To: CIR Expert Panel Members and Liaisons
From: Bart Heldreth, Executive Director, CIR
Subject: 146th Meeting of the CIR Expert Panel — Monday and Tuesday, March 5-6, 2018
Date: February 9, 2018

Welcome to the March 2018 CIR Expert Panel Meeting. We have been very fortunate to hire 2 new writers and find some great candidates for the staff toxicologist position; so you will see at least 2 fresh faces at this meeting and possibly a 3rd. We are all set and ready for our first Panel meeting of 2018.

Enclosed are the agenda and accompanying materials for the 146th CIR Expert Panel Meeting to be held on March 5-6, 2018. The location is the same as the last meeting – the Darcy Hotel, 1515 Rhode Island Avenue, NW, Washington, District of Columbia, 20005-5595. Phone: (202) 232-7000.

The meeting agenda includes the consideration of 13 reports advancing in the review process, including 6 final reports, 2 tentative reports, 4 draft reports, and 1 re-review. Two of these reports are not included herein, but will be available in Wave 2 supplemental materials (draft report on Parabens and the re-review of Acrylates Copolymers).

Following up on the Panel’s request for additional expertise regarding reproductive and developmental toxicology of parabens, we have a great speaker for this meeting who will present on his personal experience assessing the safety of these ingredients. Our speaker, Dr. George Daston, is the Victor Mills Society Research Fellow at The Procter & Gamble Company. His current research efforts are in the areas of toxicogenomics and mechanistic toxicology, particularly in addressing how findings in these fields can improve risk assessment for chemicals and the development of non-animal alternatives. The title of Dr. Daston’s presentation to the Panel is Assessing the Developmental and Reproductive Toxicity of Parabens.

Schedule and hotel accommodations

We have reserved rooms for the nights of Sunday, March 4th and Monday, March 5th at the Darcy 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. Triphenyl Phosphate (agenda and flash drive name – Triphenyl Phosphate) – This is the first time that the Panel is seeing this report on Triphenyl Phosphate. In January 2018, a Scientific Literature Review (SLR) was issued with an invitation for submission of data on this ingredient. According to the Dictionary, this ingredient functions as a plasticizer in cosmetics. Concentration of use data and comments were received from the Council and addressed. Summaries of 5 human repeat insult patch tests (HRIPTs), and an in-use study wherein Triphenyl Phosphate was tested at up to 7.0% in nail products, were also provided.

   According to 2017 VCRP data, Triphenyl Phosphate is used in 372 leave-on manicuring preparations, with the majority of the uses (327) reported in nail polishes and enamels. The results of the concentration of use survey conducted in 2017 by the Council indicate that...
Triphenyl Phosphate is used in leave-on manicuring preparations at a maximum use concentration range of 1% to 14.5%, with the highest maximum concentration of use reported to be in polish strips.

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. If the available data are insufficient, the Panel should issue an Insufficient Data Announcement (IDA), specifying the data needs therein.

2. Polyol Phosphates (agenda and flash drive name – Polyol Phosphates). This is the first time that the Panel is seeing this report on 10 polyol phosphate ingredients. In December 2017, the SLR was posted for public comment with a request for additional data. Concentration of use data; comments; unpublished data on the skin and ocular irritation potential of Sodium Phytate; and unpublished data on the production method, impurities, and in vitro skin/ocular irritation potential of Phytic Acid were received from the Council and addressed.

Also included are data that may potentially be useful for read across - human dermal penetration data on Potassium Phytate (potential read-across for Sodium Phytate, Phytic Acid, and Phytin) and tumor promotion data on phytic acid hexamagnesium salt n-hydrate (potential read-across for Phytin, the calcium and magnesium salt of Phytic Acid). The potential use of these chemicals for read-across is presented in Table 2 of the safety assessment for the Panel’s consideration.

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. If the available data are insufficient, the Panel should issue an IDA, specifying the data needs therein.

3. Fluoropolymers (agenda and flash drive name – Fluoropolymers). This is the first time that the Panel is seeing these 13 fluorinated polymers as used in cosmetic formulations. In January 2018, the SLR was posted for public comment with a request for additional data. Concentration of use data, additional data, and comments were received from the Council and addressed.

Each ingredient in this report is a synthetic polymer, likely of significant average molecular weight (e.g., the range of molecular weight for PTFE is 400,000 to 10,000,000 Daltons (Da)) and size, and is synthesized utilizing at least one fluorinated monomer. Unless there is reason to believe that one or more of these polymers is small enough to allow dermal penetration, the primary emphasis of this safety assessment should focus on local effects, such as irritation and sensitization, and the presence of impurities (e.g., potentially dermally penetrable residual fluorinated monomer).

If the data included in this report adequately address the safety of these ingredients, the Panel should be prepared to formulate a tentative conclusion, provide the rationale to be described in the Discussion, and issue a Tentative Report for public comment. If the data are not sufficient for making a determination of safety, then an IDA should be issued that provides a listing of the additional data that are needed.

4. Parabens (agenda and Wave2 file name – Parabens). Updates to the Parabens report are yet in process and the Draft Report will be made available in the Wave 2 supplemental files distribution.
Tentative Reports – there are 2 draft tentative reports.

1. *Eucalyptus globulus* (Eucalyptus)-Derived Ingredients (agenda and flash drive name – Eucalyptus). In December 2017, the Panel issued an IDA for this safety assessment of 6 ingredients. The data needs were:

   - Sensitization at maximum concentration of use (i.e., Eucalyptus Globulus Leaf Oil at 5.5%)
   - Impurity data on all ingredients
   - Margin of safety (MOS) calculations for inhalation and dermal exposure using the Eucalyptus Globulus Leaf Oil and/or the major constituent, eucalyptol (1,8-cineole)

The Council has provided a specification technical data sheet and an MSDS on a trade name mixture containing 10% Eucalyptus Globulus Leaf Extract and an HRIPT on a lipstick containing Eucalyptus Globulus Leaf Oil (0.5%). Wave 2 data from December 2017 (irritation, sensitization, and photosensitization) have been added to the report. These data have been marked with lines in the margins. No other data have been submitted.

The data on eucalyptol that the Panel examined in December (for potential inference to Eucalyptus Globulus Leaf Oil), as well as a few additional studies (acute inhalation, oral toxicity, sensitization, oral carcinogenicity), have been incorporated into the report and those data are also marked with lines in the margins.

The Panel should consider and discuss the data and the draft Abstract and Discussion presented in this report and issue a Tentative Report.

2. *Ginkgo biloba* (Ginkgo)-Derived Ingredients (agenda and flash drive name – Ginkgo). In December 2017, the Panel issued an IDA for these 10 ingredients. The Panel’s data needs were:

   - Method of manufacturing for each of these *Ginkgo biloba*-derived cosmetic ingredients
   - Composition and impurities data for each of these *Ginkgo biloba*-derived cosmetic ingredients
   - 28-Day dermal toxicity data
   - Dermal irritation and sensitization data at leave-on use concentrations (i.e., up to 1% Ginkgo Biloba Leaf Extract)
   - Ocular irritation data, if available
   - Genotoxicity data
   - Developmental and reproductive toxicity data
   - Data on the absorption spectra or phototoxicity of these cosmetic ingredients

Since the December Panel meeting, CIR has received the following requested data, which have been incorporated into the report and have been designated with [brackets] in the text or highlighting in the tables.

   - HRIPT on a lotion containing 0.2% Ginkgo Biloba Leaf Extract
   - Certificate of analysis for a Ginkgo Biloba Leaf Extract
   - Composition, method of manufacturing, and toxicity data on Ginkgo Biloba Meristem Cell
   - Absorption spectra for of a Ginkgo Biloba Leaf Extract
   - Summaries of HRIPTs, phototoxicity/photoallergy, and in vitro ocular tests on Ginkgo Biloba Leaf Extract

Additional data from the published literature have also been incorporated in the report and designated appropriately.

Comments provided by the Council prior to the December meeting on the draft report have been
addressed. Additionally, comments provided by the American Herbal Products Association (AHPA) at the meeting have been addressed. The AHPA also provided their comments on the 2-year gavage studies performed by the NTP.

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

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. Alkane Diols (agenda and flash drive name – Alkane Diols). At the December 2017 meeting, the Panel issued its second Revised Tentative Report, with a conclusion that 7 (of the 10) alkane diols are safe in cosmetics in the present practices of use and concentration described in the safety assessment.

The Panel also determined that the data are insufficient to determine the safety of 1,4-Butanediol, 2,3-Butanediol, and Octanediol for use in cosmetic formulations. Concentration of use data are needed to evaluate the safety of 1,4-Butanediol. Because 1,4-Butanediol can be metabolized into gamma-hydroxybutyric acid (GHB), a controlled substance in the United States, and because maximum reported concentrations of use of other ingredients in this report are as high as 40%, the Panel stated that it is necessary to have these data in order to determine safety for use in cosmetic formulations.

For 2,3-Butanediol and Octanediol, the following data are needed:

- Concentration of use data;
- 28-day dermal toxicity studies;
- Developmental and reproductive toxicity data; and
- Mammalian genotoxicity studies (if these ingredients are used at low concentrations, these data may not be needed).

Council comments received prior to the December meeting, and most of those received in response to the Revised Tentative Report that was issued following that meeting, have been addressed. The Council noted that a draft NTP inhalation study on diacetyl (a potential metabolite of 2,3-Butanediol) is available, but the data from that study had not yet been included in the report; those data are now included and highlighted. At the request of the Panel, neurotoxicity mechanism data have been added to the report. The comment yet to be addressed refers to a paragraph in the Discussion, and Panel input is sought to resolve the concern.

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

2. *Hamamelis virginiana* (Witch Hazel)-Derived Ingredients (agenda and flash drive name – Witch Hazel). In December 2017, the Panel issued a Tentative Report with the conclusion that these 8 ingredients 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.

No new data have been submitted. Council comments have been addressed.

After reviewing these documents, the Panel should review the Abstract, Discussion, and Conclusion, and be prepared to issue a Final Report.

3. Malic Acid and Sodium Malate (agenda and flash drive name – Malic Acid). In December 2017, the CIR Expert Panel issued a Tentative Amended Report with the conclusion that Malic Acid and Sodium Malate are safe in cosmetics in the present practices of use and concentration described in this safety assessment.

Since the December meeting, additional data on Sodium Malate (reported as DL) from the Food
Chemicals Codex have been incorporated into the report. No other new data have been discovered or received. Comments provided by the Council prior to the December meeting and on the Tentative Amended Report have been addressed.

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

4. *Mentha piperita* (Peppermint)-Derived Ingredients (agenda and flash drive name – Peppermint). At the December 2017 meeting, the Panel issued a Revised Tentative Amended Report for public comment with a safe when formulated to be non-sensitizing conclusion on 7 of the 10 *Mentha piperita* (peppermint)-derived ingredients:

Mentha Piperita (Peppermint) Oil
Mentha Piperita (Peppermint) Extract
Mentha Piperita (Peppermint) Leaf
Mentha Piperita (Peppermint) Leaf Cell Extract
Mentha Piperita (Peppermint) Leaf Extract
Mentha Piperita (Peppermint) Leaf Juice
Mentha Piperita (Peppermint) Leaf Water

Therein, the Panel also concluded that the available data are insufficient to make a determination of safety for the following 3 ingredients: Mentha Piperita (Peppermint) Flower/Leaf/Stem Extract, Mentha Piperita (Peppermint) Flower/Leaf/Stem Water, and Mentha Piperita (Peppermint) Meristem Cell Culture. The data needed are:

- Composition data
  - Depending on the composition data that are received, other toxicological endpoints may be needed
- Skin irritation and sensitization data

Comments on this safety assessment that were received from the Council prior to the December 2017 Panel and in response to the Tentative Amended Report that was issued after the Panel meeting have been addressed. No responses to data requests pertaining to the insufficient data conclusion on Mentha Piperita (Peppermint) Flower/Leaf/Stem Extract, Mentha Piperita (Peppermint) Flower/Leaf/Stem Water, and Mentha Piperita (Peppermint) Meristem Cell Culture have been received.

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

5. Alkyl Sulaines (agenda and flash drive name – Sultaines). In December 2017, the Panel issued a Tentative Report with the conclusion that the 13 alkyl sulaines are safe in cosmetics in the present practices of use and concentration described in this safety assessment.

Since the December meeting, no new data have been received. Comments provided by the Council prior to the December meeting and on the Tentative Report have been addressed.

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

6. Zinc Salt Ingredients (agenda and flash drive name – Zinc Salts). In December 2017, the Panel issued a Tentative Report for public comment with the conclusion that the 27 zinc salts are safe in cosmetics in the present practices of use and concentration described in the safety assessment when formulated to be non-irritating. The Scientific Literature Review (SLR) that was issued for this group of ingredients included Zinc Sulfide. Because Zinc Sulfide is chemically different from the other ingredients included in this safety assessment (e.g., is not a dissociable salt), the Panel removed Zinc Sulfide from the report.

The majority of the zinc salts are not reported to be irritating. However, because irritation was reported in testing with 1% Zinc Chloride and the threshold for irritation is not known, the Panel specified that products containing zinc salts must be formulated to be non-irritating. The Panel noted that Zinc Sulfate reduced hair shaft melanin content in an oral exposure study, and that hair
shaft depigmentation was observed during multiple hair cycles in treated animals. However, the Panel noted that this study was conducted at high concentrations and therefore the results were not toxicologically significant to the safety of use in cosmetics.

Since the issuance of the Tentative Report, the CIR SSC provided a number of comments including their position that it should be clarified in the report that oral exposure to zinc products was considered. The concentration of zinc in lipstick and oral care products has been added to the report.

The CIR SSC also proposed that Zinc Oxide should be added to the report. However, the bonds between zinc and oxygen therein bear considerable covalent character (covalent bonding was the rationale for excluding Zinc Sulfide from the report). Additionally, this report is in a very late stage, ready for finalization by the Panel, and addition of a new ingredient would require the report to be amended and brought back to the Panel for at least one more iteration.

Other comments (from the CIR SSC and other stakeholders), and submitted data, including HRIPTs on Zinc Laurate, Zinc Myristate, and Zinc Chloride, have been addressed accordingly. Additional published data have also been incorporated. All new data are highlighted in the report.

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

Re-Review – there is 1 Re-Review Report

1. Acrylates Copolymers (agenda and Wave2 file name – Acrylates Copolymers). Drafting of the Acrylates Copolymers report is yet in process and the Re-Review will be made available in the Wave 2 supplemental files distribution.

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-review; and the Draft 2019 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

146th Cosmetic Ingredient Review Expert Panel Meeting
March 5th-6th, 2018
The Darcy Hotel
1515 Rhode Island Avenue, NW,
Washington, District of Columbia, 20005-5595

Monday, March 5th

8:00 am CONTINENTAL BREAKFAST

8:30 am WELCOME TO THE 146th EXPERT PANEL TEAM MEETINGS
Drs. Bergfeld/Heldreth

8:45 am PRESENTATION – Parabens and Spermatogenesis
→ Assessing the Developmental and Reproductive Toxicity of Parabens
Dr. George Daston, P&G

10:00 am TEAM MEETINGS
Drs. Marks/Belsito

Dr. Marks’ Team

Admin (BH) Priorities
DR (LB/BH) Parabens
TR (LB) Eucalyptus
FR (LB) Witch Hazel
DR (WJ) Fluropolymers
DR (WJ) Polyl Phosphates
FAR (WJ) Peppermint
RR (MF) Acrylates Copolymers
FR (MF) Zinc Salts
FR (MF) Alkane Diols
DR (CB) Triphenyl Phosphate
TR (CB) Ginkgo
FR (CB) Sultaines
FAR (CB) Malic Acid

Dr. Belsito’s Team*

FR (MF) Alkane Diols
FR (MF) Zinc Salts
RR (MF) Acrylates Copolymers
TR (CB) Eucalyptus
DR (LB/BH) Parabens
FAR (WJ) Peppermint
DR (WJ) Polyl Phosphates
DR (WJ) Fluropolymers
FR (LB) Witch Hazel
Admin (BH) Priorities

F(A)R: Final (Amended) Report
TR: Tentative Report
DR: Draft Report
RR: Re-Review

NOTE: The order of presentation and discussion of each topic will be maintained. However, the scheduled times may be accelerated or delayed depending upon the time required for the Expert Panel to complete its review of each subject.

*Team moves to breakout room.
**Tuesday, March 6th**

8:00 am  **CONTINENTAL BREAKFAST**

8:30 am  **WELCOME TO THE 146th FULL CIR EXPERT PANEL MEETING**  Dr. Bergfeld

8:45 am  **Admin MINUTES OF THE DECEMBER 2017 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

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<tr>
<td>FR (LB)</td>
<td>Witch Hazel – Dr. Belsito Reports</td>
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<td>FAR (WJ)</td>
<td>Peppermint – Dr. Marks Reports</td>
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<td>FR (MF)</td>
<td>Alkane Diols – Dr. Belsito Reports</td>
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<td>Zinc Salts – Dr. Marks Reports</td>
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### Reports Advancing

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<td>Triphenyl Phosphate – Dr. Marks Reports</td>
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<td>Parabens – Dr. Marks Reports</td>
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<td>DR (WJ)</td>
<td>Polyl Phosphates – Dr. Belsito Reports</td>
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### Other Item

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**ADJOURN** - Next meeting *Monday and Tuesday, June 4th – 5th, 2018*, at The Darcy Hotel, 1515 Rhode Island Avenue, NW, Washington, District of Columbia, 20005-5595

F(A)R: Final (Amended) Report
TR: Tentative Report
DR: Draft Report
RR: Re-Review
## ONE HUNDRED FORTY-FIFTH MEETING

### OF THE

### EXPERT PANEL

December 4-5, 2017

Darcy Hotel

Washington, D.C.

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<tr>
<th>Expert Panel Members</th>
<th>Liaison Representatives</th>
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<tr>
<td>Wilma F. Bergfeld, M.D., Chair</td>
<td><strong>Consumer</strong></td>
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<td>Donald V. Belsito, M.D.</td>
<td>Thomas Gremillion, J.D.</td>
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<td>Ronald A. Hill, Ph.D.</td>
<td><strong>Industry</strong></td>
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<td>Curtis D. Klaassen, Ph.D.</td>
<td>Jay Ansell, Ph.D.</td>
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<td>Daniel C. Liebler, Ph.D.</td>
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<td>James G. Marks, Jr., M.D.</td>
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<td>Ronald C. Shank, Ph.D.</td>
<td><strong>Government</strong></td>
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<td>Thomas J. Slaga, Ph.D.</td>
<td>Linda Katz, MD., M.P.H.</td>
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<td>Paul W. Snyder, D.V.M., Ph.D.</td>
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**Adopted (Date)**

Wilma F. Bergfeld, M.D.
Others Present at the Meeting

Alice Akinsulie            CIR
Jay Ansell                PCPC
Robena Aziz               FDA
Lillian Becker            CIR
Don Bjerke                P & G
Roshil Budhram            L-Brands
Christina Burnett         CIR
Jamie Coleman             Kao USA
Kapal Dewan               FDA
Carol Eisenmann           PCPC
Monice Fiume              CIR
Kevin Fries               CIR
Dave Gossai               L’Oreal
Thomas Gremillion         CFA
Bart Heldreth             CIR
Carla Jackson             CIR
Wilbur Johnson, Jr.       CIR
May Krasteva              L’Oreal
Dennis Laba               Presperse
Jon Lacko                 Estee Lauder
Julia Linthicum           CIR
Linda Loretz              PCPC
Stanley R. Milstein       Milstein & Milstein Associates
Goran Periz               FDA
Yolanda Sales             CIR
David Steinberg           Steinberg and Associates
Merle Zimmermann          AHPA
MINUTES FROM THE 145th CIR EXPERT PANEL MEETING

CHAIRMAN’S OPENING REMARKS

Dr. Bergfeld welcomed the attendees to the 145th meeting of the Cosmetic Ingredient Review (CIR) Expert Panel. She stated that 14 ingredient reports (8 final reports and 6 advancing to another level in the review process) were reviewed in Teams on the preceding day. Three of the 6 reports advancing to another level were on botanical ingredients and the need for additional data was discussed. Dr. Bergfeld also noted that both Teams reviewed and commented on the latest draft of the CIR Hair Dye Epidemiology document, and heard 2 presentations that are relevant to this topic. One of the presentations was on the chemistry of hair dyes, and the other was on an alternative allergy alert test.

Dr. Bergfeld thanked the CIR staff for all of the work that was done in preparing for this Panel meeting.

APPROVAL OF MINUTES

Dr. Belsito called the Panel’s attention to a sentence in the minutes stating that CIR has developed boilerplates that relate to read-across information. Dr. Heldreth confirmed that the sentence should be revised to state that the process of developing these boilerplates has been initiated and remains in progress. The minutes of the September 11-12, 2017 CIR Expert Panel meeting were then unanimously approved.

DIRECTOR’S REPORT

Dr. Heldreth expressed gratitude for the Panel’s and other stakeholders’ continuing support of Cosmetic Ingredient Review program.

Dr. Heldreth thanked the appropriate parties for two cogent presentations made to the Panel at this meeting, and the significant discussion involving issues associated with hair dyes. He also discussed the finalized status with regard to 3 ingredients that had previously been classified with insufficient data conclusions. Specifically, Hydrolyzed Carrageenan and MEA-Hydrolyzed Silk have been moved to the “zero-use category,” and Silkworm Cocoon Extract has been moved to the “use not supported” category.

With regard to visibility of CIR, Dr. Heldreth mentioned that since the last Panel meeting, Ms. Fiume made a presentation at the 7th Cosmetic Compliance Conference, in New York, NY, in November, sharing the structure of CIR and the safety assessment process performed herein (https://cosmeticscompliance.iqpc.com/).

Final Safety Assessments

Ammonia and Ammonium Hydroxide

The Cosmetic Ingredient Review Expert Panel (Panel) issued a final report with the conclusion that Ammonia and Ammonium Hydroxide are safe as used in hair dyes and colors, and safe in cosmetics applied directly to the skin in the present practices of use and concentration described in the safety assessment when formulated to be non-irritating.

It was noted that Ammonia and Ammonium Hydroxide, well-known skin irritants, are indistinguishable from each other in aqueous formulation. Furthermore, since the only cosmetic function of Ammonia applicable to this safety assessment is pH adjuster (which by default means aqueous formulations only) and Ammonium Hydroxide (which is also functions as a denaturant) does not exist outside of water, regardless of which ingredient is added, the final formulations will contain an equilibrium of molecular Ammonia and the ions of Ammonium Hydroxide in water. Thus, whether toxicity data is reported for Ammonia or Ammonium Hydroxide, it is applicable to both (as the test articles would have had this same equilibrium).

Because the use of hair dyes can be irritating, the Panel stated that skin contact should be minimized when using such products.
Persulfates

The Panel issued a final amended report with the conclusion that Ammonium Persulfate, Potassium Persulfate, and Sodium Persulfate are safe as used as oxidizing agents in hair colorants and hair lighteners designed for brief discontinuous use followed by thorough rinsing from the hair and skin. The Panel also concluded that the available data are insufficient for determining the safety of these ingredients in leave-on products and dentifrices.

The additional data needed to evaluate the safety of these ingredients in leave-on products and dentifrices are:

- No-Observed-Adverse Effect-Level (NOAEL) for sensitization and urticarial reactions
- Concentrations of use in leave-on products and dentifrices.

The data needs stated above are the same as those issued from the June 2017 meeting and no data have been received in response thereto. Regarding the “safe as used” part of the current conclusion (stated above), “in hair colorants and lighteners” was changed to “in hair colorants and hair lighteners” to clarify that this conclusion did not apply to skin lighteners.

Specific to dentifrices, the Panel learned of an FDA public health notification concerning the risk of allergic reactions in users of denture cleansers containing Sodium Persulfate, and the risks of misusing these products, prior to initially determining the data needed for completion of this safety assessment. The Panel determined that not enough information (e.g., maximum concentration of use) had been provided to determine the safety of these ingredients for this use. As with toothpastes and mouthwashes, cosmetic use of dentifrices is only applicable in the absence of formulation with fluoride.

Polysilsesquioxanes

The Panel issued a final report with the conclusion that the following 18 polysilsesquioxanes are safe in cosmetics in the present practices of use and concentration described in the safety assessment

<table>
<thead>
<tr>
<th>Acryloyloxypropyl Polysilsesquioxane*</th>
<th>Methacryloyloxypropyl Polysilsesquioxane*</th>
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<td>Dimethicone/Silsesquioxane Copolymer</td>
<td>Polymethylsiloxane</td>
</tr>
<tr>
<td>Dimethiconol/Caprylylsilsesquioxane/Silicate Crosspolymer*</td>
<td>Polydimethylsiloxane PEG/ PPG-24/19 Butyl Ether Silsesquioxane</td>
</tr>
<tr>
<td>Ethyl Polysilsesquioxane*</td>
<td>Polydimethylsiloxane PPG-13 Butyl Ether Silsesquioxane*</td>
</tr>
<tr>
<td>Hydrogen Dimethicone/Octyl Silesquoxane Copolymer</td>
<td>Polymethylsiloxane/Trimethylsiloxysilicate*</td>
</tr>
<tr>
<td>Isobutyl/Methoxy PEG-10 Polysilsesquioxane*</td>
<td>Polypropylsilsesquioxane</td>
</tr>
<tr>
<td>Isobutyl Polysilsesquioxane*</td>
<td></td>
</tr>
</tbody>
</table>

*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 noted a lack of systemic toxicity data (i.e. reproductive and developmental toxicity and carcinogenicity data), but agreed that these ingredients are large, insoluble molecules that share dominant features/structures, and are not expected to penetrate the skin. The Panel also agreed that the weight of the evidence alleviated concerns about the potential for local effects, such as dermal irritation and sensitization. This was reinforced by newly submitted data that included negative acute oral toxicity, genotoxicity, and dermal irritation on additional ingredients. However, manufacturers should continue to use current good manufacturing practices to ensure that the levels of monomers and other source materials are minimized in the final products.

Polymethylsiloxanes was reported to be used in 397 formulations, i.e., 374 in leave-on formulations, 22 in rinse-off formulations, and 1 diluted for the bath formulation. All other ingredients reportedly in use were specified
to be used in 14 formulations or fewer. Polymethylsilsesquioxane had the highest reported maximum concentration of use; it was used at up to 55.2% in the category of other makeup preparations. The rest of the ingredients reportedly in use were stated to be used at 4.9% (e.g., C30-45 Alkylidimethylsilyl Polypropylsilsesquioxane in foundations) or less.

**Triglycerides**

The Panel issued a final amended report with the conclusion that the 51 triglycerides listed below are safe in cosmetics in the present practices of use and concentration described in the safety assessment.

| Triglyceride                                                                 | Acetic/Linoleic/Palmitic Triglyceride* | C12-18 Acid Triglyceride | C18-36 Acid Triglyceride | C8-12 Acid Triglyceride* | Capric/Lauric/Myristic/Oleic Triglyceride* | Caprylic/Capric Triglyceride | Caprylic/Capric/Lauric Triglyceride | Caprylic/Capric/Linoleic Triglyceride | Caprylic/Capric/Myristic/Stearic Triglyceride | Caprylic/Capric/Palmitic/Stearic Triglyceride* | Caprylic/Capric/Stearic Triglyceride | C10-40 Isoalkyl Acid Triglyceride | Cod Liver/Mink/Tallow Triglyceride* | C10-18 Triglycerides | Docosahexenoic/Docosapentenoic/Oleic/Palmitic Triglyceride* | Glyceryl Stearate Diacetate* | Glyceryl Triacetyl Hydroxystearate | Glyceryl Triacetyl Ricinoleate | Glyceryl Tri-Hydrogenated Rosinate | Glyceryl Tripalmitate/Palm | Hydrogenated C12-18 Triglycerides | Isomerized Safflower Glycerides* | Jojoba Oil/Caprylic/Capric Triglyceride Esters* | Lauric/Palmitic/Oleic Triglyceride* | Oleic/Linoleic Triglyceride* |
|------------------------------------------------------------------------------|----------------------------------------|-------------------------|-------------------------|--------------------------|-------------------------------------------|-------------------------------|-------------------------------------|-----------------------------------|------------------------------------------------|------------------------------------------------|---------------------------|---------------------|-----------------------------|-----------------------------|-------------------------------|-----------------------------|----------------------------|--------------------------|-----------------------------|-----------------------------|--------------------------|
| Oleic/Palmitic/Lauric/Myristic/Linoleic Triglyceride*                         | C12-18 Acid Triglyceride               | C18-36 Acid Triglyceride | C8-12 Acid Triglyceride* | Capric/Lauric/Myristic/Oleic Triglyceride* | Caprylic/Capric Triglyceride | Caprylic/Capric/Lauric Triglyceride | Caprylic/Capric/Linoleic Triglyceride | Caprylic/Capric/Myristic/Stearic Triglyceride | Caprylic/Capric/Palmitic/Stearic Triglyceride* | Caprylic/Capric/Stearic Triglyceride | C10-40 Isoalkyl Acid Triglyceride | Cod Liver/Mink/Tallow Triglyceride* | C10-18 Triglycerides | Docosahexenoic/Docosapentenoic/Oleic/Palmitic Triglyceride* | Glyceryl Stearate Diacetate* | Glyceryl Triacetyl Hydroxystearate | Glyceryl Triacetyl Ricinoleate | Glyceryl Tri-Hydrogenated Rosinate | Glyceryl Tripalmitate/Palm | Hydrogenated C12-18 Triglycerides | Isomerized Safflower Glycerides* | Jojoba Oil/Caprylic/Capric Triglyceride Esters* | Lauric/Palmitic/Oleic Triglyceride* | Oleic/Linoleic Triglyceride* |
| Oleic/Palmitic/Lauric/Myristic/Linoleic Triglyceride*                         | C12-18 Acid Triglyceride               | C18-36 Acid Triglyceride | C8-12 Acid Triglyceride* | Capric/Lauric/Myristic/Oleic Triglyceride* | Caprylic/Capric Triglyceride | Caprylic/Capric/Lauric Triglyceride | Caprylic/Capric/Linoleic Triglyceride | Caprylic/Capric/Myristic/Stearic Triglyceride | Caprylic/Capric/Palmitic/Stearic Triglyceride* | Caprylic/Capric/Stearic Triglyceride | C10-40 Isoalkyl Acid Triglyceride | Cod Liver/Mink/Tallow Triglyceride* | C10-18 Triglycerides | Docosahexenoic/Docosapentenoic/Oleic/Palmitic Triglyceride* | Glyceryl Stearate Diacetate* | Glyceryl Triacetyl Hydroxystearate | Glyceryl Triacetyl Ricinoleate | Glyceryl Tri-Hydrogenated Rosinate | Glyceryl Tripalmitate/Palm | Hydrogenated C12-18 Triglycerides | Isomerized Safflower Glycerides* | Jojoba Oil/Caprylic/Capric Triglyceride Esters* | Lauric/Palmitic/Oleic Triglyceride* | Oleic/Linoleic Triglyceride* |

*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 listed in blue were previously reviewed by the Panel. The conclusion reached by the Panel at this meeting reaffirmed the original conclusions of safety.

According to the web-based International Cosmetic Ingredient Dictionary and Handbook, a reported potential function of Docosahexenoic/Docosapentenoic/Oleic/Palmitic Triglyceride is as a skin bleaching agent. However, in the U.S., skin bleaching agent is not considered a cosmetic function, and therefore use in that manner was not assessed in this report.

Finally, the Panel recognized that, reportedly, Triolein and Triacrylylin can enhance the skin penetration of other chemicals. Therefore, 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 a concern.
Panthenol, Pantothenic Acid, and Derivatives

The Panel issued a final report with the conclusion that the following 7 ingredients are safe in the present practices of use and concentration described in the safety assessment:

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Derivative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Panthenol</td>
<td>Panthenyl Triacetate</td>
</tr>
<tr>
<td>Pantothenic Acid</td>
<td>Calcium Pantothenate</td>
</tr>
<tr>
<td>Panthenyl Ethyl Ether</td>
<td>Sodium Pantothenate*</td>
</tr>
<tr>
<td>Panthenyl Ethyl Ether Acetate*</td>
<td></td>
</tr>
</tbody>
</table>

*Not reported to be in current use. Were the ingredients in this group not currently in 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 also noted that these ingredients may contain residual amine impurities, and thus cautioned that these ingredients should not be used in cosmetic products in which N-nitroso compounds can be formed.

Panthenol, Panthenyl Ethyl Ether, Panthenyl Ethyl Ether Acetate, and Panthenyl Triacetate can be metabolized to Pantothenic Acid, an essential nutrient. The Panel recognized that exposures from absorbed amounts of these compounds are below what would be typical from dietary intake, thereby underscoring the safety of the ingredients.

Tentative Safety Assessments

Malic Acid and Sodium Malate

The Panel issued a tentative amended report for public comment with the conclusion that Malic Acid and Sodium Malate are safe in cosmetics in the present practices of use and concentration described in the safety assessment.

The Panel noted that there are no sensitization data for Malic Acid at the maximum leave-on use concentration of 2.1%. The results of a human repeated insult patch test (HRIPT) found that Malic Acid at 1% in formulation did not induce dermal sensitization. Based on the experience of the clinicians on the Panel and the fact that Malic Acid and Sodium Malate are common chemicals in human biology, the Panel concluded that these ingredients would not induce sensitization at use concentrations.

The Panel also noted that Malic Acid is an ocular irritant and use as a hair spray has been reported. The Panel thus advises consumers to minimize incidental ocular exposure to hair sprays containing Malic Acid.

Mentha piperita (Peppermint)-Derived Ingredients

The Panel issued a revised tentative amended report for public comment with a conclusion that 7 of the 10 Mentha piperita (peppermint)-derived ingredients are safe in cosmetics in the present practices of use and concentration described in the safety assessment when formulated to be non-sensitizing:

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Derivative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mentha Piperita (Peppermint) Oil</td>
<td>Mentha Piperita (Peppermint) Leaf Extract</td>
</tr>
<tr>
<td>Mentha Piperita (Peppermint) Extract</td>
<td>Mentha Piperita (Peppermint) Leaf Juice*</td>
</tr>
<tr>
<td>Mentha Piperita (Peppermint) Leaf</td>
<td>Mentha Piperita (Peppermint) Leaf Water</td>
</tr>
<tr>
<td>Mentha Piperita (Peppermint) Leaf Cell Extract*</td>
<td></td>
</tr>
</tbody>
</table>

*Not reported to be in use. Were the ingredients in this group not currently in 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 noted that, because botanical ingredients are complex mixtures, there is concern that multiple botanical ingredients in one formulation may each contribute to the final concentration of a single shared constituent. Therefore, when formulating products, manufacturers should avoid reaching levels, in final formulations, of botanical constituents that may cause sensitization or other adverse effects.
The Panel also concluded that the available data are insufficient to make a determination of safety for Mentha Piperita (Peppermint) Flower/Leaf/Stem Extract, Mentha Piperita (Peppermint) Flower/Leaf/Stem Water**, and Mentha Piperita (Peppermint) Meristem Cell Culture.** (**Not reported to be in use.)

The following data needed to formulate a conclusion of safety:

- Composition data on each of the 3 ingredients above
  - Depending on the composition data that are received, other toxicological endpoints may be needed
- Skin irritation and sensitization data

At the September 2017 Panel meeting, the Panel issued a tentative amended conclusion stating that Mentha Piperita (Peppermint) Oil is safe in the present practices of use and concentration when formulated to be non-sensitizing, but that the available data were insufficient for making a determination of safety for the remaining 9 ingredients. A revised tentative amended report is being issued at this meeting because the Panel determined that the data on Mentha Piperita (Peppermint) Leaf Extract and Mentha Piperita (Peppermint) Extract that were received in response to the data needs associated with the insufficient data conclusion support the safe use of Mentha Piperita (Peppermint) Extract, Mentha Piperita (Peppermint) Leaf, and the 4 ingredients that are derived from the leaf, when these ingredients are formulated to be non-sensitizing. However, the available data remain insufficient for making a determination of safety in cosmetic products for Mentha Piperita (Peppermint) Flower/Leaf/Stem Extract, Mentha Piperita (Peppermint) Flower/Leaf/Stem Water, and Mentha Piperita (Peppermint) Meristem Cell Culture.

Alkyl Sultaines

The Panel issued a tentative report for public comment with the conclusion that the following 13 ingredients are safe in cosmetics in the present practices of use and concentration described in the safety assessment:

- Capryl Sultaine
- Cetyl/Lauryl/Myristyl Hydroxysultaine*
- Coco-Hydroxysultaine*
- Coco-Sultaine*
- Lauryl Hydroxysultaine
- Lauril Sultaine
- Myristyl Sultaine*
- Cocamidopropyl Hydroxysultaine
- Erucamidopropyl Hydroxysultaine
- Lauramidopropyl Hydroxysultaine*
- Oleamidopropyl Hydroxysultaine*
- Tallowamidopropyl Hydroxysultaine*

*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 expressed concern that 3,3-dimethylaminopropylamine (DMAPA) and related amines that may exist as impurities in the amidopropyl hydroxysultaine ingredients could cause sensitization. Dermal sensitization was not observed in animal or human studies of Cocamidopropyl Hydroxysultaine and Lauramidopropyl Hydroxysultaine; and suppliers have reported that DMAPA impurities are at extremely low levels (< 3 ppm). To ensure that sensitization does not occur in consumers, the Panel urges manufacturers to minimize the content of DMAPA and related sensitizing agents in cosmetic formulations.

Zinc Salts

The Panel issued a tentative report for public comment with the conclusion that the 27 zinc 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:

- Zinc Acetate
- Zinc Ascorbate
- Zinc Ascorbate Hydroxide*
- Zinc Aspartate
- Zinc Carbonate
- Zinc Carbonate Hydroxide*
Zinc Chloride
Zinc Chloride Hydroxide*
Zinc Citrate
Zinc Cysteinate*
Zinc Gluconate
Zinc Glutamate*
Zinc Glycinate
Zinc Hexametaphosphate*
Zinc Hydroxide
Zinc Lactate
Zinc Laurate
Zinc Myristate
Zinc Neodecanoate*
Zinc Nitrate*
Zinc Palmitate*
Zinc Phosphate
Zinc Ricinoleate
Zinc Salicylate
Zinc Stearate
Zinc Sulfate
Zinc Undecylenate

*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 Scientific Literature Review (SLR) that was issued for this group of ingredients included Zinc Sulfide. Because Zinc Sulfide is chemically different from the other ingredients included in this safety assessment (e.g., is not a dissociable salt), the Panel removed Zinc Sulfide from the report.

The majority of the zinc salts are not reported to be irritating. However, because irritation was reported in testing with 1% Zinc Chloride and the threshold for irritation is not known, the Panel specified that products containing zinc salts must be formulated to be non-irritating.

The Panel noted that Zinc Sulfate reduced hair shaft melanin content in an oral exposure study, and that hair shaft depigmentation was observed during multiple hair cycles in treated animals. However, the Panel noted that this study was conducted at high concentrations and therefore the results were not toxicologically significant to the safety of use in cosmetics.

Alkane Diols

The Panel issued a revised tentative report for public comment, with a split conclusion of safety for this ingredient family. The Panel concluded that the following 7 (of 10 total) alkane diols are safe in cosmetics in the present practices of use and concentration described in the safety assessment.

Butyl Ethyl Propanediol
1,10-Decanediol
Hexanediol
Isopentyldiol
Methylpropanediol
1,5-Pentanediol*
Propanediol

*Not reported to be in current use. Were the ingredients in this group not currently in 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 also determined that the data are insufficient to determine the safety of 1,4-Butanediol, 2,3-Butanediol (not reported to be in current use), and Octanediol for use in cosmetic formulations.

Concentration of use data are needed to evaluate the safety of 1,4-Butanediol. Because 1,4-Butanediol can be metabolized into gamma-hydroxybutyric acid (GHB), a controlled substance in the United States, and because maximum reported concentrations of use are as high as 40%, the Panel stated that it is necessary to have this data in order to determine safety for use in cosmetic formulations.

For 2,3-Butanediol and Octanediol, the following data are needed:

- Concentration of use
- 28-Day dermal toxicity studies
• Developmental and reproductive toxicity data
• Mammalian genotoxicity studies (if these ingredients are used at low concentrations, these data may not be needed)

In the previous tentative report, 1,5-Pentanediol was listed as having insufficient data. However, because the report includes metabolism data, acute oral toxicity data, negative Ames test data, and negative irritation, sensitization, and photosensitization data, the Panel determined that the data were no longer considered insufficient.

**Hamamelis virginiana (Witch Hazel)-Derived Ingredients**

The Panel issued a tentative report with the conclusion that the following 8 *Hamamelis virginiana* (witch hazel)-derived ingredients 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.

<table>
<thead>
<tr>
<th>Hamamelis Virginiana (Witch Hazel) Bark/Leaf Extract*</th>
<th>Hamamelis Virginiana (Witch Hazel) Extract</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hamamelis Virginiana (Witch Hazel) Bark/Leaf</td>
<td>Hamamelis Virginiana (Witch Hazel) Flower Water</td>
</tr>
<tr>
<td>Hamamelis Virginiana (Witch Hazel) Bark/Leaf/Twig Extract</td>
<td>Hamamelis Virginiana (Witch Hazel) Leaf Extract</td>
</tr>
<tr>
<td>Hamamelis Virginiana (Witch Hazel) Bark/Twig Extract*</td>
<td>Hamamelis Virginiana (Witch Hazel) Leaf Water</td>
</tr>
<tr>
<td>Hamamelis Virginiana (Witch Hazel) Bark/Twig</td>
<td>Hamamelis Virginiana (Witch Hazel) Water</td>
</tr>
</tbody>
</table>

* 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’s concerns included the presence of geraniol and the oxidation products of linalool in cosmetics, which could result in potential dermal sensitization, as well as other constituents of concern. At the reported concentrations of use of these *Hamamelis virginiana* (witch hazel)-derived ingredients, the constituents that may cause these effects are present far below levels of concern, including for sensitization. However, the Panel noted that, because botanical ingredients are complex mixtures, there is concern that multiple botanical ingredients in one formulation may each contribute to the final concentration of a single shared constituent. Therefore, when formulating products, manufacturers should avoid reaching levels, in final formulations, of botanical constituents that may cause sensitization or other adverse effects. Also, these ingredients are astringents and are reported to be used in products used around the eyes; and thus, these ingredients may be irritating.

Hamamelis Virginiana (Witch Hazel) Water is reported to be used in 386 formulations (255 in leave-on formulations, 122 in rinse-off formulations, and 9 in formulations that are diluted for the bath). Hamamelis Virginiana (Witch Hazel) Extract is reported to be used in 359 formulations and Hamamelis Virginiana (Witch Hazel) Leaf Extract is reported to be used in 218 formulations. All other in-use ingredients are reported to be used in 128 or fewer formulations. Hamamelis Virginiana (Witch Hazel) Water has the highest reported maximum concentration of use; it is used at up to 43% (in the category of other skin care preparations). All other in-use ingredients are reported to be used at up to 4.3% or less.

**Insufficient Data Announcements**

**Ginkgo biloba-Derived Ingredients**

The Panel issued an Insufficient Data Announcement (IDA) for the following ingredients:

| Ginkgo Biloba Leaf Extract | Ginkgo Biloba Leaf Water |
| Ginkgo Biloba Biflavones | Ginkgo Biloba Meristem Cell |
| Ginkgo Biloba Leaf | Ginkgo Biloba Nut Extract |
| Ginkgo Biloba Leaf Cell Extract | Ginkgo Biloba Root Extract |
| Ginkgo Biloba Leaf Powder | Ginkgo Leaf Terpenoids |

The data needed for these cosmetic ingredients are:
• Method of manufacturing for each of these Ginkgo biloba-derived cosmetic ingredients
• Composition and impurities data for each of these Ginkgo biloba-derived cosmetic ingredients
• 28-Day dermal toxicity data
• Dermal irritation and sensitization data at leave-on use concentrations
• Ocular irritation data, if available
• Genotoxicity data
• Developmental and reproductive toxicity data
• Data on the absorption spectra or phototoxicity of these cosmetic ingredients

**Eucalyptus globulus** (Eucalyptus)-Derived Ingredients

The Panel issued an IDA for the following *Eucalyptus globulus*-derived ingredients.

- Eucalyptus Globulus Leaf
- Eucalyptus Globulus Leaf Extract
- Eucalyptus Globulus Leaf Oil
- Eucalyptus Globulus Leaf Powder
- Eucalyptus Globulus Leaf/Twig Oil
- Eucalyptus Globulus Leaf Water

The data needs are:

- Sensitization on Eucalyptus Globulus Leaf Oil at 5.5% or greater
- Impurity data on all ingredients
- Margin of safety (MOS) calculations for inhalation and dermal exposure using the Eucalyptus Globulus Leaf Oil and/or the major constituent, eucalyptol (1,8-cineole)

**Tabled Assessment**

**Polyaminopropyl Biguanide (aka polyhexamethylene biguanide hydrochloride)**

The draft final report on this ingredient was tabled in response to a commitment from the cosmetics industry to complete a 100-person human repeated insult patch test of a product containing Polyaminopropyl Biguanide. The task force that will be overseeing this project is being formed, and the Panel will receive ongoing updates relating to this project. The Panel requested that a progress report be given at the March 2018 Panel meeting.

At the September 2017 Panel meeting, the Panel issued a tentative report with a conclusion stating that the available data are insufficient to make a determination that Polyaminopropyl Biguanide is safe under the intended conditions of use in cosmetic formulations. The data that are needed to complete the safety assessment of this ingredient are:

- HRRIPT on Polyaminopropyl Biguanide involving a diverse population (i.e., with a range of Fitzpatrick skin types) of 100 subjects tested with a dose of 1,000 μg/cm² (and recommend to test at 500 μg/cm² as well)
- Consumer use data on pump and propellant hair sprays, for use in estimating the extent of exposure to Polyaminopropyl Biguanide during spray product use

In response to a previous IDA, a spray model and a no observed adverse effect concentration (NOAEC) were used to calculate a margin of safety (MOS). MOS values for both pump hair sprays and propellant hair sprays were calculated. In reviewing this risk assessment, the Panel noted that the exposure scenario (e.g., sprayed over 6 hours) in one of the underlying experimental studies was not representative of pump and propellant hair spray product use. Thereby, consumer use data on these product types are needed to determine a dose, if the safe use of this ingredient is to be determined for products that are intended to be sprayed. However, this ingredient might not actually be in use in products that are intended to be sprayed. Indeed, one supplier submitted a comment that their company would not consider using this ingredient in such applications.

A quantitative risk assessment (QRA) yielded a no expected sensitization induction level (NESIL) of 1000 μg/cm², which theoretically supports the use of this ingredient at concentrations of ≤ 0.1%. However, the Panel noted that the
HRIPT study utilized to support this NESIL may not be adequately diverse, and suggested that an HRIPT (> 100 subjects) on a more diverse study population at a dose of 500 and 1000 μg/cm² is needed to derive an acceptable NESIL.

**CIR Precedent (Guidance Document)**

**Hair Dye Epidemiology**

The Panel reviewed the latest draft of the Hair Dye Epidemiology document. The previous draft was reviewed by the Panel at the September 2017 meeting. Comments on the previous draft were addressed and a few additional studies were added to the document. The Panel noted the presentations on hair dye self-testing and hair dye chemistry at this meeting. The Panel approved the current revisions. However, the Panel concluded that the services of an expert epidemiologist, with experience specifically relevant to factors associated with breast cancer, should be retained. Specifically, this expert would be asked to evaluate all of the currently available epidemiology studies that investigated the potential association between hair dye use and breast cancer, reconcile the disparities in the results of those studies, and provide the Panel with a concise summary for inclusion in this Precedents document.
Presentations

The Panel requested further expert input on the topics of hair dye chemistry and allergy testing. In response, two presentations were made at this meeting. Dr. Carsten Goebel presented a briefing titled “Chemistry of Coloring.” Dr. Goebel is currently responsible for the safety evaluation of the professional hair care division at Coty.

Therein, he demonstrated that common precursors and couplers and precursors used in oxidative hair dye formulations. And, Dr. Goebel showed the common reaction pathways and reaction products, resulting in dimer and trimer products.

According to Dr. Goebel, consumer exposure is limited to unreacted precursors and couplers, plus expected reaction products. He stressed that self-coupling products and intermediates can be ruled out and that the maximum external exposure to reaction products is in the range of 0.02 to 0.33% (concentration in formulation).

Finally, Dr. Goebel detailed the results of various in vitro and in vivo genotoxicity tests on oxidative hair dye reaction products. DEREK alerts had indicated that some of these products had the potential for positive genotoxicity. However, even though Ames and micronucleus tests seemed to concur with these alerts in some cases, none of the in vivo test results were indicative of genotoxicity.
Dr. Maya Krasteva then presented a briefing titled “Allergy Alert Test: Proof of Concept Study.” Dr. Krasteva is a Eurotox registered dermatologist and is currently a Senior Scientist at L’Oreal, involved with safety evaluation, postmarketing safety, and regulatory affairs. Dr. Krasteva emphasized that in the results of this study on hair dye allergy alert testing, there were no statistically significant differences between 1) consumer self-assessment and dermatological assessment, 2) testing site results behind the ear or on the forearm, and 3) assessment between day 2 or day 4. She also concluded that these new parameters for hair dye allergy testing would adequately alert consumers with allergies to hair dye ingredients to avoid hair dyeing.

### Case study: Subject AU01
- 21 year-old male
- Declared a reaction to a dark shade in real use conditions (mean concentration 0.75% PPD)
- Severity of clinical reaction: mild
- Patch test to PPD (2012): weakly positive (+)
- Noticed 14.5 hours post-AAT reactions developing on both sites to Product C (0.75%): reddening and itching; swelling developed later.

Reactions to Product C (0.75% PPD), Day 2

The results of this study demonstrated that an alternative test methodology (alternative to the standard hair dye patch test) could adequately alert consumers with hair dye allergies to avoid hair dyeing, but very importantly, tested in a location that is easier to self-assess (forearm as opposed to behind the ear) and tested with a much shorter exposure time (45 minutes as opposed to 24 hours in the standard patch test). Potentially, this shorter exposure time might result in a reduced potential to self-sensitize the consumer with the test itself.

### Main conclusions of the study
- Open testing under realistic hair dye use conditions (AAT design) was efficient to cause a reaction noticeable by the majority of study subjects (39/42 subjects available for analysis) within 48 hours. This was objectified by dermatological evaluation. In addition, the dermatological evaluation did not find significant differences between Day 2 and Day 4. Therefore, a self-evaluation period of 2 days is feasible.
- Comparison of the two test sites (response rate of 90.5% on forearm and 93% behind the ear) did not reveal statistically significant differences, both by self-assessment and when combined with dermatological assessment.
- All subjects (19/19) with the highest reactivity to PPD (+++) reacted already to PPD concentrations between 0.05 and 0.75% in the AAT, indicating that they would be adequately alerted to avoid hair dyeing.
Date: February 9, 2018

From: Bart Heldreth, Ph.D., Executive Director

To: CIR Expert Panel Members, Liaisons, and members of CIR Science and Support Committee

Re: Draft 2019 Priority List

The CIR Procedures require preparation of the Draft 2019 Priority List for public comment by June 1, 2018. The Draft 2019 Priority list has been prepared and 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 FDA on February 5, 2018; and on CIR staff and Panel workflow. While this list includes only the lead ingredients, potential groupings are provided for each on the following pages. The Expert Panel will have the opportunity to review any revisions to this list and any public comments at the June 2018 meeting, at which time a Final 2019 Priority List will be issued. CIR will select a number of ingredients/ingredient groups from this list, including a proposed hair dye yet to be submitted by the Hair Dye Technical Committee, for review in 2019; but, CIR is not committing to begin all of these reports by year-end 2019. Indeed, high priority reports already in process may preempt the start of these proposed reports.

There are seventeen reports covering 171 ingredients on the Draft 2019 Priorities List. Reports previously prioritized and on the CIR docket at the end of 2018, as well as a number of re-reviews of previous assessments, will supplement the total number of ingredients to be assessed in 2019.

The first 2 ingredients listed below have been proposed for cause. The first, Benzisothiazolinone, is considered to take primacy with the ever shrinking palette of preservatives. The second, Caprylhydroxamic Acid, is a chelating agent that has seen some attention as a potential allergen in a recent study (Contact Dermatitis 77:159-162, 2017), and may warrant the Panel’s attention sooner rather than later.

The remaining cosmetic ingredients listed in the table are 1) those with the highest frequencies of use and not previously reviewed by CIR; and 2) are not the purview of another safety assessment body (e.g., RIFM for fragrance only ingredients, or FDA for certain color ingredients).

CIR welcomes and considers all suggestions for cosmetic ingredient additions to the priority list for cause, regardless of frequency of use or listing herein. Such submissions and suggestions will be welcomed prior to the June 2018 CIR Expert Panel Meeting.
## Draft 2019 Priorities List

<table>
<thead>
<tr>
<th>Per interest</th>
<th>Frequency of Use (FOU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzisothiazolinone – potentially a new preservative</td>
<td>not reported in 2018 VCRP (6 uses in 2015)</td>
</tr>
<tr>
<td>Caprylhydroxamic Acid – per Finnish Study</td>
<td>147</td>
</tr>
<tr>
<td><strong>Per FOU</strong></td>
<td></td>
</tr>
<tr>
<td>SACCHARIDE ISOMERATE</td>
<td>365</td>
</tr>
<tr>
<td>PORTULACA OLERACEA (PURSLANE) EXTRACT</td>
<td>363</td>
</tr>
<tr>
<td>SODIUM LEVULINATE</td>
<td>331</td>
</tr>
<tr>
<td>GLUCONOLACTONE</td>
<td>329</td>
</tr>
<tr>
<td>ACETYL HEXAPEPTIDE-8</td>
<td>318</td>
</tr>
<tr>
<td>CHONDRUS CRISPUS (CARRAGEENAN) EXTRACT</td>
<td>299</td>
</tr>
<tr>
<td>ROSA DAMASCENA (DAMASK ROSE) FLOWER OIL</td>
<td>298</td>
</tr>
<tr>
<td>SALVIA OFFICINALIS (SAGE) LEAF EXTRACT</td>
<td>292</td>
</tr>
<tr>
<td>ROSA DAMASCENA (DAMASK ROSE) FLOWER WATER</td>
<td>289</td>
</tr>
<tr>
<td>DICAPRYLYL ETHER</td>
<td>288</td>
</tr>
<tr>
<td>PEG/PPG-8/3 DIISOSTEARATE</td>
<td>277</td>
</tr>
<tr>
<td>POLYQUATERNIUM-51</td>
<td>274</td>
</tr>
<tr>
<td>ACETYL GLUCOSAMINE</td>
<td>265</td>
</tr>
<tr>
<td>POLYQUATERNIUM-6</td>
<td>265</td>
</tr>
<tr>
<td>OLEA EUROPAEA (OLIVE) LEAF EXTRACT</td>
<td>257</td>
</tr>
</tbody>
</table>
Draft 2019 Priorities Reports

Proposed 2019 Reports – per interest

Benzisothiazolinone – per request
Definition: Benzisothiazolinone is the heterocyclic compound that conforms to the structure:

![Benzisothiazolinone Structure](image)

Reported Functions: Preservatives
Notes: This isothiazolinone-type preservative differs significantly in structure from others as a bicyclic aromatic (isothiazolinone structure: \( \text{S} \text{NH} \text{CON} \text{H} \)). The \( \alpha,\beta \)-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

Caprylhydroxamic Acid – per Contact Dermatitis 77:159-162, 2017
Definition: Caprylhydroxamic Acid is the organic compound that conforms to the structure:

![Caprylhydroxamic Acid Structure](image)

Reported Functions: Chelating Agents (i.e. prevent oxidative deterioration of formula)
Notes: The study authors in Finland concluded that they, “found a new contact allergen, caprylhydroxamic acid, which caused an epidemic of allergic contact dermatitis in patients using moisturizers containing this preservative”
Grouping proposal: None. There are other hydroxamic acid chelating agents in the ingredient Dictionary. However, all of those are aromatic (whereas this ingredient is aliphatic) and not reported to be in use in the 2018 snapshot of the FDA VCRP.
**Proposed 2019 Reports – per FOU**

### Saccharide Isomerate

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

![Saccharide Isomerate](image)

**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, xylolbiose, and xylene were found safe as used in 2014 ([Final Report](#)).

**Grouping proposal:** Saccharide Humectants (10 ingredients, 1453 combined FOU)

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>FOU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saccharide Isomerate (FOU priority ingredient)</td>
<td>365</td>
</tr>
<tr>
<td>Saccharide Hydrolysate (mix of saccharides)</td>
<td>21</td>
</tr>
<tr>
<td>Anhydrogalactose</td>
<td>-</td>
</tr>
<tr>
<td>Anhydroglucitol</td>
<td>-</td>
</tr>
<tr>
<td>Anhydroxylitol</td>
<td>112</td>
</tr>
<tr>
<td>Arabinose</td>
<td>-</td>
</tr>
<tr>
<td>Honey (mix of saccharides)</td>
<td>949</td>
</tr>
<tr>
<td>Hydrogenated Honey (mix of saccharides)</td>
<td>6</td>
</tr>
<tr>
<td>Hydrolyzed Honey (mix of saccharides)</td>
<td>-</td>
</tr>
<tr>
<td>Psicose</td>
<td>-</td>
</tr>
</tbody>
</table>
Portulaca Oleracea Extract

**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, 363 combined FOU)

- Portulaca Oleracea Extract (FOU priority ingredient) 363
- Portulaca Oleracea Flower/Leaf/Stem Extract -
- Portulaca Oleracea Juice -
- Portulaca Oleracea Water -
**Sodium Levulinate**

**Definition:** Sodium Levulinate is the sodium salt of Levulinic Acid

![Chemical Structure of Sodium Levulinate]

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

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

**Grouping proposal:** Levulinic Acid and Sodium Levulinate (2 ingredients, 425 combined FOU)

- Sodium Levulinate (FOU priority ingredient) 331
- Levulinic Acid 94
Gluconolactone

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

![Chemical Structure of Gluconolactone]

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, 329 combined FOU)

Gluconolactone (FOU priority ingredient) 329
Galactonolactone -
Glucarolactone -
Glucoheptonolactone -
Ribonolactone -
Acetyl Hexapeptide-8

**Definition:** Acetyl Hexapeptide-8 is a 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, 318 combined FOU)

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>FOU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetyl Hexapeptide-8 (FOU priority ingredient)</td>
<td>318</td>
</tr>
<tr>
<td>Acetyl Hexapeptide-8 Amide</td>
<td>-</td>
</tr>
</tbody>
</table>
Chondrus Crispus Extract

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 (72 ingredients, combined 876 FOU)

Chondrus Crispus Extract (FOU priority ingredient) 299
Chondrus Crispus (aka “Irish moss” in VCRP) 5
Chondrus Crispus Powder 28
Hydrolyzed Chondrus Crispus Extract 2
Ahnfeltiopsis Concinna Extract (aka AHNFELTIA CONCINNA EXTRACT) 13
Asparagopsis Armata Extract 42
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 69
Corallina Officinalis Powder -
<table>
<thead>
<tr>
<th>Extract</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digenea Simplex Extract</td>
<td>1</td>
</tr>
<tr>
<td>Dilsea Carnosa Extract</td>
<td>-</td>
</tr>
<tr>
<td>Eucheuma Serra Extract</td>
<td>-</td>
</tr>
<tr>
<td>Eucheuma Serra/Grateloupi Sparsa/Saccharina Angustata/Undaria Pinna</td>
<td>-</td>
</tr>
<tr>
<td>Linza/Undaria Pinnatifida Extract</td>
<td>-</td>
</tr>
<tr>
<td>Eucheuma Serra/Saccharina Angustata/Undaria Linza Extract</td>
<td>-</td>
</tr>
<tr>
<td>Furcellaria Lumbricalis Extract</td>
<td>-</td>
</tr>
<tr>
<td>Galaxaura Rugosa Extract</td>
<td>-</td>
</tr>
<tr>
<td>Galaxaura Rugosa/Sargassum Pacificum/Turbinaria Ornata Extract</td>
<td>-</td>
</tr>
<tr>
<td>Gelidiella Acerosa Extract</td>
<td>89</td>
</tr>
<tr>
<td>Gelidium Amansii Extract</td>
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<tr>
<td>Gelidium Cartilagineum Extract</td>
<td>22</td>
</tr>
<tr>
<td>Gelidium Sesquipedale Extract</td>
<td>-</td>
</tr>
<tr>
<td>Gigartina Skottsbergii Extract</td>
<td>-</td>
</tr>
<tr>
<td>Gigartina Stellata Extract</td>
<td>9</td>
</tr>
<tr>
<td>Gigartina Stellata/Kappaphycus Alvarezii Extract</td>
<td>-</td>
</tr>
<tr>
<td>Gloiopeltis Furcata Extract</td>
<td>-</td>
</tr>
<tr>
<td>Gloiopeltis Tenax Extract</td>
<td>-</td>
</tr>
<tr>
<td>Gloiopeltis Tenax Powder</td>
<td>-</td>
</tr>
<tr>
<td>Gracilaria Vermiculophylla Extract</td>
<td>-</td>
</tr>
<tr>
<td>Gracilaria Verrucosa Extract</td>
<td>-</td>
</tr>
<tr>
<td>Gracilaripsis Chorda Extract</td>
<td>-</td>
</tr>
<tr>
<td>Grateloupi Sparsa Extract</td>
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</tr>
<tr>
<td>Grateloupi Sparsa Extract</td>
<td>-</td>
</tr>
<tr>
<td>Hydrolyzed Asparagopsis Armata Extract</td>
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<tr>
<td>Hydrolyzed Corallina Officinalis</td>
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</tr>
<tr>
<td>Hydrolyzed Corallina Officinalis Extract</td>
<td>5</td>
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<tr>
<td>Hydrolyzed Gracillariopsis Chiangii Extract</td>
<td>-</td>
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<tr>
<td>Hydrolyzed Porphyra Yezoensis</td>
<td>-</td>
</tr>
<tr>
<td>Hydrolyzed Rhodophyceae Extract</td>
<td>25</td>
</tr>
<tr>
<td>Hypnea Musciformis Extract</td>
<td>122</td>
</tr>
<tr>
<td>Kappaphycus Alvarezii Extract</td>
<td>5</td>
</tr>
<tr>
<td>Lithothamnion Calcareum Extract</td>
<td>12</td>
</tr>
<tr>
<td>Lithothamnion Calcareum Powder</td>
<td>11</td>
</tr>
<tr>
<td>Lithothamnion Coralliodes Powder</td>
<td>-</td>
</tr>
<tr>
<td>Mesophyllum Lichenoides Extract</td>
<td>-</td>
</tr>
<tr>
<td>Palmaria Palmata Extract</td>
<td>72</td>
</tr>
<tr>
<td>Palmaria Palmata Powder</td>
<td>-</td>
</tr>
<tr>
<td>Phymatolithon Calcareum Extract</td>
<td>-</td>
</tr>
<tr>
<td>Pikea Robusta Extract</td>
<td>-</td>
</tr>
<tr>
<td>Polysiphonia Brodiei Extract</td>
<td>-</td>
</tr>
<tr>
<td>Polysiphonia Elongata Extract</td>
<td>-</td>
</tr>
<tr>
<td>Polysiphonia Lanosa Extract</td>
<td>-</td>
</tr>
<tr>
<td>Porphyra Columbina Extract</td>
<td>-</td>
</tr>
<tr>
<td>Porphyra Linearis Extract</td>
<td>-</td>
</tr>
<tr>
<td>Porphyra Tenera Extract</td>
<td>-</td>
</tr>
<tr>
<td>Product Name</td>
<td>Quantity</td>
</tr>
<tr>
<td>--------------------------------------------------</td>
<td>----------</td>
</tr>
<tr>
<td>Porphyra Umbilicalis Extract</td>
<td>36</td>
</tr>
<tr>
<td>Porphyra Umbilicalis Powder</td>
<td>-</td>
</tr>
<tr>
<td>Porphyra Yezoensis Extract</td>
<td>9</td>
</tr>
<tr>
<td>Porphyra Yezoensis Powder</td>
<td>-</td>
</tr>
<tr>
<td>Rhodymenia Palmata Extract (synonym for Palmaria Palmata Extract?)</td>
<td>-</td>
</tr>
<tr>
<td>Rissoella Verruculosa Extract</td>
<td>-</td>
</tr>
<tr>
<td>Sarcodiotheca Gaudichaudii Extract</td>
<td>-</td>
</tr>
<tr>
<td>Sodium Porphyra Yezoensis Extract</td>
<td>-</td>
</tr>
</tbody>
</table>
**Rosa Damascena Flower Oil**

**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, 806 combined FOU)

- Rosa Damascena Flower Oil (FOU priority ingredient) 298
- Hydrolyzed Rosa Damascena Flower Extract -
- Rosa Damascena Bud Extract -
- Rosa Damascena Extract 48
- Rosa Damascena Flower 3
- Rosa Damascena Flower Extract 148
- Rosa Damascena Flower Powder -
- Rosa Damascena Flower Water 289
- Rosa Damascena Flower Water Extract -
- Rosa Damascena Flower Wax 20
Salvia Officinalis (Sage) Leaf Extract

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 (9 ingredients, 309 combined FOU)

Salvia Officinalis (Sage) Leaf Extract (FOU priority ingredient) 292
Salvia Officinalis (Sage) Extract -
Salvia Officinalis (Sage) Flower/Leaf/Stem Extract -
Salvia Officinalis (Sage) Flower/Leaf/Stem Juice -
Salvia Officinalis (Sage) Flower/Leaf/Stem Water -
Salvia Officinalis (Sage) Leaf 8
Salvia Officinalis (Sage) Leaf Water 9
Salvia Officinalis (Sage) Root Extract -
Salvia Officinalis (Sage) Water -
Dicaprylyl Ether

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

![Structure](image)

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

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

**Grouping proposal:** Fatty Ethers (8 ingredients, 304 combined FOU)

Dicaprylyl Ether (FOU priority ingredient) 288

Dicetyl Ether -
Didecyl Ether -
Diisononyl Ether -
Dilauryl Ether -
Dimyristyl Ether -
Distearyl Ether 16
Cetyl Dimethylbutyl Ether
**PEG/PPG-8/3 Diisostearate**

**FOU = 277**

**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.

![Chemical Structure](Image)

**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, 282 combined FOU)

<table>
<thead>
<tr>
<th>PEG/PPG-8/3 Diisostearate (FOU priority ingredient)</th>
<th>277</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEG-15 Butylene Glycol Diisostearate</td>
<td>-</td>
</tr>
<tr>
<td>PEG-10 Glyceryl Diisostearate</td>
<td>-</td>
</tr>
<tr>
<td>PEG-20 Glyceryl Diisostearate</td>
<td>-</td>
</tr>
<tr>
<td>PEG-30 Glyceryl Diisostearate</td>
<td>-</td>
</tr>
<tr>
<td>PEG-60 Glyceryl Diisostearate</td>
<td>-</td>
</tr>
<tr>
<td>PEG-12 Glyceryl Dimyristate</td>
<td>-</td>
</tr>
<tr>
<td>PEG-12 Glyceryl Dioleate</td>
<td>-</td>
</tr>
<tr>
<td>[PEG-3 Glyceryl Distearate] (VCRP listing only)</td>
<td>1</td>
</tr>
<tr>
<td>PEG-4 Glyceryl Distearate</td>
<td>-</td>
</tr>
<tr>
<td>PEG-12 Glyceryl Distearate</td>
<td>4</td>
</tr>
<tr>
<td>PEG-23 Glyceryl Distearate</td>
<td>-</td>
</tr>
<tr>
<td>PEG-4 Polyglyceryl-2 Distearate</td>
<td>-</td>
</tr>
</tbody>
</table>
Polyquaternium-51  

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

![Chemical Structure](image)

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

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

**Grouping proposal:** Acryloyloxyethyl Phosphorylcholine Polymers (8 ingredients, 303 combined FOU)

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>FOU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyquaternium-51 (FOU priority ingredient)</td>
<td>274</td>
</tr>
<tr>
<td>Polyquaternium-61</td>
<td>9</td>
</tr>
<tr>
<td>Polyphosphorylcholine Glycol Acrylate</td>
<td>20</td>
</tr>
<tr>
<td>Acrylic Acid/Phosphorylcholine Glycol Acrylate Crosspolymer</td>
<td>-</td>
</tr>
<tr>
<td>C4-18 Alkyl Methacrylate/Methacryloyloxyethyl Phosphorylcholine Copolymer</td>
<td>-</td>
</tr>
<tr>
<td>Hydroxyethylcellulose/Phosphorylcholine Glycol Acrylate Copolymer</td>
<td>-</td>
</tr>
<tr>
<td>Phosphorylcholine Glycol Methacrylate/PEG-10 Dimethacrylate Crosspolymer</td>
<td>-</td>
</tr>
<tr>
<td>Polyquaternium-10/Phosphorylcholine Glycol Acrylate Copolymer</td>
<td>-</td>
</tr>
</tbody>
</table>

*Distributed for comment only -- do not cite or quote*
Acetyl Glucosamine

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

![Chemical Structure](image)

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

**Notes:**

**Grouping proposal:** Glucosamine and Acetyl Glucosamine (3 ingredients, 403 combined FOU)

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>FOU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetyl Glucosamine (FOU priority ingredient)</td>
<td>265</td>
</tr>
<tr>
<td>Glucosamine</td>
<td>7</td>
</tr>
<tr>
<td>Glucosamine HCl</td>
<td>131</td>
</tr>
</tbody>
</table>
**Polyquaternium-6**

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

```
CH₂=CHCH₂N(CH₂CH₂CH₂)⁺Cl⁻
```

**DADMAC:**

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

**Notes:** homopolymer

**Grouping proposal:** None
**Olea Europaea (Olive) Leaf Extract**

**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 (21 ingredients, 502 combined FOU)*

- Olea Europaea (Olive) Leaf Extract (FOU priority ingredient) - 257
- 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 - 6
- Olea Europaea (Olive) Fruit Extract
- Olea Europaea (Olive) Fruit Juice
- Olea Europaea (Olive) Fruit Oil Ethyl Ester
- Olea Europaea (Olive) Fruit Unsaponifiables - 36
- Olea Europaea (Olive) Fruit Water
- Olea Europaea (Olive) Husk Powder
- Olea Europaea (Olive) Leaf
- Olea Europaea (Olive) Leaf Cell Extract
- 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