ADMIN

Memo

Agenda

Minutes

EXPERT PANEL MEETING
December 7-8, 2020

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MEMORANDUM

To: The Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Bart Heldreth, Ph.D., Executive Director, Cosmetic Ingredient Review
Subject: 156th Meeting of the Expert Panel — Monday and Tuesday, December 7-8, 2020
Date: November 13, 2020

Welcome to the last Panel Meeting of 2020! Please join me in welcoming our new team leader, Dr. David E. Cohen!

The agenda and accompanying materials for the 156th Expert Panel Meeting to be held on December 7-8, 2020, are now available. The location is the ***same*** – this meeting will be held virtually! Invitations (3 of them) to join the meeting will arrive separately in your email inbox. Panel members and liaisons will be registered ***automatically***. However, other interested parties may register to attend in advance of the meeting at the meeting page:

https://www.cir-safety.org/meeting/156th-expert-panel-meeting

The meeting agenda includes the consideration of 15 reports advancing in the review process, including 5 final reports, 4 tentative reports, and 6 draft reports.

Team Meetings

Draft Reports - there are 6 draft reports for review – Sufficient data to proceed or issue an IDA?

1. Barley – DR (Christina) – This is the first time the Expert Panel for Cosmetic Ingredient Safety (Panel) is reviewing the safety of these 16 botanical ingredients derived from various species of barley. The Council provided concentration of use survey data, method of manufacturing, composition and impurities, and HRIPT data on Hordeum Vulgare Seed Extract; method of manufacturing and impurities on Hordeum Distichon (Barley) Extract; method of manufacturing on Hordeum Vulgare Seed Water; and ocular irritation and HRIPT data on Hordeum Vulgare Extract. No comments on the Notice to Proceed (NTP; issued August 5, 2020) were received from the Council.

   According to 2020 VCRP survey data, Hordeum Vulgare Extract has the most reported uses in cosmetic products, with a total of 383 formulations; the majority of the uses are in leave-on skin care products. Hordeum Distichon (Barley) Extract has the second greatest reported number of uses in this safety assessment, with 91 formulations; the majority of the uses are also in leave-on skin care products. The other 2 in-use ingredients are reported to be used in much smaller numbers. The results of the concentration of use survey conducted by the Council indicate that the highest concentration of use for Hordeum Vulgare Extract is 1.5% in leave-on body and hand skin care products. Hordeum Distichon (Barley) Extract is reported to be used at up to 1.8% in leave-on moisturizing products. No concentrations of use were reported for the other 2 in-use barley-derived ingredients in this report. There are 12 ingredients not reported to be in use, according to the VCRP and industry surveys.

   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. *Equisetum arvense* – DR (Wilbur) – This is the first time the Panel is reviewing the safety of these 5 *Equisetum arvense*-derived ingredients. Comments on the Scientific Literature Review (SLR; announced on March 20, 2020), use concentration data, and data on Equisetum Arvense Extract relating to methods of production and skin irritation and sensitization potential, were received from the Council; and, the draft report has been revised to address these comments and data.

   According to 2020 FDA VCRP data, Equisetum Arvense Extract is reported to be used in 340 cosmetic products (227 leave-on products, 111 rinse-off products, and 2 products that are diluted for (bath) use). Of the *Equisetum arvense*-derived ingredients that are being reviewed in this safety assessment, this is the greatest reported use frequency. The results of a concentration of use survey completed in 2018 and provided by the Council in 2019 indicate that Equisetum Arvense Extract is being used at maximum use concentrations up to 0.4% in leave-on products (body and hand products (not spray)), and at maximum use concentrations up to 0.00078% in rinse-off products (skin cleansing products). Equisetum Arvense Extract is the only *Equisetum arvense*-derived ingredient in this safety assessment for which use concentration data were provided in response to the Council survey. Additionally, according to both VCRP and Council survey data, Equisetum Arvense Juice and Equisetum Arvense Leaf Powder are not reported to be used in cosmetic products.

   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, unsafe, or split conclusion, and Discussion items should be identified. If the available data are insufficient, the Panel should issue an IDA, specifying the data needs therein.

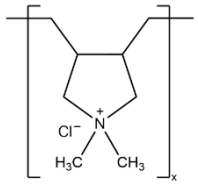
3. Tea Tree – DR (Monice) – This is the first time the Panel is seeing the safety assessment on these 8 *Melaleuca alternifolia* (tea tree)-derived ingredients. You will notice that all abbreviations are defined at the front of the document, rather than in the text of the report. Please provide comments as to whether you prefer the abbreviations presented up front (as in this document) or in the body of the text (as we have normally done).

Comments on the SLR (announced on August 4, 2020) and the following unpublished data were received and are included in the report: concentration of use by FDA product category; a safety data sheet on Tea Tree (*Melaleuca alternifolia*) leaf oil; and irritation and sensitization for a tradename mixture comprising 10% Melaleuca Alternifolia (Tea Tree) Leaf Oil in caprylic/capric triglyceride on human skin.

A concentration of use survey was originally conducted in 2015. Although these data are not included in the safety assessment, they are included with this submission to provide the Panel with information regarding changes in use over the last few years. VCRP data have increased significantly for the Leaf Oil (more than doubling, from 336 uses in 2015 to 724 uses in 2020), but the number of categories for which concentrations of use were reported for the *Melaleuca alternifolia*-derived ingredients, as well as the maximum reported concentration of use for the Leaf Oil, decreased notably. (For example, the maximum concentration of use for the Leaf Oil decreased from 15% (in face and neck products) in 2015 to 0.63% (in cuticle softeners) in 2019.)

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 IDA, specifying the data needs therein.

4. Polyquaternium-6 – DR (Wilbur) – This is the first time the Panel is reviewing the safety of this ingredient. In response to the NTP (announced on September 17, 2020), the following unpublished data were received: molecular weight; method of manufacture, composition, and impurities; use concentrations; acute dermal, oral, and inhalation toxicity; short-term oral toxicity; subchronic dermal toxicity; in vitro genotoxicity; skin irritation (animal); skin sensitization (guinea pig and human); photoallergenicity (animal); and ocular irritation (animal).



According to 2020 VCRP data, Polyquaternium-6 is reported to be used in 282 cosmetic products (16 leave-on products, 265 rinse-off products, and 1 product diluted for bath use). The results of a concentration of use survey completed in 2019 - 2020, and provided by the Council in 2020, indicate that Polyquaternium-6 is used at maximum use concentrations up to 1.2% in leave-on products (tonics, dressings, and other hair grooming aids) and at maximum use concentrations up to 3% in rinse-off products (hair straighteners). Cosmetic products containing Polyquaternium-6 may be applied to the skin/hair (at concentrations up to 3%) and may come in contact with mucous membranes (at concentrations up to 0.25% in bath soaps and detergents).

After reviewing this document, 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 IDA, specifying the data needs therein.

5. *Portulaca oleracea* – DR (Preethi) – This is the first time the Panel is seeing a safety assessment of these 4 *Portulaca oleracea*-derived Ingredients. In addition to comments on the SLR (announced on July 15, 2020), the following data were received: concentration of use data; certificates of origin and method of manufacture for a water/butylene glycol extract of *Portulaca oleracea* and water extract of *Portulaca oleracea*; a human patch test (product containing 0.1% Portulaca Oleracea Extract; summary of a clinical use test of a product containing 0.1% Portulaca Oleracea Extract; and an evaluation of the contact sensitization potential of a product containing 0.1% Portulaca Oleracea Extract.

Portulaca Oleracea Extract is the only ingredient included in this report that is currently reported to be used in cosmetic formulations. According to 2020 VCRP survey data, Portulaca Oleracea Extract is reported to be used in 579 formulations, of which 189 uses are in face and neck products, and 133 uses are in moisturizing products. The results of the concentration of use survey conducted by the Council in 2018 indicate that the reported maximum concentration of use for Portulaca Oleracea Extract is 0.008%, in leave-on, moisturizing formulations. According to VCRP and Council survey data, Portulaca Oleracea Flower/Leaf/Stem Extract, Portulaca Oleracea Juice, and Portulaca Oleracea

Water were not reported to be in use in cosmetic products.

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 IDA, specifying the data needs therein.

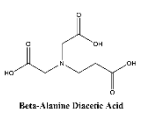
6. Sugarcane – DR (Priya) – This is the first time the Panel is reviewing the safety assessment on these 4 *Saccharum officinarum* (sugarcane)-derived ingredients. In addition to comments on the SLR (announced on September 17, 2020), concentration of use data, method of manufacturing information, and chemical properties data were received.

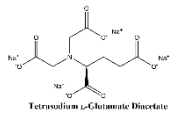
According to 2020 VCRP survey data, Saccharum Officinarum (Sugarcane) Extract is reported to be used in 466 formulations (245 of which are leave-on formulations). The results of concentration of use surveys conducted by the Council indicate Saccharum Officinarum (Sugarcane) Extract also has the highest concentration of use in leave-on formulations; it is used at up to 2.4% in foot powders and sprays. Use concentration data were reported for Saccharum Officinarum (Sugarcane) Wax and Saccharum Officinarum (Sugarcane) Juice Extract, but no uses were reported in the VCRP; it should be presumed there is at least one use for the category in which the concentration is reported. No uses were reported for Saccharum Officinarum (Sugarcane) Bagasse Powder.

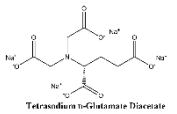
After reviewing these documents, if the available data are deemed sufficient to make a determination of safety, the Panel should issue a tentative report with a safe as used, safe with qualifications, or unsafe conclusion, and Discussion items should be identified. If the available data are insufficient, the Panel should issue an IDA, specifying the data needs therein.

Draft Tentative Reports – there are 4 draft tentative reports for consideration.

1. Amino Acid Diacetates – TR (Christina) – At the September 2020 meeting, the Panel issued a second IDA for this report. The additional data needed to determine safety were:





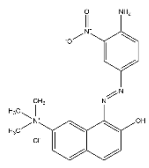


   - 28-day dermal toxicity on Beta-Alanine Diacetic Acid
     - o If positive, DART, genotoxicity, and dermal irritation and sensitization may be needed.

   Since the issuance of the IDA, CIR has not received any new data. CIR staff have included the IARC report on *Nitrotriacetic Acid and Its Salts* in this report package for the Panel to review. The staff seeks guidance on what, if any, data on this structurally similar chemical to Beta-Alanine Diacetic Acid should be included in this report.

   Based on the proceedings and comments from the June and September 2020 meetings, a draft Discussion has been included. The Panel should carefully consider and discuss the data (or lack thereof) 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.

2. Basic Brown 17 – TR (Christina) – At the June 2020 meeting, the Panel issued an IDA for this ingredient. The additional data needed to determine safety were concentration of use and reported function for the non-coloring hair product uses that were reported in the FDA VCRP database. Since the issuance of the IDA, CIR has not received any new data.



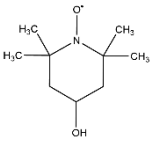
   Based on the proceedings and comments from the June 2020 meeting, a draft Discussion has been included. The Panel should carefully consider and discuss the data (or lack thereof) and the draft Abstract and Discussion presented in this report, and issue a tentative report with a safe, safe with qualifications, unsafe, insufficient data, or split conclusion.

3. Papaya – TR (Priya) – At the June 2020 meeting, the Panel issued an IDA for this ingredient group, and requested irritation and sensitization data on Carica Papaya (Papaya) Fruit Extract at the reported maximum use concentration of 0.25%. In addition, the Panel requested impurities, genotoxicity, and irritation/sensitization data on Carica Papaya (Papaya) Leaf Extract.

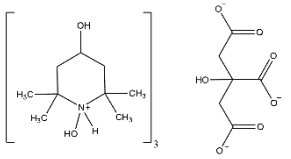
Since the June Panel meeting, unpublished data have been received and incorporated. These data include: five HRIPTs on formulations containing up to 0.0586% Carica Papaya (Papaya) Fruit Extract; two 5-d cumulative irritation patch tests on formulations containing up to 0.003% Carica Papaya (Papaya) Fruit Extract; two photosensitization/ phototoxicity assays on an SPF 50 lotion containing 0.0075% Carica Papaya (Papaya) Fruit Extract; and corrected concentration of use data for Carica Papaya (Papaya) Fruit Extract (hair conditioners are now reported to be used at up to 0.0006% (no previous concentration of use reported) and depilatories are used at up to 0.01% (previously reported to be used at up to 0.05%)).

The Panel should carefully consider and discuss the data (or lack thereof), and the draft Abstract and draft Discussion presented in this report. A tentative report with a safe, safe with qualifications, unsafe, insufficient data, or split conclusion should then be issued.

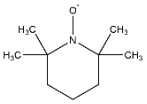
4. TrisTetramethylhydroxypiperidinol – TR (Preethi) – At the June 2020 Panel meeting, a draft report was presented to the Panel. Upon review, the Panel issued an IDA for method of manufacture and impurities, for which no data have been received.



The first time the Panel saw this assessment, it was a single-ingredient report (only Tris(Tetramethylhydroxypiperidinol) Citrate). The Council proposed the addition of two chemically-similar substances, Hydroxy Tetramethylpiperidine Oxide (a cosmetic ingredient) and tetramethylpiperidine nitroxide (not a cosmetic ingredient), which the Panel agreed upon. The newly added data have been added to the report. These data include 2020 concentration of use data received for Hydroxy Tetramethylpiperidine Oxide.

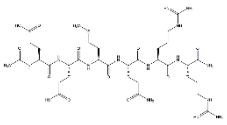


The Panel should carefully consider and discuss the data (or lack thereof), and the draft Abstract and draft Discussion presented in this report. A tentative report with a safe as used, safe with qualifications, insufficient, or unsafe conclusion should then be issued.



Draft Final Reports - there are 5 draft final reports for consideration. After reviewing these drafts, especially the rationales provided in the Discussion sections, the Panel should issue these as final reports, as appropriate.

1. Acetyl Hexapeptide-8 Amide – FR (Wilbur) – The safety of Acetyl Hexapeptide-8 Amide (synonymous with Acetyl Hexapeptide-8 (sans "Amide")), as used in cosmetics, is reviewed in this safety assessment. Acetyl Hexapeptide-8 Amide is synonymous with the in-use name, Acetyl Hexapeptide-8, and both names are found in the International Cosmetic Ingredient Dictionary and Handbook (Dictionary). The following synonyms have been retired or deleted from the *Dictionary*: Acetyl Hexapeptide-3, Acetyl Hexapeptide-24, and Acetyl Hexapeptide-24 Amide. Since the name, "Acetyl Hexapeptide-8 Amide," is more descriptive and its definition more accurate (i.e. includes the amidation), this name was chosen for use throughout the report (i.e., instead of Acetyl Hexapeptide-8).

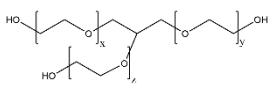


A tentative report with the following conclusion was issued at the September 2020 Panel meeting: Acetyl Hexapeptide-8 Amide is safe in cosmetics in the present practices of use and concentration described in this safety assessment. Comments on the tentative report were received from the Council, and the draft final report has been revised to address these comments.

The Panel should carefully consider the Abstract, Discussion, and Conclusion presented in this report. After reviewing these documents, the Panel should issue a final report with the conclusion

that is stated in the paragraph above.

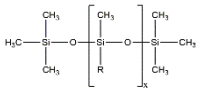
2. Glycerin Ethoxylates – FR (Preethi) – At the June 2020 meeting, the Panel expressed concerns about low level reactions occurring in HRIPT studies in the absence of fully disclosed experimental details. Thus, the Panel issued a tentative report with an insufficient conclusion, requesting full experimental details for previously received summaries, or, newly completed HRIPT experimental data, at or above maximum concentrations of use, with n ≥ 100 participants.



In response to the stated data needs, the following were submitted and have been incorporated: results for an HRIPT on a product containing 3% Glycereth-26; results for an HRIPT on a product containing 8.75% Glycereth-26; and experimental details and clarification for previously submitted HRIPT study summaries. Comments on the tentative report, received from Council after the June 2020 meeting, have also been addressed and incorporated where appropriate.

After reviewing these documents, if the available data are deemed sufficient to make a determination of safety, the Panel should identify any additional matters to be addressed in the Discussion and then issue a final report with a safe as used, safe with qualifications, or unsafe conclusion. If, however, the available data remain insufficient, the Panel should issue a final report with a conclusion of insufficient data, discussing the rationale therein.

3. Methicones – FAR (Preethi) – At the June 2020 Panel meeting, a Draft Amended Report was presented to the Panel, along with 11 additional ingredient suggestions from the CIR Science and Support Committee. The Panel approved the addition of 10 ingredients, excluding Simethicone. Due to an observed potential for irritation at the present concentrations of use, the Panel issued a tentative amended report for these 30 ingredients (20 original, plus 10 add-ons), with a conclusion of safe as used when formulated to be non-irritating to the skin and the eye.



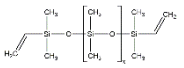
This is the first time that the Panel has issued a conclusion with the caveat, “when formulated to be non-irritating to the skin and the eye.” Three issues make formulating to be “non-irritating to the eye” a departure from prior Panel conclusions. The first is that eye exposure is incidental; thus, formulating for accidental exposures of unknown doses creates a unique challenge. The second issue is that most of the reported uses for these ingredients are not categorized for use in the “eye area.” The third issue is that the Panel has historically utilized conclusion caveats based on concentration or use/product types, instead of organ exposures. For instance, with regard to formaldehyde, the Panel concluded (emphasis added):

> …that formaldehyde and methylene glycol are safe for use in cosmetics **when formulated to ensure use at the minimal effective concentration**, but in no case should the formalin concentration exceed 0.2% (w/w), which would be 0.074% (w/w) calculated as formaldehyde or 0.118% (w/w) calculated as methylene glycol. Additionally, formaldehyde and methylene glycol are safe in the present practices of use and concentration **in nail hardening products**. However, formaldehyde and methylene glycol are unsafe in the present practices of use and concentration **in hair smoothing products** (a.k.a. hair straightening products).

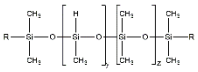
It is, of course, the prerogative of the Panel to continue with a new conclusion type if they deem such is warranted. However, the Panel should consider if a historically more common approach may equally/better serve the Panel’s intentions. For example, it has been stated in the past that the caveat of “when formulated to be non-irritating” was in meant to address dermal and/or ocular irritation.

Since the last review, concentration and frequency of use data for the added ingredients, as well as newly identified published data, have been incorporated into the report. Additionally, comments on the tentative amended report were received from the Council and have been considered.
The Panel should consider the newly added data, and review the Abstract, Discussion, and Conclusion. The Panel should be prepared to issue a final amended report.

4. Polysilicone-11 – FR (Priya) – At the September 2020 meeting, the Panel issued a tentative report with the conclusion that Polysilicone-11 is safe in cosmetics in the present practices of use and concentration as described in the safety assessment. Comments on the tentative report, but no new data, were received.



bis-vinyldimethicone



hydrogen dimethicone

The Panel should carefully consider the Abstract, Discussion, and Conclusion presented in this report. If these are satisfactory, the Panel should issue a final report.

5. Wheat – FR (Christina) – At the June 2020 meeting, the Panel reviewed the safety of the 27 ingredients in this report and issued a tentative report with the conclusion that the available data are insufficient to make a determination of safety under the intended conditions of use in cosmetic formulations. The Panel's needs were: method of manufacturing data, and dermal irritation and sensitization data at a test concentration of 13% for Triticum Vulgare (Wheat) Sprout Extract

Since the June Panel meeting, CIR staff have received method of manufacturing data on Triticum Vulgare (Wheat) Germ Extract and a technical data sheet and a summary of a single insult patch test on a mixture containing approximately 5% Triticum Vulgare (Wheat) Gluten and sodium laureth sulfate. These data, and additional information from published literature on wheat allergy, have been incorporated into this draft.

The Panel should review the Abstract, Discussion, and Conclusion, and issue a final report.

Administrative Items - none.

Full Panel Meeting

The Panel will consider the 5 reports to be issued as final safety assessments, followed by the remaining reports advancing in the process (including the tentative reports and draft reports).

Please remember, the meeting starts at 8:30 am on day 1 and on day 2. It is likely that the full Panel session will conclude before lunch on day 2.

Looking forward to seeing you all (virtually)!

Agenda
156th Meeting of the Expert Panel for Cosmetic Ingredient Safety
December 7th - 8th, 2020

Virtual via Microsoft Teams

Monday, December 7th

8:30 AM	**WELCOME TO THE 156th EXPERT PANEL TEAM MEETINGS**	**Drs. Bergfeld/Heldreth**
8:40 AM	**TEAM MEETINGS**	**Drs. Cohen/Belsito**

Dr. Cohen Team		**Dr. Belsito Team***	
FR (CB)	Wheat	FR (WJ)	Acetyl Hexapeptide-8 Amide
TR (CB)	Amino Acid Diacetates	DR (WJ)	Equisetum arvense
TR (CB)	Basic Brown 17	DR (WJ)	Polyquaternium-6
DR (CB)	Barley	FAR (PR)	Methicones
FR (PC)	Polysilicone-11	FR (PR)	Glycerin Ethoxylates
TR (PC)	Papaya	TR (PR)	TrisTetramethylhydroxypiperidinol
DR (PC)	Sugarcane	DR (PR)	Portulaca oleracea
DR (MF)	Tea Tree	DR (MF)	Tea Tree
FR (WJ)	Acetyl Hexapeptide-8 Amide	FR (CB)	Wheat
DR (WJ)	Equisetum arvense	TR (CB)	Amino Acid Diacetates
DR (WJ)	Polyquaternium-6	TR (CB)	Basic Brown 17
FAR (PR)	Methicones	DR (CB)	Barley
FR (PR)	Glycerin Ethoxylates	FR (PC)	Polysilicone-11
TR (PR)	TrisTetramethylhydroxypiperidinol	TR (PC)	Papaya
DR (PR)	Portulaca oleracea	DR (PC)	Sugarcane

The purpose of the Cosmetic Ingredient Review and the Expert Panel for Cosmetic Ingredient Safety 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

(CB): Christina Burnett || (BH) Bart Heldreth || (MF): Monice Fiume || (PC): Priya Cherian || (WJ): Wilbur Johnson || (PR): Preethi Raj || (JZ): Jinqiu Zhu

*Team moves to breakout room (for a virtual meeting, this means a separate Microsoft Teams meeting).

Tuesday, December 8th			
8:30 am	**WELCOME TO THE 156th FULL EXPERT PANEL MEETING**		**Dr. Bergfeld**
8:45 am	Admin	**MINUTES OF THE SEPTEMBER 2020 EXPERT PANEL MEETING**	**Dr. Bergfeld**
9:00 am	**DIRECTOR'S REPORT**		**Dr. Heldreth**
9:10 am	**FINAL REPORTS, REPORTS ADVANCING TO THE NEXT LEVEL**		

Final Reports

FR (PC)	Polysilicone-11 – *Dr. Belsito Reports*
FR (WJ)	Acetyl Hexaeptide-8 Amide – *Dr. Cohen Reports*
FAR (PR)	Methicones – *Dr. Belsito Reports*
FR (CB)	Wheat – *Dr. Cohen Reports*
FR (PR)	Glycerin Ethoxylates – *Dr. Belsito Reports*

Reports Advancing

TR (PR)	TrisTetramethylhydroxypiperidinol – *Dr. Cohen Reports*
DR (PR)	Portulaca oleracea – *Dr. Belsito Reports*
DR (WJ)	Equisetum arvense – *Dr. Cohen Reports*
DR (WJ)	Polyquaternium-6 – *Dr. Belsito Reports*
DR (PC)	Sugarcane – *Dr. Cohen Reports*
TR (PC)	Papaya – *Dr. Belsito Reports*
TR (CB)	Amino Acid Diacetates – *Dr. Cohen Reports*
DR (CB)	Barley – *Dr. Belsito Reports*
TR (CB)	Basic Brown 17– *Dr. Cohen Reports*
DR (MF)	Tea Tree – *Dr. Belsito Reports*

ADJOURN - *Next meeting **Thursday and Friday**, March 11-12, 2021, will also be held virtually. Please check the CIR website for details as the meeting approaches.*

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

(CB): Christina Burnett || (BH) Bart Heldreth || (MF): Monice Fiume || (PC): Priya Cherian || (WJ): Wilbur Johnson || (PR): Preethi Raj || (JZ): Jinqiu Zhu

ONE HUNDRED FIFTY-FIFTH MEETING

OF THE

EXPERT PANEL FOR COSMETIC INGREDIENT SAFETY

September 14-15, 2020

Microsoft Teams Virtual Meeting

Expert Panel Members

Wilma F. Bergfeld, M.D., Chair

Donald V. Belsito, M.D.

Curtis D. Klaassen, Ph.D.

Daniel C. Liebler, Ph.D.

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

Lisa A. Peterson, Ph.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

Alex Kowcz, M.B.A.

Government

Nakissa Sadrieh, Ph.D.

Adopted (Date)

Wilma F. Bergfeld, M.D.

CIR Staff

Administration
Bart Heldreth, Ph.D. - Executive Director

Monice Fiume, M.B.A. - Senior Director

Carla Jackson - Administrative Coordinator

Subject Matter Expertise
Jinqiu Zhu, Ph.D., D.A.B.T, E.R.T. - Toxicologist

Analysis
Christina L. Burnett, M.S.E.S - Senior Scientific Analyst

Wilbur Johnson, Jr., M.S. - Senior Scientific Analyst

Preethi S. Raj, M.S. - Senior Scientific Analyst

Priya Cherian - Scientific Analyst

Information Services
Kevin Stone Fries, M.L.S. - Information Services Manager

Others Present at the Meeting

Maria Alonso	ASAP Testing
Jay Ansell	PCPC
Wafaa Ayad	Church Dwight, Inc
Lakendra Barajas	Earthjustice
Sage Begolly	DuPont
Don Bjerke	P & G
Ron Brown	Risk Science Consortium, LLC
Roshil Budhram	Bath & Body Works
Lina Bueno	DuPont
Alejandro Camacho	Castri Universidad de los Andes
Wei Chen	Mast Global
Anne Corriou	Givaudan
Christine Crincoli	Cargill, Inc.
Nava Dayan	Dr. Nava Dayan, LLC
Marta Dias	Groupe GM Cosmética Portugal
Carol Eisenmann	PCPC
Michael Fevola	INOLEX, Inc.
Valerie George	John Paul Mitchell Systems
John Gormley	Grant Industries
Marita Grothus	IKW
Craig Harvey	Colgate-Palmolive
Rashimi Joglekar	Earthjustice
Ashish Kapoor	JDM Scientific Research Organization Pvt Ltd
Cunie Lamb	J Strickland & Co
Solenn Le Bruchec	Gerontopole
Linda Loretz	PCPC
L. Manjunath	WNS Global Services
Tim McCarthy	J&J Consumer
Dawn Morales	Personal
Damani Parran	Nouryon Chmicals LLC
Rajendra Patil	Colgate
David Plimpton	INOLEX
Pheona Radcliffe	Givaudan Fragrances
L. Ramalingam	Intertek India Pvt Ltd
Kyle Saitta	J & J
Kumar Sambhav	Evalueserve
Alexandra Scranton	Women's Voices for the Earth
Jahsh Sha	Reckitt Benckiser
Prajakta Shimpi	Church & Dwight
Lawrence Smith	High Ridge Brands
Jan Summers	Sanofi
Sanjay Talreja	Intertek
Sandra Tamara	Soluciones Regulatorias SAS
Izabel Villela	InnVitro
Theresa Vuskovich	University of Florida
Leigh Wilson	J & J
Michael K.Wyatt	FDA
Merle Zimmermann	American Herbal Products Association

MINUTES FROM THE 155th EXPERT PANEL FOR COSMETIC INGREDIENT SAFETY MEETING

CHAIRMAN'S OPENING REMARKS

Dr. Bergfeld welcomed the attendees to the 155th meeting of the Expert Panel for Cosmetic Ingredient Safety (Panel). She then announced that this is Dr. James Marks, Jr's last meeting as a Panel member, and noted that he has done a splendid job and will be missed greatly. Dr. Bergfeld wished Dr. Marks much happiness and luck in all future endeavors. Individually, the Panel members expressed their appreciation for Dr. Marks' service and wished him well.

Dr. Bergfeld welcomed Dr. David Cohen as a new member of the Panel, and noted that he would be formally introduced in the Director's report.

Concerning today's agenda, Dr. Bergfeld noted that 16 ingredient reports are scheduled for review, including 8 new drafts, 3 tentative drafts, and 5 finals. Two re-review summaries and the 2021 CIR Priority List are also being considered. She added that comments received from the CIR Science and Support Committee will be incorporated. Both the CIR Staff and the CIR Science and Support Committee were thanked by Dr. Bergfeld for the increased quality of the documents that are being reviewed.

APPROVAL OF MINUTES

The minutes of the June 8-9, 2020 (154th) 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. As he mentioned in June, Dr. Heldreth noted that this meeting would be Dr. Marks' last Panel meeting, as he is retiring hereto. Dr. Marks served this Panel for 19 years, lending his great expertise, leadership, and geniality. The CIR Staff and Members of the Panel are extremely grateful to have worked with him for so long. The CIR Steering Committee met this summer, and elected an expert to fill this team leader role. Thus, starting with the December 2020 meeting, the Panel will have a new team leader, Dr. David E. Cohen. Dr. Cohen completed his undergraduate work at the City University of New York, and is a graduate of the State University of New York at Stony Brook, School of Medicine (M.D.) and Columbia University School of Public Health (M.P.H.). He completed his dermatology residency at the New York University Medical Center and Columbia University School of Public Health. He is currently Chief - Allergy Section/Contact Dermatitis (among other titles) at NYU. Dr. Cohen has also served on, and led, numerous professional and scientific associations and committees, including the American Contact Dermatitis Society, the International Eczema Council, the American Dermatological Association, & the American Academy of Dermatology. More information about the Panel may be found at their website: https://ingredientsafetyexpertpanel.org/

Final Safety Assessments

Caprylhydroxamic Acid

The Panel issued a Final Report with the conclusion that Caprylhydroxamic Acid is safe in cosmetics in the present practices of use and concentration described in this safety assessment.

The Panel was concerned with inconsistent outcomes regarding dermal sensitization. However, upon further review, the Panel determined that cases of increased sensitization with the use of a moisturizer in Finland (a product that had been reformulated to include Caprylhydroxamic Acid) appeared to be related to use on damaged skin, which most likely resulted in increased penetration. Therefore, the Panel stated that caution should be taken with use of Caprylhydroxamic Acid in a manner that would result in increased penetration, such as formulations with penetration enhancers. This is especially important in product types with a margin of safety (MOS), based on an acceptable exposure level/consumer exposure level (AEL/CEL) ratio at or near 1, as calculated in a quantitative risk assessment (QRA). According to the results of a QRA that was submitted to CIR, product types with an AEL/CEL

of 1 include baby lotions, oils, and creams; the weight of evidence (WoE) no expected sensitization induction level (NESIL) used in the QRA was 1056 μg/cm^2. This QRA did not consider penetration enhancers or damaged skin. Previously, the Panel had also discussed the theoretical possibility of *N*-nitrosation. However, upon further review, the Panel found nitrosamine formation unlikely.

Adenosine Ingredients

The Panel issued a Final Report with the conclusion that Adenosine, Adenosine Phosphate, Adenosine Triphosphate, Disodium Adenosine Phosphate, and Disodium Adenosine Triphosphate are safe in the present practices of use and concentration described in the safety assessment. The safety of this ingredient group was supported by sufficient impurities data, negative animal oral toxicity assays, negative human dermal irritation/sensitization assays, and low concentrations of use. The Panel noted the effects of Adenosine administered via a nebulizer in asthmatic patients and determined that these effects would not be pertinent to cosmetic exposure as delivery of Adenosine via cosmetic products would result in a much lower exposure than that of a nebulizer.

Methylisothiazolinone

The Panel issued a Final Amended Report with the conclusion that Methylisothiazolinone (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 (QRA).

The Panel's recommendations for MI in rinse-off and leave-on cosmetic products are intended to prevent the induction of sensitization to MI. However, the Panel cautioned that following these recommendations may not necessarily prevent the elicitation of allergic reactions in individuals who are already allergic to MI. Individuals sensitized to MI should avoid products that contain MI.

In response to concerns of reports of adverse events observed in infants following inhalation exposure to humidifier disinfectants that contained the preservative mixture Methylchloroisothiazolinone/Methylisothiazolinone (MCI/MI), the Panel moved to reopen the safety assessment of MI in September 2019. A search of inhalation toxicity to MI (separate from the combination of MCI/MI) did not yield any new published literature; however, studies were detailed in the MCI/MI report. The Panel reviewed a 13-wk repeated-dose inhalation study of MCI/MI in rats and determined that the data mitigated concern for the use of MI at the reported concentrations in cosmetic products that could be incidentally inhaled following use. The Panel also reviewed a draft risk assessment for MCI/MI produced by the US EPA and determined that the analyses of exposures to paints, textile, and household cleaning products were not relevant to the assessment of cosmetic safety due to exposure duration and concentrations of application being magnitudes greater than those of cosmetic use.

Ascorbyl Glucoside Ingredients

The Panel concluded that Ascorbyl Glucoside and Sodium Ascorbyl Glucoside are safe in cosmetics in the present practices of use and concentration described in the safety assessment, and issued a Final Report.

Ascorbyl Glucoside has been identified as an ingredient in commercial bleaching cosmetics (also contain kojic acid), at concentrations of ~2%. After reviewing in vitro data relating to a potential skin depigmentation effect, the Panel stated that this ingredient may not actually be a skin bleaching agent. The Panel noted that skin lightening is considered to be a drug effect in the US, and should not occur during the use of cosmetic products. Based on the current use concentrations of Ascorbyl Glucoside in cosmetic products (up to 5% in leave-on products), the results of the in vitro experiment, and clinical experience, concern for this effect in cosmetics was mitigated. Nevertheless, the Panel noted that cosmetic formulators should only use Ascorbyl Glucoside in products in a manner that does not cause depigmentation.

The Panel also noted the absence of developmental and reproductive toxicity data on Ascorbyl Glucoside and Sodium Ascorbyl Glucoside. However, concern over the lack of these data was mitigated, considering that Ascorbyl Glucoside is metabolized into ascorbic acid and glucose in the skin, and would not be absorbed, intact, in an

appreciable quantity. Additionally, concern was further mitigated because both of these substances are essential constituents of the body.

Finally, the Panel discussed the issue of incidental inhalation exposure from the use of Ascorbyl Glucoside in pump and aerosol hair spray formulations and in face powders; the maximum reported concentration of use in these types of products is 0.01% in hair sprays and 2% in face powders. The Panel stated that droplets/particles deposited in the nasopharyngeal or bronchial regions of the respiratory tract present no toxicological concerns based on the properties of Ascorbyl Glucoside or Sodium Ascorbyl Glucoside.

***Scutellaria baicalensis*-Derived Ingredients**

The Panel concluded that Scutellaria Baicalensis Root Extract and Scutellaria Baicalensis Root Powder are safe in cosmetics in the present practices of use and concentration described in the safety assessment, and issued a Final Report.

However, the Panel also concluded that the available data are insufficient to make a determination that Scutellaria Baicalensis Extract and Scutellaria Baicalensis Sprout Extract are safe under the intended conditions of use in cosmetic formulations. The data needed to determine the safety of these two ingredients comprise method of manufacture, composition, impurities, dermal absorption, 28-day dermal toxicity, genotoxicity, phototoxicity, skin irritation, and sensitization data.

The Panel initially expressed concern over the statistically significant, dose-dependent increase in the incidence of skeletal variations (presence of lumbar ribs) in developmental and reproductive toxicity studies on a *Scutellaria baicalensis* root extract (aqueous extract) involving Sprague-Dawley rats. However, after further review of the data, the Panel agreed that the study results suggest that the appearance of lumbar ribs induced by the test material was a transient fetal variation rather than teratogenicity or maternal toxicity.

The genotoxicity of *Scutellaria baicalensis* root extracts (methanol extract and aqueous extract) was evaluated in the *Bacillus subtilis* rec-assay using strains H17 Rec+ and M45 Rec- without metabolic activation. Results were positive for the methanol extract and negative for the aqueous extract. However, in Ames tests, results were positive for the aqueous extract and negative for the methanol extract. After an initial review of these data, the Panel noted that, given the mixed results, a repeat of these assays and the addition of another assay (mammalian system) would be needed in order to develop a weight of evidence approach for evaluating the genotoxicity of Scutellaria Baicalensis Root Extract. Subsequently, negative Ames test results on a trade name mixture containing 33.33% Scutellaria Baicalensis Root Extract (aqueous extract) were received, and the Panel agreed that these data support the safety of Scutellaria Baicalensis Root Extract in cosmetic products.

In vitro studies indicated that ethanol and methanol extracts (but not n-hexane, ethyl acetate, and water extracts) could have an inhibitory effect on melanogenesis. However, the Panel noted that skin lightening is considered to be a drug effect and should not occur during the use of cosmetic products. Because of that caveat, and based on the low concentrations of use of Scutellaria Baicalensis Root Extract in cosmetic products, the results of these in vitro experiments on Scutellaria Baicalensis Root Extract, and clinical experience, concern for this effect in cosmetics was mitigated. Nevertheless, the Panel noted that cosmetic formulators should only use Scutellaria Baicalensis Root Extract in products in a manner that does not cause depigmentation.

After considering that Scutellaria Baicalensis Root Extract is being used in suntan products and the in vitro data on the potential inhibitory effect of Scutellaria Baicalensis Root Extract on melanogenesis, the Panel noted that phototoxicity data on Scutellaria Baicalensis Root Extract and other *Scutellaria baicalensis*-derived ingredients may be needed. In response to this concern, negative in vitro phototoxicity data on a trade name mixture containing 33.33% Scutellaria Baicalensis Root Extract (aqueous extract) were received, mitigating these concerns.

Tentative Safety Assessments

Acetyl Hexapeptide-8 Amide

The Panel concluded that Acetyl Hexapeptide-8 Amide is safe in cosmetics in the present practices of use and concentration described in the safety assessment, and issued a Tentative Report.

Acetyl Hexapeptide-8 Amide (CAS No. 616204-22-9), the subject of this safety assessment, is defined as the product obtained by the acetylation of hexapeptide-8 in which the C-terminus is an amide. The sequence for this acetylated and amidated peptide is Ac-Glu-Glu-Met-Gln-Arg-Arg-NH2.

The Panel noted the absence of systemic toxicity and genotoxicity data on Acetyl Hexapaptide-8 Amide. However, concern over the lack of these data was mitigated, after considering the peptide structure of this ingredient and associated low log Ko/w value of -7.68 (i.e. percutaneous absorption is unlikely), and the low maximum use concentration of 0.005% in leave-on cosmetic products. The Panel determined that these findings support the safe use of Acetyl Hexapeptide-8 Amide in cosmetic products.

Finally, the Panel discussed the issue of incidental inhalation exposure from the use of Acetyl Hexapeptide-8 Amide in face powders at concentrations up to 0.0001%. It was noted that conservative estimates of inhalation exposures to respirable particles during the use of loose powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace.

Benzophenones

The Panel published a safety assessment of benzophenones with the following conclusion in 1983: On the basis of the available animal data and clinical human experience presented in this report, the Panel concluded that Benzophenones-1, -3, -4, -5, -9, and -11 are safe for topical application to humans in the present practices of use and concentration in cosmetics. During the same year, the Panel also published an addendum to this published safety assessment, having concluded that Benzophenones-2, -6, and -8 are not mutagenic or genotoxic and that the published conclusion on Benzophenones-1, -3, -4, -5, -9, and -11 is applicable to these 3 ingredients.

The Panel elected to defer its next rereview of these ingredients until the National Toxicology Program (NTP) completed an assessment of benzophenone carcinogenicity. An NTP oral carcinogenicity study on Benzophenone-3 was published in May 2020, and results from this study have been reviewed by the Panel, along with other safety test data on this ingredient and the other ingredients in this report that have been identified in the published literature since the original safety assessment was published in 1983. After considering new studies and updated use data on these ingredients, the Panel determined that the safety assessment should be reopened and issued a Tentative Amended Report with the conclusion that Benzophenones-1, -2, -3, -4, -5, -6, -8, -9, -10, -11, and -12 are safe in cosmetics in the present practices of use and concentration described in this safety assessment.

The Panel reviewed a number of systemic toxicity studies on benzophenones. However, the Panel noted that these studies were performed at high concentrations that are not relevant to cosmetic exposure. The NTP oral carcinogenicity study on Benzophenone-3 reviewed by the Panel involved rats and mice. Results indicated equivocal evidence of carcinogenicity, i.e., male rats with benign thyroid tumors and malignant meningiomas in the absence of a dose response, and no evidence of carcinogenicity in mice. Based in part on these results, the Panel expressed a lack of concern over the carcinogenic potential of benzophenones as used in cosmetic products.

In Europe, Benzophenone-3 is permitted in cosmetics at concentrations up to 0.5% to protect formulations from photodegradation, and at concentrations up to 6% as a sunscreen ingredient. The Panel agreed that it should be recognized that sunscreens are classified as cosmetics in Europe, but are classified as over-the-counter drugs in the United States. Furthermore, the Panel emphasized that, in the United States, Benzophenone-3 functions only as a light stabilizer in cosmetic products.

The issue of incidental inhalation exposure from the use of Benzopheone-3 and Benzophenone-4 in cosmetic products was discussed by the Panel. Benzophenone-3 is being used in aerosol hair spray (maximum concentration of 0.014%), pump hair spray (maximum concentration of 0.05%), and in pump deodorant spray (at maximum

concentration of 0.08%). Benzophenone-4 is also being used in aerosol hair spray (maximum concentration of 0.015%) and pump hair spray (maximum concentrations of 0.001% to 0.1%). Relative to these uses, the Panel stated that droplets/particles deposited in the nasopharyngeal or bronchial regions of the respiratory tract present no toxicological concerns based on the properties of Benzophenone-3 or Benzophenone-4. Benzophenone-3 is also being used in face powders (use concentrations unknown). The Panel noted that conservative estimates of inhalation exposures to respirable particles during the use of loose powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace.

Coconut-Derived Ingredients

The Panel issued a Tentative Report for public comment with the conclusion that the following 7 *Cocos nucifera* (coconut)-derived ingredients are safe in the present practices of use and concentration described in the safety assessment:

Cocos Nucifera (Coconut) Fruit
Cocos Nucifera (Coconut) Fruit Extract
Cocos Nucifera (Coconut) Fruit/Fruit Juice Extract
Cocos Nucifera (Coconut) Fruit Juice
Cocos Nucifera (Coconut) Fruit Powder
Cocos Nucifera (Coconut) Fruit Water
Cocos Nucifera (Coconut) Liquid Endosperm

However, the Panel also concluded that the available data are insufficient to make a determination that the following 3 ingredients are safe under the intended conditions of use in cosmetic formulations:

Cocos Nucifera (Coconut) Flower Extract
Cocos Nucifera (Coconut) Flower Nectar Extract
Cocos Nucifera (Coconut) Shell Powder

The additional data needed for these cosmetic ingredients are:

- Composition and impurities data for Cocos Nucifera (Coconut) Flower Extract, Cocos Nucifera (Coconut) Flower Nectar Extract, and Cocos Nucifera (Coconut) Shell Powder
- Data on Cocos Nucifera (Coconut) Flower Extract, Cocos Nucifera (Coconut) Flower Extract, and Cocos Nucifera (Coconut) Shell Powder on the following endpoints:
    - 28-day dermal toxicity, and if positive, developmental and reproductive toxicity may be needed
    - Genotoxicity
    - Dermal irritation and sensitization

Polysilicone-11

The Panel issued a Tentative Report for public comment with the conclusion that Polysilicone-11 is safe in the present practices of use and concentration described in the safety assessment. The safety of this ingredient was supported by sufficient data on residual monomer concentrations and dermal sensitization/irritation, and lack of clinical reports. In addition, as this ingredient is reported to have a large molecular weight, it is unlikely to penetrate the epidermis, mitigating the concern for systemic toxicity.

According to 2020 VCRP data, Polysilicone-11 is reported to be used in 440 formulations, 432 of which are leave-on formulations. Results of the concentration of use survey conducted by the Council in 2018, and updated in 2019, indicate Polysilicone-11 is used at a maximum concentration of up to 19.9% in other skin care preparations.

Insufficient Data Announcements

Saccharide Humectants

The Panel issued an Insufficient Data Announcement (IDA) with for the following saccharide humectants that are listed below:

Anhydrogalactose	Arabinose	Saccharide Isomerate
Anhydroglucitol	Psicose	
Anhydroxylitol	Saccharide Hydrolysate	

- Method of manufacture, impurities, and composition data on all ingredients/ingredient mixtures
- Confirmation of the lack of skin penetration of these ingredients/ingredient mixtures
- Composition of glucose and fructose in the ingredient mixtures; if the 2 monosaccharides are present in sufficient amounts, the available negative data on glucose and fructose skin penetration can be used to evaluate the skin penetration potential of saccharide humectant ingredient mixtures
- 28-day dermal toxicity data on Saccharide Isomerate at cosmetic use concentrations up to 2.8%

Levulinic Acid

The Panel issued an IDA for Levulinic Acid and Sodium Levulinate. The additional data needs to determine safety for these cosmetic ingredients are:

- Impurities
- 28-day dermal toxicity data (and, if found to be absorbed other endpoints may be needed, e.g. developmental and reproductive toxicity (DART))
- Ocular irritation data at, or above, the highest reported leave-on concentration, 0.57%

Ubiquinone

The Panel issued an IDA for Disodium Ubiquinone, Hydroxydecyl Ubiquinone, Ubiquinol, and Ubiquinone. The additional data needs to determine safety for these cosmetic ingredients are:

- Method of manufacture for Hydroxydecyl Ubiquinone and Ubiquinol
- Concentration of use data for Hydroxydecyl Ubiquinone

Amino Acid Diacetates

The Panel issued an IDA for Beta-Alanine Diacetic Acid and Tetrasodium Glutamate Diacetate. The additional data needed to determine safety for these cosmetic ingredients are:

- 28-day dermal toxicity on Beta-Alanine Diacetic Acid
    - If positive, DART, genotoxicity, and dermal irritation and sensitization may be needed

Silicates

The Panel issued an IDA for the following 24 silicate ingredients:

Aluminum Calcium Sodium Silicate	Lithium Magnesium Silicate
Aluminum Iron Calcium Magnesium Germanium Silicates	Lithium Magnesium Sodium Silicate
	Magnesium Aluminometasilicate
Aluminum Iron Calcium Magnesium Zirconium Silicates	Magnesium Aluminum Silicate
	Magnesium Silicate
Aluminum Iron Silicates	Magnesium Trisilicate
Aluminum Silicate	Potassium Silicate
Ammonium Silver Zinc Aluminum Silicate	Pyrophyllite
Calcium Magnesium Silicate	Sodium Magnesium Aluminum Silicate
Calcium Silicate	Sodium Magnesium Silicate

Sodium Metasilicate
Sodium Potassium Aluminum Silicate
Sodium Silicate
Sodium Silver Aluminum Silicate
Zinc Silicate
Zirconium Silicate

The additional data needed to determine safety for these cosmetic ingredients are:

- Method of manufacturing, with specific focus to the origin of raw materials (synthetic versus mined derivation)
- Composition and impurities data, specifically percent quantification of any crystalline silica/silicate
- Inhalation toxicity data

Diacetone Alcohol

The Panel issued an IDA for Diacetone Alcohol. In order to determine safety for this cosmetic ingredient, the Panel requested impurities and purity level data on this ingredient, as used in cosmetics.

Red Algae

The Panel issued an IDA for the following 60 red algae ingredients:

Ahnfeltiopsis Concinna Extract
Asparagopsis Armata Extract
Betaphycus Gelatinum Extract
Botryocladia Occidentalis Extract
Calliblepharis Ciliata Extract
Ceramium Kondoi Extract
Ceramium Rubrum Extract
Chondracanthus Teedei Powder
Chondrus Crispus
Chondrus Crispus Extract
Chondrus Crispus Powder
Corallina Officinalis Extract
Corallina Officinalis Powder
Corallina Officinalis Thallus Extract
Cyanidium Caldarium Extract
Delesseria Sanguinea Extract
Digenea Simplex Extract
Dilsea Carnosa Extract
Furcellaria Lumbricalis Extract
Gelidiella Acerosa Extract
Gelidium Amansii Extract
Gelidium Amansii Oligosaccharides
Gelidium Cartilagineum Extract
Gelidium Pulchrum Protein
Gelidium Sesquipedale Extract
Gigartina Skottsbergii Extract
Gigartina Stellata Extract
Gloiopeltis Tenax Extract
Gloiopeltis Tenax Powder
Gracilaria Verrucosa Extract
Gracilariopsis Chorda Extract
Grateloupia Livida Powder
Hydrolyzed Asparagopsis Armata Extract
Hydrolyzed Chondrus Crispus Extract
Hydrolyzed Corallina Officinalis
Hydrolyzed Corallina Officinalis Extract
Hydrolyzed Porphyra Yezoensis
Hypnea Musciformis Extract
Kappaphycus Alvarezzi Extract
Lithothamnion Calcareum Extract
Lithothamnion Calcareum Powder
Lithothamnion Corallioides Powder
Mesophyllum Lichenoides Extract
Palmaria Palmata Extract
Palmaria Palmata Powder
Phymatolithon Calcareum Extract
Pikea Robusta Extract
Polysiphonia Lanosa Extract
Porphyra Linearis Powder
Porphyra Tenera Extract
Porphyra Tenera Sporophyte Extract
Porphyra Umbilicalis Extract
Porphyra Umbilicalis Powder
Porphyra Yezoensis Extract
Porphyra Yezoensis Powder
Porphyridium Cruentum Culture Conditioned Media
Porphyridium Cruentum Extract
Porphyridium Purpureum Extract
Rhodymenia Palmata Extract
Sarcodiotheca Gaudichaudii Extract

It was noted that several ingredients evaluated in this report are generally recognized as safe (GRAS) or used in foods. Since systemic exposure via ingestion would be far greater than exposure via cosmetics, the Panel deferred the need for systemic toxicity data on these ingredients, but requested the addition of dermal sensitization data where absent. For those ingredients without a GRAS designation, composition/impurities data are needed. In addition, the Panel requested a 28-day dermal toxicity assay on Corallina Officinalis Extract at the current maximum concentration of use (2%), as this ingredient is used at the highest concentration; if positive, systemic toxicity data such as DART and genotoxicity may be needed.

Re-Review Summaries

Quaternium-18 and Quaternium-18 Bentonite

The Panel approved the re-review summary of these ingredients, concluding that the data on Quaternium-18 and Quaternium-18 Bentonite were sufficient to re-affirm the original conclusion that these ingredients are safe as cosmetic ingredients in the present practices of use and concentration. This conclusion was originally published in 1982. In 2001, after considering new studies and updated use data on these ingredients, the Panel determined to not reopen the safety assessment. It should be noted that Quaternium-18 Hectorite was also included in the 1982 safety assessment and 2001 re-review consideration. However, Quaternium-18 Hectorite is not included in the current assessment because it was recently (2013) part of a separate assessment (Safety Assessment of Ammonium Hectorites as Used in Cosmetics).

Sulfites

The Panel approved the re-review summary of the following 7 sulfite ingredients, affirming their original conclusion that these ingredients are safe as used in cosmetic formulations.

Ammonium Bisulfite
Ammonium Sulfite*
Potassium Metabisulfite
Potassium Sulfite
Sodium Bisulfite
Sodium Metabisulfite
Sodium Sulfite

** Not reported to be in current use. Were this ingredient 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.*

The Panel first reviewed the safety of sulfites in 2003. The Panel considered the increased ingredient use frequency, reports of dermal sensitization, enhanced asthmatic responses to dust mites, and mutagenic effects in the published literature.

Final 2021 Priorities

The CIR Procedures require preparation of the 2021 Draft Priority List for public comment by June 1, 2020. This list was provided to the Panel and reviewed at the June 2020 meeting; comments made at the June meeting were considered and incorporated into a 2021 Draft Final Priority List, presented at the September 2020 meeting. The priority list is typically based on stakeholder requests (e.g., a hair dye) and frequency of use (FOU) data from FDA's Voluntary Cosmetic Registration Program (VCRP); this year, VCRP data were received from the FDA on January 13 (in response to a Freedom of Information Act request).

While this list includes only the lead ingredients, groupings of botanical or other organism-sourced mixture-type ingredients (e.g., Rosa Centifolia Flower Extract), are drafted in the 2021 Active Priority List available at https://cir-safety.org/sites/default/files/Final_2021_Active_Priority_List.pdf. For organic chemicals, the list of lead ingredients was forwarded to the newly convened Expert Panel Grouping/Clustering Working Group for consideration; the Working Group's comments were considered and incorporated, where appropriate. These groupings are also drafted in the 2021 Active Priority List.

There are 11 reports proposed (2 of the 12 lead ingredients below are proposed to be reviewed together in 1 report) on the 2021 Final Priorities List. Reports previously prioritized and on the CIR docket at the end of 2020, as well as a number of re-reviews of previous assessments, will supplement the total number of reports to be assessed in 2021.

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
- Genotoxicity data; if positive, carcinogenicity data may be needed
- Dermal irritation and sensitization data at maximum concentration of use

For the review of botanical ingredients, additional data needs 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) as used in cosmetics.

Ingredients	**Frequency of Use (FOU) Data Year 2020**
For cause	
Basic Yellow 57 – a hair dye	45
Per FOU	
Yeast Extract	736
Glyceryl Acrylate/Acrylic Acid Copolymer	519
Hydroxyacetophenone	409
Glyceryl Polymethacrylate	364
Acrylates/Octylacrylamide Copolymer	361
Hydroxypropyl Starch Phosphate	353
Sodium Lauroamphoacetate	344
Zingiber Officinale (Ginger) Root Extract	326
Leuconostoc/Radish Root Ferment Filtrate	322
Rosa Centifolia Flower Extract	321
Phytosteryl/Octyldodecyl Lauroyl Glutamate	313