated Tallow Amide*
PEG-5 Lanolinamide*
PEG-2 Lauramide*
PEG-3 Lauramide*
PEG-5 Lauramide
PEG-6 Lauramide
PEG-11 Lauramide*
PEG-3 Oleamide*
PEG-4 Oleamide*
PEG-5 Oleamide*
PEG-6 Oleamide*
PEG-7 Oleamide*
PEG-9 Oleamide*
PEG-4 Rapeseedamide
PEG-4 Stearamide*
PEG-10 Stearamide*
PEG-15 Stearamide*
PEG-50 Stearamide*
PEG-5 Tallow Amide*
PEG-8 Tallow Amide*
PEG-50 Tallow Amide
PEG-2 Tallowamide DEA*
Polyglyceryl-4-PEG-2 Cocamide*
PPG-2 Cocamide
PPG-1 Hydroxyethyl Caprylamide*
PPG-2 Hydroxyethyl Cocamide
PPG-2 Hydroxyethyl Coco/Isostearamide
PPG-3 Hydroxyethyl Soyamide*

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

The ingredients included in this family are structurally related as *N*-alkoxylated simple amides. Although a few of the ingredients in this are di-*N,N*-alkoxyl- substituted amides, most of these alkoxylated fatty amides are mono-*N*-alkoxyl-substituted. One ingredient that was inadvertently included in the Scientific Literature Review (SLR), PEG-5 Oleamide Dioleate, is a tertiary amide; that ingredient has been deleted from the report.

At its September 2018 meeting, the Panel issued an Insufficient Data Announcement (IDA) for this group. In response to the IDA, sufficient methods of manufacture and impurities data were received. The IDA had also included a request for dermal absorption data, and if absorbed, 28-day dermal toxicity data may be needed. However, the Panel has since determined that the 28-day oral toxicity data and the oral developmental and reproductive toxicity data that are described in the report, combined with the fact that leave-on dermal concentrations of use are very low, mitigate any concerns about systemic toxicity potential. Additionally, the Panel considered that subchronic test data on PEG-4 Rapeseedamide and PPG-2 Hydroxyethyl Cocamide could be read-across to the entire group. The lack of carcinogenicity data was noted; concerns were mitigated by the sufficient, negative genotoxicity studies and lack of structural alerts for carcinogenicity.

The Panel was concerned that the potential exists for dermal irritation with the use of products formulated using the ingredients named in this assessment. Therefore, the Panel specified that products containing the ingredients listed above must be formulated to be non-irritating.

CIR has issued reports on the component parts of the ingredients named in this report. Therefore, to be consistent with existing conclusions for some of the components, specifically the diethanolamides, these ingredients should not be used in cosmetic products in which *N*-nitroso compounds can be formed. Additionally, the levels of free diethanolamine (DEA) are not to exceed the present practices of use and concentration of DEA itself.

Also, the Panel discussed other impurities that could be of concern with this group of ingredients. The possible presence of 1,4-dioxane as an impurity is one concern. The Panel stressed that the cosmetics industry should continue to use the necessary procedures to limit this impurity in alkoxylated fatty amide ingredients before blending them into cosmetic formulations. Because some of the alkoxylated fatty amides may be manufactured from plant- or animal-derived constituents, the Panel stressed that the cosmetics industry should continue to use the necessary procedures to sufficiently limit pesticide residues and heavy metal impurities in these ingredient before blending them into cosmetic formulations. Additionally, the Panel considered the risks inherent in using animal-derived ingredients, namely the transmission of infectious agents. While tallow may be used in the manufacture of some ingredients in this safety assessment and is clearly animal-derived, the Panel noted that tallow is highly processed, and tallow derivatives even more so. The Panel agreed with determinations by the US FDA that tallow derivatives are not risk materials for transmission of infectious agents.

Insufficient Data Announcements

Silica & Silicates

The Panel issued an IDA for the following 40 ingredients:

Activated Clay
Aluminum Calcium Sodium Silicate
Aluminum Iron Calcium Magnesium Germanium Silicates
Aluminum Iron Calcium Magnesium Zirconium Silicates
Aluminum Iron Silicates
Aluminum Silicate
Ammonium Silver Zinc Aluminum Silicate
Ammonium Silver Zeolite
Attapulgite
Bentonite
Calcium Magnesium Silicate
Calcium Silicate
Fuller's Earth
Gold Zeolite
Hectorite
Hydrated Silica
Kaolin
Lithium Magnesium Silicate
Lithium Magnesium Sodium Silicate
Magnesium Aluminometasilicate
Magnesium Aluminum Silicate
Magnesium Silicate
Magnesium Trisilicate
Montmorillonite
Potassium Silicate
Pyrophyllite
Silica
Silver Copper Zeolite
Sodium Magnesium Aluminum Silicate
Sodium Magnesium Silicate
Sodium Metasilicate
Sodium Potassium Aluminum Silicate
Sodium Silicate
Sodium Silver Aluminum Silicate
Titanium Zeolite
Tromethamine Magnesium Aluminum Silicate
Zeolite
Zinc Silicate
Zinc Zeolite
Zirconium Silicate

Ingredients in blue were previously reviewed by the Panel.

The additional data needed for the safety assessment of these cosmetic ingredients are:

- The range of particle sizes for all silica and silicate ingredients that are used in spray and powder formulations
- Chemical characterization, composition, and impurities data for all ingredients, except Silica
- Method of manufacturing and/or source data for all ingredients, except Silica and Hydrated Silica.

Other Items:

Re-Review Summary – Triacetin

The Panel approved the re-review summary of Triacetin, reaffirming that Triacetin is safe as used in cosmetics. This conclusion was originally published by CIR in 2003. Limited new data (a developmental and reproductive toxicity screening test and two genotoxicity studies) that were identified in the published literature, as well as updated information regarding frequencies of use, provided by the FDA, and maximum use concentrations of use, provided by the Council, were reviewed by the Panel.

Strategy Document – Polyaminopropyl Biguanide

The draft final report on Polyaminopropyl Biguanide was tabled at the June 2018 meeting, pending the completion and subsequent availability of the human repeated insult patch test (HRIPT) that the Council agreed to provide. However, an additional data insufficiency determined by the Panel remained:

- Consumer use data on pump and propellant hair sprays, for use in determining the extent of exposure to Polyaminopropyl Biguanide during product use

Thus, a strategy memo was issued at this meeting, to provide the Panel with an opportunity to review, in detail, the exposure parameters that are associated with pump and propellant spray use with this ingredient. Upon completion of this review, the Panel confirmed that the consumer use data are yet insufficient to accurately calculate an inhalation margin of safety.

Strategy Document – Hair Dye Epidemiology Resource Document

At the June 2018 meeting, with regard to the Hair Dye Epidemiology Resource Document, the Panel requested that Dr. Luigi Naldi, Director of the Department of Dermatology, San Bortolo Hospital in Vicenza, Italy, comment on the two newly discovered studies on the potential breast cancer-hair dye association. Furthermore, the Panel requested a clarifying statement on the types of further investigations that are necessary to examine the association between hair dye use and the incidence of breast cancer. At this meeting, the Panel reviewed the revised document as well as Dr. Naldi's comments and his professional opinions on further investigations that are necessary to examine the association between hair dye use and the incidence of breast cancer. The Panel concluded that the available hair dye epidemiology data do not provide sufficient evidence for a causal relationship between personal hair dye use and cancer. The Panel determined to continue monitoring upcoming epidemiological data on the link between personal use of hair dyes and cancer risk and the conclusion of the document would be re-evaluated based upon the new information on a regular period basis. The Panel finalized this document.

Strategy Document – Respiratory Exposure from Cosmetic Ingredients Resource Document

New particle/droplet size information, developed by companies marketing propellant hair sprays and deodorant sprays, was included in this revision. Importantly, a tiered approach to assessment of inhalation exposure has been incorporated into the document. Accordingly, the language was revised to reflect less reliance on particle size and more emphasis on exposure levels from spray cosmetic products by the inhalation route.

The Panel recommended changing the document title to "Respiratory Exposure from Cosmetic Ingredients." The Panel concluded that the document must be further revised to address the comments received on the document to date. The Panel noted that particle size distributions are product specific; however, data are currently insufficient to assess the inhalation exposure assessment of some types of cosmetic sprays. The Panel requested collection and analysis of particle size distributions data of such spray products. In addition, the Panel concluded that, while particle/droplet size is an important parameter, the physicochemical properties of ingredients in a spray formulation, as well as the realistic exposure factors under in-use conditions also play significant roles in evaluating inhalation safety of ingredients as spray formulation. When spray parameters are absent or provide an insufficient basis to support a robust inhalation exposure assessment, the Panel would request additional information from Industry and further evaluate the sufficiency of other exposure data that may be available on a case-by-case basis. Finally, the Panel determined that after all the concerns and received comments are addressed, the revisions should be reviewed by an external expert on inhalation toxicology before finalizing the document.

Since some readers of the document may take certain sentences out of context and misconstrue the inherent meaning of the whole, further edits will be forthcoming in an attempt to prevent such misnomers (misnomers such as: particle size is the only factor; incidental inhalation of any cosmetic product is unlikely to ever result in respiratory harm; this document is applicable to occupational exposures; etc.).

Cosmetic Ingredient Review

Commitment & Credibility since 1976

Memorandum

Date: March 15th, 2019

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

To: All stakeholders

Re: Draft 2020 Priority List

The CIR Procedures require preparation of the Draft 2020 Priority List for public comment by June 1, 2019. The Draft 2020 Priority List is being issued for public comment earlier in the process to allow more time for the acquisition of data. The list is based on stakeholder requests; frequency of use data (FOU) from FDA's Voluntary Cosmetic Registration Program (VCRP) received from the FDA on February 5, 2018; and on CIR staff and Panel workflow. While this list has been updated with 2019 frequency of use data, and a report in progress has been removed from the list, the Draft Priorities for 2020 are the same as those finalized for 2019. Most of the ingredients herein have increased in FOU. Of those that decreased, Calcium Sulfate decreased the most and may be considered for deletion. While no new ingredients are being proposed for addition to the CIR docket, submissions of ingredients for cause are welcome, as always.

While this list includes only the lead ingredients, groupings are provided for each on the following pages of this document. There are twenty-five reports covering 186 ingredients on the Draft 2020 Priorities List. Reports previously prioritized and on the CIR docket at the end of 2019, as well as a number of re-reviews of previous assessments, will supplement the total number of ingredients to be assessed in 2020.

Interested parties are encouraged to submit pertinent data to the CIR, as soon as possible, for use in the development of the Scientific Literature Reviews for these ingredients. Although the specific data needs vary for each safety assessment, the following are typical data that the Panel reviews for each safety assessment.

- Chemistry, impurities, and method of manufacture
- Toxicokinetics data, specifically dermal absorption and/or penetration
- Repeated-dose toxicity data
- Inhalation toxicity data, if the ingredient is used in a product that can be incidentally inhaled
- Reproductive/developmental toxicity data

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- Genotoxicity data; if positive, carcinogenicity data may be needed
- Dermal irritation and sensitization data

For the review of botanical ingredients, the additional data needed include: species, plant part, extraction method, solvent, and data on component chemical characterization. It is important that these data are specific for the ingredient(s).

Draft 2020 Priorities List

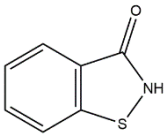
Ingredients	Frequency of Use (FOU) Data	
	Year 2018	Year 2019
For cause		
BENZISOTHIAZOLINONE - preservative	*Not reported since 2016*	
BASIC BROWN 17 – a hair dye	45	51↑
Per FOU		
HONEY	949	1002↑
SACCHARUM OFFICINARIUM (SUGARCANE) EXTRACT	406	447↑
EQUISETUM ARVENSE EXTRACT	369	338↓
SACCHARIDE ISOMERATE	365	455↑
PORTULACA OLERACEA (PURSLANE) EXTRACT	363	481↑
UBIQUINONE	343	374↑
DIATOMACEOUS EARTH	337	213↓
SODIUM LEVULINATE	331	390↑
GLUCONOLACTONE	329	369↑
ACETYL HEXAPEPTIDE-8	318	379↑
CALCIUM SULFATE	317	178↓
HONEY EXTRACT	306	359↑
CHONDRUS CRISPUS EXTRACT	299	350↑
ROSA DAMASCENA FLOWER OIL	298	328↑
SALVIA OFFICINALIS (SAGE) LEAF EXTRACT	292	325↑
ROSA DAMASCENA FLOWER WATER	289	331↑
DICAPRYLYL ETHER	288	344↑
PEG/PPG-8/3 DIISOSTEARATE	277	290↑
POLYQUATERNIUM-51	274	310↑
DIACETONE ALCOHOL	268	223↓
ACETYL GLUCOSAMINE	265	276↑
POLYQUATERNIUM-6	265	280↑
OLEA EUROPAEA (OLIVE) LEAF EXTRACT	257	279↑

Draft 2020 Priorities Groupings for New Reports

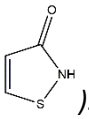
Proposed 2020 Reports – per cause

Benzisothiazolinone – per request **FOU = not reported**

Definition: Benzisothiazolinone is the heterocyclic compound that conforms to the structure:



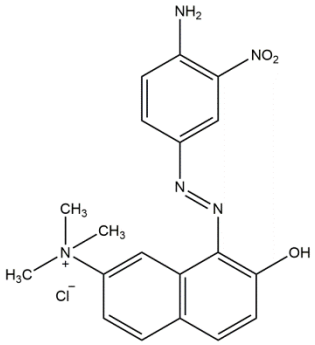
Reported **Function**: Preservative

Notes: *This isothiazolinone-type preservative differs significantly in structure from others as a bicyclic aromatic (isothiazolinone structure:*  *). The α,β-unsaturated carbonyl of this ingredient makes it a Michael-Acceptor (i.e. alert for sensitization potential), but the aromatic ring is likely to attenuate that activity in comparison to the other isothiazolinone-type preservatives.*

Grouping proposal: *None*

Basic Brown 17 – *per PCPC HCTC* **FOU = 51**

Definition: Basic Brown 17 is the monoazo color that conforms to the formula:



Reported **Function**: Hair Colorant

Notes: *Since FOU might not be a very accurate surrogate for exposure, with regard to hair dyes, the PCPC HCTC proposes one hair dye ingredient annually for CIR review.*

Grouping proposal: None

Proposed 2020 Reports – per FOU (all 2019 data)

Honey

FOU = 1002

Definition: Honey is a saccharic secretion gathered and stored by honey bees of the species, *Apis mellifera*, *Tetragonisca angustula*, *Scaptotrigona pectoralis*, or *Melipona Becheii.*

Reported **Functions**: Flavoring Agents; Humectants; Skin-Conditioning Agents - Humectant; Solvents

Notes: *Primarily saccharides, but a complex mixture of proteins, amino acids, vitamins, minerals, etc.*

Grouping proposal: *Honey Ingredients (7 ingredients; 1,373 combined FOU)*

Honey (FOU priority ingredient)	**1002**
Honey Extract	**359**
Hydrogenated Honey (mix of saccharides)	**6**
Hydrolyzed Honey (mix of saccharides)	**-**
Honey Cocoates	**-**
Honey Powder	**6**
Hydrolyzed Honey Protein	**-**

Saccharum Officinarum (Sugarcane) Extract

FOU = 447

Definition: Saccharum Officinarum (Sugarcane) Extract is the extract of the sugar cane, *Saccharum officinarum.*

Reported **Functions**: Exfoliants; Skin-Conditioning Agents - Miscellaneous; Solvents

Notes: *Sugarcane wax is used as a commercial source of long chain fatty alcohols, acids, esters, aldehydes, and ketones. Policosanols and D-003 along with some steroids and terpenoids have also been identified and isolated from sugarcane wax. Policosanols are a mixture of long chain primary aliphatic alcohols (1 - 8) ranging from 2.5 - 80%. Octacosanol constitutes 50 - 80% of the total policosanoles. Other major pharmacologically active components of sugarcane wax are long chain aliphatic fatty acids (9 - 18) present at lower concentrations. Although fatty acid and fatty alcohol are reported as major constituents various phytosterols, steroids, and higher terpenoids have also been reported in sugarcane wax.* *Pharmacognosy Reviews*. 2015;9(17):45-54

Grouping proposal: *Saccharum officinarum-Derived Ingredients (2 ingredients; 447 combined FOU)*

Saccharum Officinarum (Sugarcane) Extract (FOU priority ingredient)	**447**
Saccharum Officinarum (Sugarcane) Wax	**-**

Equisetum Arvense Extract

FOU = 338

Definition: Equisetum Arvense Extract is the extract of the whole herb, *Equisetum arvense*.

Reported **Functions**: Skin-Conditioning Agents - Miscellaneous

Notes:

Grouping proposal: *Horsetail Ingredients (6 ingredients, 368 combined FOU)*

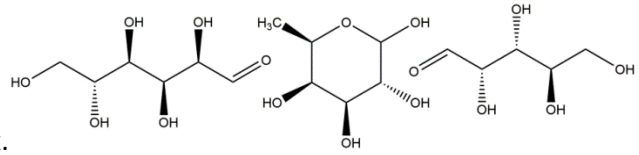
Equisetum Arvense Extract (FOU priority ingredient)	**338**
Equisetum Arvense Juice	**-**
Equisetum Arvense Leaf Extract	**8**
Equisetum Arvense Leaf Powder	**-**
Equisetum Arvense Powder	**1**
Horsetail (Equisetum Arvense) – not in INCI; VCRP only	21

Saccharide Isomerate

FOU = 455

Definition: Saccharide Isomerate is a carbohydrate complex formed from a base catalyzed rearrangement of a mixture of saccharides.

Ex.



Reported **Functions**: Skin-Conditioning Agents - Humectant

Notes: *Many of the saccharide ingredients used as humectants in cosmetic formulation have been previously assessed for safety (e.g., calcium gluconate, fructose, fucose galactose, galactosyl fructose, galacturonic acid, gluconic acid, glucose, isomalt, kefiran, lactitol lactose, lactulose, maltose, mannose, melibiose, potassium gluconate, rhamnose, ribose, sodium gluconate, sucralose, sucrose, trehalose, xylobiose, and xylose were found safe as used in 2014* (Final Report)).

Grouping proposal: *Saccharide Humectants (7 ingredients, 636 combined FOU)*

Saccharide Isomerate (FOU priority ingredient)	**455**
Saccharide Hydrolysate (mix of saccharides)	**30**
Anhydrogalactose	**-**
Anhydroglucitol	**-**
Anhydroxylitol	**151**
Arabinose	**-**
Psicose	**-**

Portulaca Oleracea Extract

FOU = 481

Definition: Portulaca Oleracea Extract is the extract of the whole plant, *Portulaca oleracea.*

Reported **Functions**: Skin-Conditioning Agents - Humectant

Notes: *Common name, Purslane*

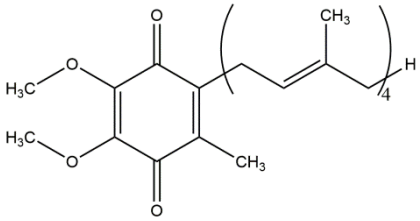
Grouping proposal: *Portulaca oleracea-Derived Ingredients (4 ingredients, 481 combined FOU)*

Portulaca Oleracea Extract (FOU priority ingredient)	**481**
Portulaca Oleracea Flower/Leaf/Stem Extract	**-**
Portulaca Oleracea Juice	**-**
Portulaca Oleracea Water	**-**

Ubiquinone

FOU = 374

Definition: Ubiquinone is the organic compound that conforms to the formula:



Reported **Functions**: Antioxidants; Skin-Conditioning Agents – Miscellaneous

Notes: *Common name is Coenzyme Q10*

Grouping proposal: *Ubiquinone Ingredients (3 ingredients, 381 combined FOU)*

Ubiquinone (FOU priority ingredient)	**374**
Disodium Ubiquinone (salt for of Ubiquinone)	**-**
Hydroxydecyl Ubiquinone (93% structural similarity to Ubiquinone)	**7**

Diatomaceous Earth

FOU = 213

Definition: Diatomaceous Earth is a mineral material consisting chiefly of the siliceous frustules and fragments of various species of diatoms, which may or may not be calcined.

Reported **Functions**: Antiacne Agents; Chelating Agents; Skin-Conditioning Agents - Miscellaneous

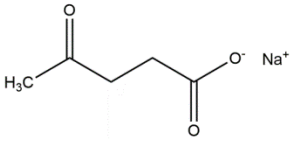
Notes:

Grouping proposal: None

Sodium Levulinate

FOU = 390

Definition: Sodium Levulinate is the sodium salt of Levulinic Acid



Reported **Functions**: Skin-Conditioning Agents - Miscellaneous

Notes: *These are "keto acids," alkyl moieties with a ketone and carboxylic acid functional group.*

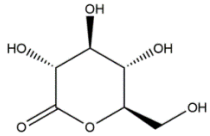
Grouping proposal: *Levulinic Acid and Sodium Levulinate (2 ingredients, 516 combined FOU)*

Sodium Levulinate (FOU priority ingredient)	**390**
Levulinic Acid	**126**

Gluconolactone

FOU = 369

Definition: Gluconolactone is the lactone that conforms to the formula:



Reported **Functions**: Antiacne Agents; Chelating Agents; Skin-Conditioning Agents - Miscellaneous

Notes: *5 such oxidized monosaccharides are found in the Dictionary.*

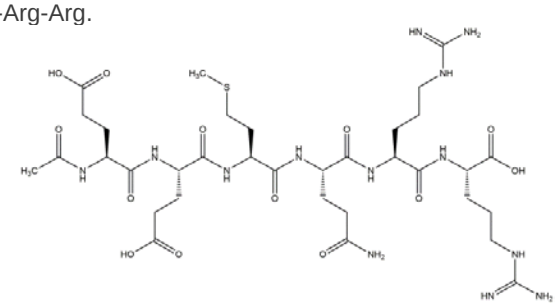
Grouping proposal: *Glycolactones (5 ingredients, 369 combined FOU)*

Gluconolactone (FOU priority ingredient)	**369**
Galactonolactone	**-**
Glucarolactone	**-**
Glucoheptonolactone	**-**
Ribonolactone	**-**

Acetyl Hexapeptide-8

FOU = 379

Definition: Acetyl Hexapeptide-8 is product obtained by the acetylation of Hexapeptide-8. Hexapeptide-8 is a synthetic peptide containing arginine, glutamic acid, glutamine and methionine. The specific sequence is Ac-Glu-Glu-Met-Gln-Arg-Arg.



Reported **Functions**: Skin-Conditioning Agents - Humectant

Notes: *These two ingredients share the same sequence and only differ at the C-terminus*

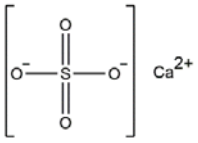
Grouping proposal: *Acetyl Hexapeptide-8 and its Amide (2 ingredients, 379 combined FOU)*

Acetyl Hexapeptide-8 (FOU priority ingredient)	**379**
Acetyl Hexapeptide-8 Amide	**-**

Calcium Sulfate

FOU = 178

Definition: Calcium Sulfate is the inorganic salt that conforms to the formula:



***Reported* Functions**: Abrasives; Bulking Agents; Opacifying Agents

Notes:

Grouping proposal: *Calcium Sulfate and its hydrate (2 ingredients, 183 combined FOU)*

Calcium Sulfate (FOU priority ingredient)	**178**
Calcium Sulfate Hydrate	**5**

Chondrus Crispus Extract

FOU = 350

Definition: Chondrus Crispus Extract is the extract of the ~~whole plant~~ [red alga], *Chondrus crispus*.

***Reported* Functions**: Skin-Conditioning Agents - Miscellaneous

Notes:

-most are from the complex cell wall

-source of stabilizers and thickeners used in: salad dressing, soft serve ice cream, puddings, icings, sauces, creamed soups, laxatives, lotions, creams, etc.

-source of Agar (safe as used by CIR (Final Report))

Grouping proposal: *Red Alga (73 ingredients, combined 865 FOU)*

Chondrus Crispus Extract (FOU priority ingredient)	**350**
Chondrus Crispus (aka "irish moss" in VCRP)	**6**
Chondrus Crispus Powder	**42**
Hydrolyzed Chondrus Crispus Extract	**2**
Ahnfeltiopsis Concinna Extract (aka AHNFELTIA CONCINNA EXTRACT)	**15**
Asparagopsis Armata Extract	**40**
Betaphycus Gelatinum Extract	**-**
Botryocladia Occidentalis Extract	**-**
Calliblepharis Ciliata Extract	**-**
Calliblepharis Jubata Extract	**-**
Ceramium Kondoi Extract	**-**
Ceramium Rubrum Extract	**-**
Chondracanthus Teedei Powder	**-**
Chondracanthus Tenellus Extract	**-**
Chondracanthus Tenellus/Saccharina Angustata/Ulva Linza Extract	**-**

Chondrus Elatus Extract	**-**
Chondrus Elatus/Saccharina Angustata/Monostroma Nitidum Thallus Extract	**-**
Corallina Officinalis Extract	**79**
Corallina Officinalis Powder	**-**
Digenea Simplex Extract	**1**
Dilsea Carnosa Extract	**-**
Eucheuma Serra Extract	**-**
Eucheuma Serra/Grateloupia Sparsa/Saccharina Angustata/Ulva Linza/Undaria Pinnatifida Extract	**-**
Eucheuma Serra/Saccharina Angustata/Ulva Linza Extract	**-**
Furcellaria Lumbricalis Extract	**-**
Galaxaura Rugosa Extract	**-**
Galaxaura Rugosa/Sargassum Pacificum/Turbinaria Ornata Extract	**-**
Gelidiella Acerosa Extract	**17**
Gelidium Amansii Extract	**-**
Gelidium Cartilagineum Extract	**27**
Gelidium Sesquipedale Extract	**-**
Gigartina Skottsbergii Extract	**-**
Gigartina Stellata Extract	**9**
Gigartina Stellata/Kappaphycus Alvarezii Extract	**-**
Gloiopeltis Furcata Extract	**-**
Gloiopeltis Tenax Extract	**-**
Gloiopeltis Tenax Powder	**-**
Gracilaria Vermiculophylla Extract	**-**
Gracilaria Verrucosa Extract	**-**
Gracilariopsis Chorda Extract	**-**
Grateloupia Elliptica Extract	**-**
Grateloupia Livida Powder	**-**
Grateloupia Sparsa Extract	**-**
Hydrolyzed Asparagopsis Armata Extract	**-**
Hydrolyzed Corallina Officinalis	**-**
Hydrolyzed Corallina Officinalis Extract	**5**
Hydrolyzed Gracilariopsis Chiangii Extract	**-**
Hydrolyzed Porphyra Yezoensis	**-**
Hydrolyzed Rhodophyceae Extract	**-**
Hypnea Musciformis Extract	**133**
Kappaphycus Alvarezii Extract	**9**
Lithothamnion Calcareum Extract	**-**
Lithothamnion Calcareum Powder	**-**
Lithothamnion Corallioides Powder	**-**
Mesophyllum Lichenoides Extract	**-**
Palmaria Palmata Extract	**78**
Palmaria Palmata Powder	**-**
Phymatolithon Calcareum Extract	**-**
Pikea Robusta Extract	**-**
Polysiphonia Brodiei Extract	**-**

Polysiphonia Elongata Extract	**-**
Polysiphonia Lanosa Extract	**-**
Porphyra Columbina Extract	**-**
Porphyra Linearis Powder	**-**
Porphyra Tenera Extract	**-**
Porphyra Umbilicalis Extract	**42**
Porphyra Umbilicalis Powder	**-**
Porphyra Yezoensis Extract	**10**
Porphyra Yezoensis Powder	**-**
Rhodymenia Palmata Extract (synonym for Palmaria Palmata Extract?)	**-**
Rissoella Verruculosa Extract	**-**
Sarcodiotheca Gaudichaudii Extract	**-**
Sodium Porphyra Yezoensis Extract	**-**

Rosa Damascena Flower Oil

FOU = 328

Definition: Rosa Damascena Flower Oil is the volatile oil obtained from the flowers of *Rosa damascena.*

Reported **Functions**: Fragrance Ingredients; Skin-Conditioning Agents - Miscellaneous

Notes: *ROSA DAMASCENA (DAMASK ROSE) FLOWER OIL according to the VCRP.*

Grouping proposal: *Rosa damascene-Derived Ingredients (10 ingredients, 888 combined FOU)*

Rosa Damascena Flower Oil (FOU priority ingredient)	**328**
Hydrolyzed Rosa Damascena Flower Extract	**-**
Rosa Damascena Bud Extract	**-**
Rosa Damascena Extract	**49**
Rosa Damascena Flower	**4**
Rosa Damascena Flower Extract	**153**
Rosa Damascena Flower Powder	**1**
Rosa Damascena Flower Water	**331**
Rosa Damascena Flower Water Extract	**-**
Rosa Damascena Flower Wax	**22**

Salvia Officinalis (Sage) Leaf Extract

FOU = 325

Definition: Salvia Officinalis (Sage) Leaf Extract is the extract of the leaves of *Salvia officinalis*.

Reported **Functions**: Oral Care Agents; Skin-Conditioning Agents - Miscellaneous

Notes:

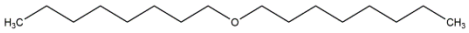
Grouping proposal: *Salvia officinalis-Derived Ingredients (8 ingredients, 423 combined FOU)*

Salvia Officinalis (Sage) Leaf Extract (FOU priority ingredient)	**325**
Salvia Officinalis (Sage) Extract	**83**
Salvia Officinalis (Sage) Flower/Leaf/Stem Extract	**-**
Salvia Officinalis (Sage) Flower/Leaf/Stem Juice	**-**
Salvia Officinalis (Sage) Flower/Leaf/Stem Water	**1**
Salvia Officinalis (Sage) Leaf	**8**
Salvia Officinalis (Sage) Leaf Water	**6**
Salvia Officinalis (Sage) Root Extract	**-**

Dicaprylyl Ether

FOU = 344

Definition: Dicaprylyl Ether is the ether that conforms to the structure:



Reported **Functions**: Skin-Conditioning Agents - Emollient

Notes: *These ingredients are all simple alkyl ethers.*

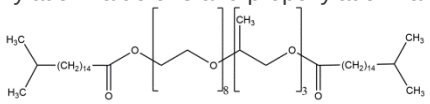
Grouping proposal: *Fatty Ethers (8 ingredients, 360 combined FOU)*

Dicaprylyl Ether (FOU priority ingredient)	**344**
Dicetyl Ether	**-**
Didecyl Ether	**-**
Diisononyl Ether	**-**
Dilauryl Ether	**-**
Dimyristyl Ether	**-**
Distearyl Ether	**16**
Cetyl Dimethylbutyl Ether	**-**

PEG/PPG-8/3 Diisostearate

FOU = 290

Definition: PEG/PPG-8/3 Diisostearate is the polyethylene glycol ether of the propoxylated diester of isostearic acid containing an average ethoxylation value of 8 and propoxylation value of 3.



Reported **Functions**: Surfactants - Emulsifying Agents

Notes: *Glycereth-7 Diisononanoate ("Glycereth" means a glyceryl PEG ether) previously assessed* (Published Report). *These ingredients are linear alkoxyl chains, capped at both ends with stearyl esters.*

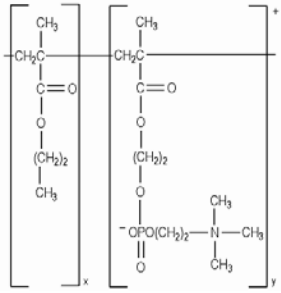
Grouping proposal: *Fatty Ester End-Capped Alkoxylates (13 ingredients, 313 combined FOU)*

PEG/PPG-8/3 Diisostearate (FOU priority ingredient)	**290**
PEG-15 Butylene Glycol Diisostearate	**-**
PEG-10 Glyceryl Diisostearate	**-**
PEG-20 Glyceryl Diisostearate	**-**
PEG-30 Glyceryl Diisostearate	**-**
PEG-60 Glyceryl Diisostearate	**-**
PEG-12 Glyceryl Dimyristate	**18**
PEG-12 Glyceryl Dioleate	**-**
[PEG-3 Glyceryl Distearate] (VCRP listing only)	**1**
PEG-4 Glyceryl Distearate	**-**
PEG-12 Glyceryl Distearate	**4**
PEG-23 Glyceryl Distearate	**-**
PEG-4 Polyglyceryl-2 Distearate	**-**

Polyquaternium-51

FOU = 310

Definition: Polyquaternium-51 is the polymeric quaternary ammonium salt that conforms generally to the formula:



Reported **Functions**: Film Formers; Skin-Conditioning Agents - Humectant

Notes: *All of these ingredients share a acryloyloxyethyl phosphorylcholine monomer in common*

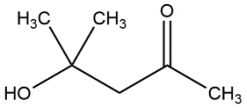
Grouping proposal: *Acryloyloxyethyl Phosphorylcholine Polymers (8 ingredients, 341 combined FOU)*

Polyquaternium-51 (FOU priority ingredient)	**310**
Polyquaternium-61	**9**
Polyphosphorylcholine Glycol Acrylate	**22**
Acrylic Acid/Phosphorylcholine Glycol Acrylate Crosspolymer	**-**
C4-18 Alkyl Methacrylate/Methacryloyloxyethyl Phosphorylcholine Copolymer	**-**
Hydroxyethylcellulose/Phosphorylcholine Glycol Acrylate Copolymer	**-**
Phosphorylcholine Glycol Methacrylate/PEG-10 Dimethacrylate Crosspolymer	**-**
Polyquaternium-10/Phosphorylcholine Glycol Acrylate Copolymer	**-**

Diacetone Alcohol

FOU = 223

Diacetone Alcohol is the ketone that conforms to the formula:



***Reported* Functions**: Fragrance Ingredients; Solvents

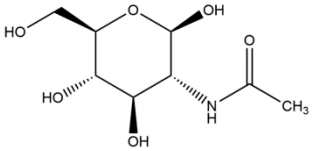
Notes:

Grouping proposal: None

Acetyl Glucosamine

FOU = 276

Definition: Acetyl Glucosamine is the organic compound that conforms to the formula:



***Reported* Functions**: Skin-Conditioning Agents – Miscellaneous

Notes:

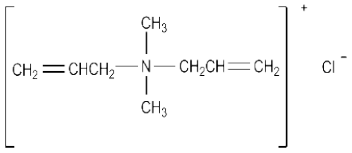
Grouping proposal: *Glucosamine and Acetyl Glucosamine (3 ingredients, 416 combined FOU)*

Acetyl Glucosamine (FOU priority ingredient)	**276**
Glucosamine	**9**
Glucosamine HCl	**131**

Polyquaternium-6

FOU = 280

Definition: Polyquaternium-6 is a polymeric quaternary ammonium salt of Diallyldimethyl Ammonium Chloride (DADMAC)

DADMAC: 

***Reported* Functions**: Antistatic Agents; Film Formers; Hair Fixatives

Notes: *homopolymer*

Grouping proposal: *None*

Olea Europaea (Olive) Leaf Extract

FOU = 279

Definition: Olea Europaea (Olive) Leaf Extract is the extract of the leaves of *Olea europaea.*

Reported **Functions**: Skin-Conditioning Agents – Miscellaneous

Notes: *Olea Europaea (Olive) Fruit Oil has been previously assessed by CIR* (Published Report)

Grouping proposal: *Olea europaea-Derived Ingredients (20 ingredients, 743 combined FOU)*

Olea Europaea (Olive) Leaf Extract (FOU priority ingredient)	**279**
Olea Europaea (Olive) Bark Extract	**-**
Olea Europaea (Olive) Branch Extract	**-**
Olea Europaea (Olive) Bud Extract	**-**
Olea Europaea (Olive) Flower Extract	**186**
Olea Europaea (Olive) Flower Water	**-**
Olea Europaea (Olive) Fruit	**19**
Olea Europaea (Olive) Fruit Extract	**202**
Olea Europaea (Olive) Fruit Juice	**-**
Olea Europaea (Olive) Fruit Oil Ethyl Ester	**-**
Olea Europaea (Olive) Fruit Unsaponifiables	**40**
Olea Europaea (Olive) Fruit Water	**-**
Olea Europaea (Olive) Husk Powder	**-**
Olea Europaea (Olive) Leaf	**-**
Olea Europaea (Olive) Leaf Powder	**3**
Olea Europaea (Olive) Leaf Water	**-**
Olea Europaea (Olive) Sap Extract	**-**
Olea Europaea (Olive) Seed	**-**
Olea Europaea (Olive) Seed Powder	**14**
Olea Europaea (Olive) Wood Extract	**-**