

ADMIN

Memo

Agenda

Minutes

EXPERT PANEL MEETING

December 6-7, 2021



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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: 159<sup>th</sup> Meeting of the Expert Panel — Monday and Tuesday, December 6-7, 2021  
Date: November 10, 2021

Welcome to the last Panel Meeting of 2021! The agenda and accompanying materials for the 159<sup>th</sup> Expert Panel Meeting to be held on December 6-7, 2021, 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/159th-expert-panel-meeting>

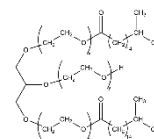
The meeting agenda includes the consideration of 17 reports advancing in the review process, including 7 final reports, 4 tentative reports, and 6 draft reports. Also on the agenda are 2 administrative items: a re-review proposal regarding certain Methacrylate Ester Monomers, and a new iteration of the Inhalation Resource Document.

## Team Meetings

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

#### 1. Fatty Ester End-Capped Alkoxylates – DR (Christina) – **Dr. Belsito reports on day 2** -

This is the first time the Expert Panel for Cosmetic Ingredient Safety (Panel) is reviewing the safety of these 14 cosmetic ingredients. A Notice to Proceed (NTP) without the preparation of a Scientific Literature Review (SLR) was issued by the Cosmetic Ingredient Review (CIR) on June 8, 2021. These ingredients are reported to function mainly as surfactants – emulsifying agents, skin-conditioning agents – emollients, and skin-conditioning agents – miscellaneous in cosmetic formulations.



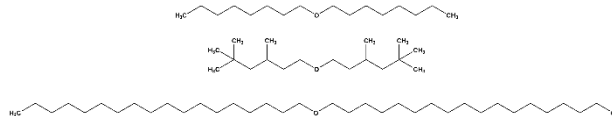
The Council provided concentration of use survey data, molecular weight, method of manufacturing, impurities, dermal penetration data, acute oral toxicity data, HRIPT data, and in vitro ocular irritation data on PEG/PPG-8/3-Diisostearate. No comments on the NTP were received from the Council.

According to 2021 VCRP survey data, PEG/PPG-8/3 Diisostearate is reported to be used in 155 formulations, with most of them being in bath soaps and detergents. All other in-use ingredients in the VCRP are reported to be used in one or two formulations. The results of the concentration of use survey conducted by the Council indicate PEG-12 Glyceryl Dimyristate has the highest concentration of use in a leave-on formulation; it is used at up to 1.8% in body and hand products. No concentration of use was reported for PEG/PPG-8/3 Diisostearate. There are 10 ingredients not reported to be in use, according to both 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, unsafe, or split 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. Fatty Ethers (Dicaprylyl Ether) – DR (Preethi) –

**Dr. Cohen reports on day 2** - This is the first time the Panel is reviewing the safety of these ingredients. An SLR was announced on February 2, 2021. Comments, skin tolerance, HRIPTs, summary information, and use concentration data were received from the Council; the draft report has been revised to address these comments and data.



According to 2021 VCRP survey data, Dicaprylyl Ether is reported to be used in 239 formulations, the majority of which are leave-on products. The only other ingredient with use reported in the VCRP is Distearyl Ether, with 4 reported uses. The results of the concentration of use survey, conducted in 2019 by the Council, indicate Dicaprylyl Ether also has the highest reported concentration of use; it is used at up to 25% in body and hand products. Cetyl Dimethylbutyl Ether is reported to be used at a maximum concentration of 19.3% in foundations. Dicetyl Ether, Didecyl Ether, Diisononyl Ether, Dilauryl Ether, and Dimyristyl Ether are not reported to be in use, according to both the VCRP and industry survey.

Additionally, Distearyl Ether has reported uses in products that may come in contact with the eyes; for example, it is used at up to 0.05% in eye lotions. Dicaprylyl Ether is used at up to 0.45% in baby lotions, oils, and creams, and has 5 reported uses in lipsticks (concentration not reported) which may lead to exposure to mucous membranes and incidental ingestion. Some of these ingredients are reported to be used in cosmetic spray formulations and could possibly be inhaled; for example, Dicaprylyl Ether is reported to be used at 10% in pump hair spray products and Dicaprylyl Ether has 1 reported use in a face powder formulation (concentration not reported).

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. Radish Root – DR (Preethi) – **Dr. Belsito reports on day 2** - This is the first time the Panel is reviewing this ingredient. The SLR NTP of this ingredient was issued by CIR on April 14, 2021. In addition to concentration of use survey data, the Council provided dermal irritation and sensitization, phototoxicity, genotoxicity, octanol/water partitioning coefficient, and composition data.

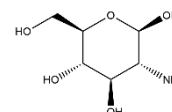


According to 2021 VCRP survey data, Leuconostoc/Radish Root Ferment Filtrate is reported to be used in 255 formulations, 104 of which are leave-on moisturizing products; Lactobacillus/Radish Root Ferment Filtrate and Raphanus Sativus (Radish) Root Extract are reported to have 2 uses each, in moisturizing and face and neck products, respectively. The results of the concentration of use survey conducted by the Council indicate that Raphanus Sativus (Radish) Root Extract has the highest reported maximum concentration of use in leave-on products, at up to 6% in lipstick; Leuconostoc/Radish Root Ferment Filtrate is used at up to 1.1% in skin cleansing products. The highest concentration of use reported for products resulting in leave-on dermal exposure is 0.03% Leuconostoc/Radish Root Ferment Filtrate in face and neck spray formulations. Use concentration data were not reported for Lactobacillus/Radish Root Ferment Filtrate, but uses were reported in the VCRP. Lactobacillus/Radish Root Ferment Extract Filtrate, Leuconostoc/Radish Root Ferment Lysate Filtrate, Raphanus Sativus (Radish) Root Juice, and Raphanus Sativus (Radish) Root Powder are not reported to be in use in either the VCRP or industry survey.

Radish root-derived ingredients have been reported to be used in products that may lead to incidental ingestion and exposure to mucous membranes; for example, Raphanus Sativus (Radish) Root Extract is reported to be used in a lipstick at up to 6%, and Leuconostoc/Radish Root Ferment Filtrate is reported to be used at up to 0.01% in other eye makeup preparations. Additionally, Leuconostoc/Radish Root Ferment Filtrate is reported to be used in products that could be potentially inhaled, e.g., Leuconostoc/Radish Root Ferment Filtrate is used in spray face and neck products at up to 0.03%.

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.

4. Glucosamine – DR (Priya) – **Dr. Cohen reports on day 2** - This is the first time the Panel is reviewing the 4 ingredients named in this report. The SLR was announced on February 5, 2021. In addition to comments and concentration of use survey data, the Council provided sensitization data. These data are enclosed and summarized in the draft report.



According to 2021 VCRP survey data, Acetyl Glucosamine is reported to be used in 117 formulations (105 leave-on formulations and 12 rinse-off formulations), and Glucosamine HCl is reported to be used in 69 formulations (57 leave-on formulations and 12 rinse-off formulations). Glucosamine is reported to be used in 4 leave-on formulations. The results of the concentration of use survey reported by the Council in 2020 indicate Acetyl Glucosamine also has the highest concentration of use in a leave-on formulation; it is used at up to 5% in face and neck products (not spray). No VCRP or concentration of use data were reported for Glucosamine Sulfate.

Incidental ingestion of Acetyl Glucosamine may occur, as it is used in lipstick formulations at concentrations up to 2%. In addition, Acetyl Glucosamine and Glucosamine HCl are used in formulations applied near the eye; for example, Acetyl Glucosamine is reported to be used at concentrations up to 2% in eye lotions. Some of these glucosamine ingredients are used in formulations that could possibly be inhaled. For example, Acetyl Glucosamine is reported to be used at 0.1% in pump hair sprays.

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.

5. Zingiber officinale (Ginger) – DR (Priya) – **Dr. Belsito reports on day 2** - This is the first time the Panel is reviewing these 9 ingredients. The SLR was announced on May 4, 2021. Since the issuance of the SLR, in addition to comments, the following data were received from Council and incorporated into the draft report: dermal patch tests, in vitro/in chemico sensitization studies, methods of manufacturing, composition, ocular irritation, and concentration of use data.



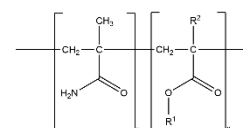
According to 2021 VCRP survey data, Zingiber Officinale (Ginger) Root Extract is reported to be used in 207 formulations (131 leave-on formulations; 75 rinse-off formulations; 1 formulation diluted for bath use) and Zingiber Officinale (Ginger) Root Oil is reported to be used in 123 formulations (84 leave-on formulations; 22 rinse-off formulations; 6 formulations diluted for bath use). All other in-use ingredients are reported to be used in 4 formulations or less. The results of the concentration of use survey conducted by the Council in 2020 indicate Zingiber Officinale (Root) Extract also has the highest concentration of use in a leave-on formulation; it is used at up to 0.2% in face and neck formulations. However, it should be noted that Zingiber Officinale (Ginger) Root Oil is reported to be used in “other fragrance preparations” as an essential oil, in which a few drops are used per teaspoon of carrier oil. The ingredients not in use according to both the VCRP and industry survey include Zingiber Officinale (Ginger) Leaf Cell Extract, Zingiber Officinale (Ginger) Root, and Zingiber and Officinale (Ginger) Root Juice.

Incidental ingestion of these ginger-derived ingredients may occur due to use in lipstick, dentifrices, and other oral hygiene product formulations (e.g. Zingiber Officinale (Ginger) Root Extract is used at up to 0.02% in lipsticks). In addition, Zingiber Officinale (Ginger) Root Extract is reported to be used in one eye lotion formulation (concentration for this formulation type was not provided). Mucous membrane exposure may also occur as Zingiber Officinale (Ginger) Root Extract and Zingiber Officinale (Ginger) Root Oil are reported to be used in bath oils, tablets and salts, at up to 0.001%. Additionally, some of these ginger-derived ingredients are used in cosmetic sprays and powders, and could possibly be inhaled; for example, Zingiber Officinale (Ginger) Root Extract is reported to be used in other fragrance preparations (up to 0.1%), and Zingiber Officinale (Ginger) Root Oil is reportedly used in pump spray body and hand formulations (up to 0.001%), and in face powders (concentration not reported).

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.

6. Acrylamide/Acrylate Copolymers – DR (Priya) – **Dr. Cohen reports on day 2** -

This is the first time the Panel is reviewing these 16 ingredients. The SLR NTP was announced on June 30, 2021. Since the issuance of the SLR NTP, the following unpublished data were received from the Council and incorporated into the draft report: composition, impurities, method of manufacture, acute oral toxicity, genotoxicity, dermal irritation and sensitization, ocular irritation, inhalation toxicity, and concentration of use data.



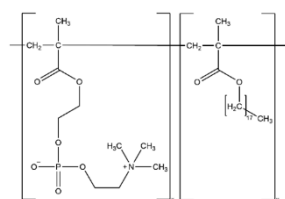
According to 2021 VCRP survey data, the ingredient with the highest number of uses, Acrylates/Octylacrylamide Copolymer, is reported to be used in 160 formulations. All other in-use ingredients are reported to be used in 14 formulations or less. The results of the concentration of use survey conducted by the Council in 2020 indicate that Acrylates/*t*-Butylacrylamide Copolymer, Acrylates/Octylacrylamide Copolymer, and Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer are used at up to 7% in leave-on formulations as aerosol hair sprays, mascaras, and tonics, dressings, and other hair grooming aids, respectively. Use concentration data were reported for Dimethylacrylamide/Lauryl Methacrylate Copolymer, but no uses were received in the VCRP; it should be presumed that there is at least one use in every category for which a concentration is reported. The 6 ingredients not in use, according to both the VCRP data and industry survey, are AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer, *t*-Butylacrylamide/Dimethylacrylamide/PEG-14 Diacrylate Crosspolymer, Butyl Acrylate/Isopropylacrylamide/PEG-18 Dimethacrylate Crosspolymer, Potassium Acrylates/Acrylamide Copolymer, Sodium Acrylates/Hydroxyethyl Acrylamide Copolymer, and Starch Acrylates/Acrylamide Copolymer.

Two ingredients are used in products that can be potentially ingested (Acrylamide/Sodium Acrylate Copolymer used in lipstick (concentration not reported) and Acrylates/Octylacrylamide Copolymer used in dentifrices (toothpaste) at up to 19.4%). Acrylates/Octylacrylamide Copolymer is also used in products used near the eye (eyeliners up to 4.6%, eye shadows up to 0.001%, and mascaras at up to 7%). In addition, mucous membrane exposure to these ingredients may occur (Acrylates/Acrylamide Copolymer is used in bath soaps and detergents (concentration not reported) and Corn Starch/Acrylamide/Sodium Acrylate Copolymer is used in bath oils, tablets, and salts (at up to 2%)). Some of these ingredients are used in cosmetic sprays and could possibly be inhaled; for example, Acrylates/*t*-Butylacrylamide Copolymer is reported to be used at 7% in aerosol hair sprays and Acrylates/Octylacrylamide Copolymer was reportedly used in face powders (concentration not reported).

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.

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

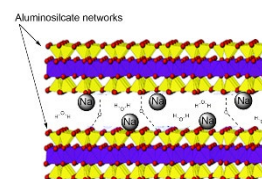
1. Acryloyloxyethyl Phosphorylcholine Polymers – TR (Wilbur) – **Dr. Belsito reports on day 2** – At the March 2021 meeting, the Panel issued an IDA for these ingredients. In order to come to a conclusion of safety, the Panel requested composition/impurities, molecular weight averages/distributions, skin sensitization data for Polyquaternium-51, and chemical structures for Hydroxyethylcellulose/ Phosphorylcholine Glycol Acrylate Copolymer and Polyquaternium-10/Phosphorylcholine Glycol Acrylate Copolymer.



In response, CIR has received the following unpublished data which have been incorporated into this iteration of the report: method of manufacture and impurities data on Phosphorylcholine Glycol Acrylate, Polyquaternium-51, and Polyquaternium-61; molecular weight averages and distribution data on Phosphorylcholine Glycol Acrylate, Polyquaternium-51, and Polyquaternium-61; guinea pig maximization test on Polyquaternium-51; guinea pig adjuvant and patch test on Polyquaternium-61; and an HRIPT on an undiluted serum containing 0.12% Polyquaternium-51. No chemical structures were provided.

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. Zeolites – TAR (Christina) – **Dr. Cohen reports on day 2** – In 2018, the Panel voted to re-open the 2003 safety assessment on several silicates, clays, and zeolites to include additional ingredients. Subsequently, the Panel decided to split off these ingredient groups into separate reports. At the September 2021 meeting, the Panel discussed the broad and uninformative definition of the ingredient Zeolite, and issued an IDA on the 6 zeolite ingredients. The additional data needs are method of manufacturing, chemical composition, particle size data, and dermal irritation/sensitization data.



Since the issuance of the IDA, CIR has received an HRIPT and an in vitro primary cutaneous tolerance test on a Zeolite material of unknown type (e.g., mined or synthetic). These data have been incorporated into the report. Additionally, CIR has found that the ECHA database has recently been updated with information for a zeolite associated with the CAS number 1318-02-1, which is the CAS number that is associated with Zeolite in the *Dictionary*. The ECHA entry describes this zeolite as “cuboidal, crystalline, synthetic, non-fibrous.” The data found under this ECHA entry have been incorporated into the safety assessment and may provide the Panel with a means to determine the scope of zeolites covered in the assessment for cosmetic safety.

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 remain insufficient, the Panel should issue a tentative report with an insufficient data conclusion, specifying the data needs in the report Discussion.

3. Salvia officinalis (Sage) – TR (Preethi) – **Dr. Belsito reports on day 2** – The Panel reviewed these 12 ingredients for the first time at the March 2021 meeting, after which an IDA was issued. The IDA included all possible data categories for the ingredient group, as well as method of manufacture information for Salvia Officinalis (Leaf) Extract and 28-d dermal toxicity data for both the Salvia Officinalis (Sage) Leaf Extract and Salvia Officinalis (Sage) Root Extract ingredients; if these ingredients were found to be absorbed, additional toxicological endpoints were to be sought.



Since the March 2021 meeting, the following data were received and have been incorporated in the report: HRIPTs for Salvia Officinalis (Sage) Leaf Extract and Oil and specifications for Salvia Officinalis (Sage) Leaf Water and Leaf Extract. Of note to the Panel, at the last meeting the placement of data included from an ECHA dossier, which generically applies to most of the ingredients (CAS No. 84082-79-1), was discussed. Although described as a *Salvia officinalis* extract (or even oil), the definition was extremely broad, and could possibly refer to the water fraction which results from the steam distillation of *Salvia officinalis* to produce oil. Hence, we had placed these data under the Salvia Officinalis Flower/Leaf/Stem Water ingredient heading, and it was agreed that more information on methods of manufacture, and the plant parts used in these methods, are needed to correctly classify this data.

**Does the Panel feel that the ECHA data should be moved under other ingredient headings, or can it remain as is?**

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. Portulaca oleracea – TR (Preethi) - **Dr. Cohen reports on day 2** – This is the second time the Panel is seeing a safety assessment of these 4 cosmetic ingredients. At the December 2020 meeting, a draft report was presented to the Panel. Upon review, the Panel issued an IDA for clarification on the current maximum concentrations of use for these ingredients, as well as a 28-d dermal toxicity study at the maximum concentration of use and an Ames test, both preferably with the ingredient in a hydroalcoholic solvent.



In response to the IDA, CIR received data on dermal sensitization for the Portulaca Oleracea Extract. Revisions to concentration of use data and updated VCRP data were also received from Council and the FDA, respectively, in 2021, and have been incorporated. The maximum concentration of use for Portulaca Oleracea Extract was verified as 0.5% in non-spray face and neck products.

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.

**Draft Final Reports - there are 7 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. Silicates – FAR (Christina) – **Dr. Cohen reports on day 2** – At the September 2021 meeting, the Panel issued a Revised Tentative Amended Report with the following conclusion on the 24 silicate ingredients:

These ingredients are safe in cosmetics in the present practices of use and concentration described in this safety assessment when formulated to be non-irritating,

with the exception that the available data are insufficient to make a determination of safety for the use of naturally-sourced (i.e., mined) silicate ingredients in products that may be incidentally inhaled.

Since the issuance of the revised tentative amended report, CIR has received no new data. Comments that were received from the Council have been addressed. After carefully reviewing the Abstract, Discussion, and Conclusion, the Panel should be prepared to issue a final amended report.

2. Barley – FR (Christina) – **Dr. Belsito reports on day 2** – At the September 2021 meeting, the Panel issued a Tentative Report with the conclusion that the 4 barley seed-derived ingredients are safe in cosmetics in the present practices of use and concentration described in the safety assessment. However, the Panel also concluded that the available data are insufficient to make a determination that the remaining 12 barley-derived ingredients are safe under the intended conditions of use in cosmetic formulations. The additional data needed to determine safety of these ingredients as used in cosmetics are:

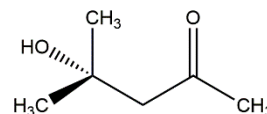


- 28-day dermal toxicity data on the whole plant extracts Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract
  - If positive, developmental and reproductive toxicity and genotoxicity data may be needed
  - Alternatively, acceptable evidence of use as a food for ingredients derived from the flower, leaf, stem, and root

Since the issuance of the tentative report, CIR has received no new unpublished data. Updated information regarding gluten content in cosmetics and use of barley grass as a developing functional food have been added to the report. Council comments on the tentative report have been addressed. In response to a Council comment on gluten and the addition of supporting references, CIR staff noted the quote from a celiac disease researcher that stated “if you have celiac disease, then the application of gluten-containing products to the skin should not be a problem, unless you have skin lesions that allow gluten to be absorbed systemically in great quantities.” There are no references cited to support this claim. **Should this information be added to the report, and if so, should the damaged skin caveat be added to this report’s conclusion?**

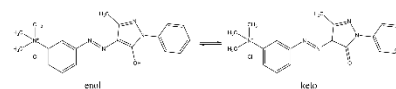
The Panel should carefully consider the Abstract, Discussion, and Conclusion presented in this report. If these are satisfactory, the Panel should issue a final report.

3. Diacetone Alcohol – FR (Priya) – **Dr. Cohen reports on day 2** – At the March 2021 meeting, the Panel issued a tentative report for public comment with the conclusion that Diacetone Alcohol is safe in the present practices of use and concentration. Comments received from the Council have been addressed. The Panel should review the Abstract, Discussion, and Conclusion, and issue a final amended report.



4. Basic Yellow 57 – FR (Christina) – **Dr. Belsito reports on day 2**

– At the September 2021 meeting, the Panel issued a tentative report with the conclusion that Basic Yellow 57 is safe for use as a hair dye ingredient in the present practices of use and concentration. Since the issuance of the Tentative Report, no additional data have been submitted. Council comments have been received and addressed. After reviewing these documents, as well as the Abstract, Discussion, and Conclusion of the report, the Panel should be prepared to issue a final report.



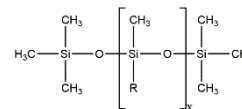


5. Saccharum officinarum (Sugarcane) – FR (Priya) – **Dr. Cohen reports on day 2** – At the September 2021 meeting, the Panel issued a Tentative Report for public comment on these 4 ingredients, with the conclusion that Saccharum Officinarum (Sugarcane) Bagasse Powder, Saccharum Officinarum (Sugarcane) Extract, Saccharum Officinarum (Sugarcane) Juice Extract, and Saccharum Officinarum (Sugarcane) Wax are safe as used in cosmetics in the present practices of use and concentration described in the safety assessment.



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.

6. Methicones – FAR (Preethi) – **Dr. Belsito reports on day 2** – At the September 2021 meeting the Panel issued a second revised tentative amended report, containing a split conclusion of safe in cosmetics in the present practices of use and concentration as described in the safety assessment when formulated to be non-irritating, with the exception that the available data are insufficient to make a determination that these ingredients are safe for use in products that may be incidentally inhaled.



Comments on the second revised tentative amended report were received from the Council and have been considered. The Panel should carefully consider the Abstract, Discussion, and Conclusion presented in this report. If these are satisfactory, the Panel should issue a final amended report.

7. Equisetum arvense – FR (Wilbur) – **Dr. Cohen reports on day 2** – At the September 2021 Panel meeting, the Panel issued a tentative report with a conclusion stating that these ingredients are safe in cosmetics in the present practices of use and concentration described in the safety assessment.



The Discussion sections in reports on botanical ingredients in which constituents of concern are identified (relative to sensitization potential) generally contain the botanical boilerplate. It should be noted that this boilerplate is included in this draft final report, though constituents of concern have not been identified. **With this in mind, the Panel should determine whether or not the boilerplate statement is needed.** The Panel should review the Abstract, Discussion, and Conclusion, and issue a final amended report.

#### Administrative Items - there is 1 resource document and 1 rereview.

1. Inhalation – Admin – separate book – (Jinjiu) – **Dr. Belsito reports on day 2** – The Panel last finalized this document at the September 2019 meeting. It has now been revised to address the comments received on exposure to airborne particles released from propellant gas sprays and airbrush application systems. Further, some new data regarding the aerosol inhalation exposure and deposited doses from various types of nanotechnology-enabled cosmetic products, including airbrush makeup foundation, have been identified since the September 2019 meeting.

In the letter dated September 9, 2021, WVE commented on the data source of particle size distributions of sprays that had been incorporated into the CIR respiratory resource document. Per the Panel's request, annotations have been added to WVE's memo to clarify each reference discussed in their comments.

At the December 2020 meeting, the Panel noted experimental evidence characterizing aerosol properties of four aerosolized nano-enabled cosmetics suggests that a fraction of airborne particles/agglomerates resulting from airbrush application systems are within the respirable range, although the particle size distribution data were not shown based on the ingredients (i.e., it is still not clear whether specific cosmetic ingredients (e.g., Methicone or Dimethicone) are in the nano-form during airbrush applications). Further physico/chemical analysis demonstrated that both the original products and collected aerosols contained micron-sized particles decorated with metal-oxide nanoparticle, such as TiO<sub>2</sub> and Fe<sub>2</sub>O<sub>3</sub>. The Panel thus considered that the currently available data indicate the usage of nano-enabled consumer products can cause aerosol/nanoparticle respiratory exposures and may pose public health risks.

At the September 2021 meeting, the Panel further discussed the particle size distribution of diverse aerosol sprays, with specific focus on propellant-driven sprays and airbrush devices. As more nano-enabled cosmetics are being formulated and released into the market, inhalation safety concerns are raised, considering prolonged duration of nanomaterial exposures in sprayable applications. Accordingly, the Panel recommended updating this Resource Document to incorporate new data on characterization of deposited dose of inhalable aerosols released from relevant sprays that might be formulated with cosmetic ingredients.

***The Panel should review the revisions and determine whether the attached draft, CIR Resource Document – Respiratory Exposure to Cosmetic Ingredients, has addressed their concerns with regard to particle size distribution and inhalation exposure parameters of spray applications that involve respirable fractions, as well as the specific considerations when assessing safety for ingredients that might be used in the product categories of propellant driven-sprays and airbrush devices. If not, the Panel should determine how, and to what extent, the Document should be revised further.***

2. Methacrylate Ester Monomers– RR (Wilbur) – ***Dr. Cohen reports on day 2*** – The Panel previously issued a conclusion stating that 22 methacrylate ester monomers are safe as used in nail enhancement products when skin contact is avoided. That conclusion also states that products containing these ingredients should be accompanied with directions to avoid skin contact, because of the sensitizing potential of methacrylates. A final report with this conclusion was published in 2005.

***Because it has been at least 15 years since the final report was published, in accordance with CIR Procedures, the Panel should consider whether the safety assessment should be reopened.*** Many of the ingredient names have changed, and one ingredient is no longer found in the Dictionary.

The results of a concentration of use survey conducted by the Council in 2020, and 2021 FDA VCRP data, are included with this submission. Collectively, these data indicate use of 8 methacrylate ester monomers in products that are applied to the nail. The most frequently used methacrylate ester monomer is HEMA, which has 149 uses and a reported maximum use concentration of 79% (in other manicuring products). Di-HEMA Trimethylhexyl Dicarbamate has a reported maximum use concentration 91.8% (in nail extenders). Of the ingredients proposed for review, this is the highest reported maximum use concentration. (In the original report, based on data received from industry in 2001, maximum use concentrations of methacrylate ester monomers was no more than 85% (reported for Methoxydiglycol Methacrylate and Ethoxyethyl Methacrylate in nail enhancement products).)

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

### **Full Panel Meeting**

The Panel will consider the 7 reports to be issued as final safety assessments, followed by the remaining reports advancing in the process (including the tentative reports and draft reports). In addition, a consensus should be reached for the 2 administrative items.

Please remember, the meeting starts at 8:30 am on day 1 and 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

## 159<sup>th</sup> Meeting of the Expert Panel for Cosmetic Ingredient Safety

### December 6<sup>th</sup> - 7<sup>th</sup>, 2021

Virtual via Microsoft Teams

Monday, December 6<sup>th</sup>

|                |   |                               |
|----------------|---|-------------------------------|
| <b>8:30 AM</b> | <b>WELCOME TO THE 159<sup>th</sup> EXPERT PANEL TEAM MEETINGS</b> | <b>Drs. Bergfeld/Heldreth</b> |
| <b>8:40 AM</b> | <b>TEAM MEETINGS</b>  | <b>Drs. Cohen/Belsito</b>     |

#### Dr. Cohen Team\*

|            |                                    |
|------------|------------------------------------|
| FR (PC)    | Diacetone Alcohol                  |
| FR (PC)    | Sugarcane                          |
| DR (PC)    | Glucosamine                        |
| DR (PC)    | Ginger                             |
| DR (PC)    | Acrylamide/Acrylate Copolymers     |
| Admin (JZ) | Inhalation                         |
| FAR (PR)   | Methicones                         |
| TR (PR)    | Sage                               |
| TR (PR)    | <i>Portulaca oleracea</i>          |
| DR (PR)    | Dicaprylyl Ether                   |
| DR (PR)    | Radish                             |
| FAR (CB)   | Silicates                          |
| TAR (CB)   | Zeolites                           |
| FR (CB)    | Basic Yellow 57                    |
| FR (CB)    | Barley                             |
| DR (CB)    | Fatty Ester End-Capped Alkoxyates  |
| FAR (WJ)   | <i>Equisetum arvense</i>           |
| TR (WJ)    | Acryloyloxyethyl Phosphorylcholine |
| RR (WJ)    | Methacrylate Ester Monomers        |

#### Dr. Belsito Team

|            |                                    |
|------------|------------------------------------|
| Admin (JZ) | Inhalation                         |
| FAR (CB)   | Silicates                          |
| TAR (CB)   | Zeolites                           |
| FR (CB)    | Basic Yellow 57                    |
| FR (CB)    | Barley                             |
| DR (CB)    | Fatty Ester End-Capped Alkoxyates  |
| FAR (WJ)   | <i>Equisetum arvense</i>           |
| TR (WJ)    | Acryloyloxyethyl Phosphorylcholine |
| RR (WJ)    | Methacrylate Ester Monomers        |
| FR (PC)    | Diacetone Alcohol                  |
| FR (PC)    | Sugarcane                          |
| DR (PC)    | Glucosamine                        |
| DR (PC)    | Ginger                             |
| DR (PC)    | Acrylamide/Acrylate Copolymers     |
| FAR (PR)   | Methicones                         |
| TR (PR)    | Sage                               |
| TR (PR)    | <i>Portulaca oleracea</i>          |
| DR (PR)    | Dicaprylyl Ether                   |
| DR (PR)    | Radish                             |

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 7<sup>th</sup>

|         |  |              |
|---------|--|--------------|
| 8:30 am | <b>WELCOME TO THE 159<sup>th</sup> FULL EXPERT PANEL MEETING</b>       | Dr. Bergfeld |
| 8:45 am | Admin <b>MINUTES OF THE SEPTEMBER 2021 EXPERT PANEL MEETING</b>        | Dr. Bergfeld |
| 9:00 am | <b>DIRECTOR'S REPORT</b>   | Dr. Heldreth |
| 9:10 am | <b>FINAL REPORTS, REPORTS ADVANCING TO THE NEXT LEVEL, OTHER ITEMS</b> |              |

**Final Reports**

|          |   |
|----------|---|
| FAR (CB) | Silicates – <i>Dr. Cohen Reports</i>                |
| FR (CB)  | Barley – <i>Dr. Belsito Reports</i>                 |
| FR (PC)  | Diacetone Alcohol – <i>Dr. Cohen Reports</i>        |
| FR (CB)  | Basic Yellow 57 – <i>Dr. Belsito Reports</i>        |
| FR (PC)  | Sugarcane – <i>Dr. Cohen Reports</i>                |
| FAR (PR) | Methicones – <i>Dr. Belsito Reports</i>             |
| FR (WJ)  | <i>Equisetum arvense</i> – <i>Dr. Cohen Reports</i> |

**Reports Advancing**

|          |   |
|----------|---|
| TR (WJ)  | Acryloyloxyethyl Phosphorylcholine – <i>Dr. Belsito Reports</i> |
| TAR (CB) | Zeolites – <i>Dr. Cohen Reports</i>                             |
| TR (PR)  | Sage – <i>Dr. Belsito Reports</i>                               |
| TR (PR)  | <i>Portulaca oleracea</i> – <i>Dr. Cohen Reports</i>            |
| DR (CB)  | Fatty Ester End-Capped Alkoxylates – <i>Dr. Belsito Reports</i> |
| DR (PR)  | Dicaprylyl Ether – <i>Dr. Cohen Reports</i>                     |
| DR (PR)  | Radish – <i>Dr. Belsito Reports</i>                             |
| DR (PC)  | Glucosamine – <i>Dr. Cohen Reports</i>                          |
| DR (PC)  | Ginger – <i>Dr. Belsito Reports</i>                             |
| DR (PC)  | Acrylamide/Acrylate Copolymers – <i>Dr. Cohen Reports</i>       |

**Other Items**

|            |  |
|------------|--|
| Admin (JZ) | Inhalation – <i>Dr. Belsito Reports</i>                |
| RR (WJ)    | Methacrylate Ester Monomers – <i>Dr. Cohen Reports</i> |

**ADJOURN** - Next meeting Monday and Tuesday, **March 7-8, 2022**, 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- EIGHTH MEETING  
OF THE  
EXPERT PANEL FOR COSMETIC INGREDIENT SAFETY

September 13-14, 2021

Microsoft Teams Virtual Meeting

Expert Panel Members

Wilma F. Bergfeld, M.D., Chairperson

Donald V. Belsito, M.D., Teamleader

David E. Cohen, M.D., Teamleader

Curtis D. Klaassen, Ph.D.

Daniel C. Liebler, Ph.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, PhD - Executive Director

Monice Fiume, MBA - Senior Director

Carla Jackson - Administrative Coordinator

Subject Matter Expertise

Jinqiu Zhu, PhD, DABT, ERT - Toxicologist

Analysis

Christina L. Burnett, MSES - Senior Scientific Analyst

Wilbur Johnson, Jr., MS - Senior Scientific Analyst

Preethi S. Raj, MS - Senior Scientific Analyst

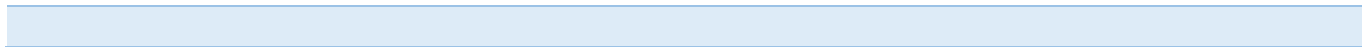
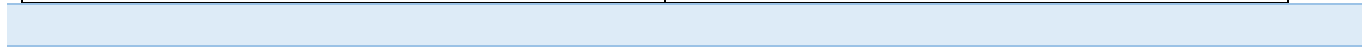
Priya Cherian - Scientific Analyst

Information Services

Kevin Stone Fries, MLS - Information Services Manager

**Others Participating in the Meeting**

|                 |  |
|-----------------|--|
| Carol Eisenmann | Personal Care Products Council                   |
| Michael Wyatt   | FDA  |
| Mark Ellis      | International Diatomite Producers Association    |
| Shripal Sharma  | Imerys   |
| Jay Ansell      | Personal Care Products Council (PCPC)            |
| Tracy Guerrero  | Silicones Environmental Health and Safety Center |
| Claudia Jackson | Carma Labs                                       |
| Zydnia Madera   | ET Browne  |



### CHAIRPERSON'S OPENING REMARKS

Dr. Bergfeld welcomed the attendees to the September 13-14, 2021 meeting of the Expert Panel for Cosmetic Ingredient Safety (158<sup>th</sup> Panel meeting). She then reflected on the fact that this year marks 20 years since 9/11, and noted that the Panel was meeting in Washington on that date.

Furthermore, Dr. Bergfeld stated that 17 ingredient reports are scheduled for review at today's meeting, and that limited data are included in the wave 2 data submission. These ingredient reports include: 7 final reports (2 of which are amended reports on Silicates and Dimethicones), 4 tentative reports, and 6 draft reports (many of which are on botanicals). She also noted that comments on silicate particles and airbrush technology were received from Women's Voices for the Earth. Silicate particle size and how these particles are delivered in an aerosol were asserted as relevant to the safety assessment of several ingredients that are scheduled for review. Regarding yesterday's Team meetings, Dr. Bergfeld recalled a discussion on the identification of toxicity potential versus biological activity, the former having been deemed more important than the latter. The 2022 CIR Priority List was also considered in Teams.

Dr. Bergfeld commented on the productivity of the CIR review process, which has yielded safety assessments involving as many as 5,000 ingredients. She then thanked the CIR staff and everyone associated with the CIR program for all of the hard work and effort involved in the preparation of safety assessments for review.

Concerning the review of Benzophenones at the March 2021 Panel meeting, Dr. Belsito stated that the minutes of that meeting do not note that environmental effects are not within the Panel's purview. This observation is based on the Panel's awareness of concerns relating to Benzophenone-3 (oxybenzone) in the environment, which was apparent during the Panel's deliberations.

### APPROVAL OF MINUTES

The minutes of the March 11-12, 2021 (157<sup>th</sup>) Expert Panel meeting were approved.

### DIRECTOR'S REPORT

Dr. Heldreth expressed gratitude for the Panel's and other stakeholders' continued support of the CIR program. He noted that 2021 has been a rather interesting year, and 2022 promises to be just as so. Hopefully, he remarked, sometime in 2022, we can again be in person for these meetings. While it looks like we have a sound group of new ingredients to assess next year, there will be a significant quantity of re-reviews in 2022. And with over 5,500 ingredients reviewed by this Panel, the priority focus will shift away from quantity to smaller groups of interest in the years to come. Although the cosmetic ingredient Dictionary lists some 20,000 to 30,000 potential ingredients, the use data we rely on demonstrate that the number of ingredients in use is much closer to 6000 to 7000. However, Dr. Heldreth remarked, please do not let this give you the impression that we are almost done. This industry is so innovative, and explores so many new ingredients every year, that this safety assessment body will never run out of ingredients to review.

### Final Safety Assessments

#### **Red Algae-Derived Ingredients**

The Panel issued a Final Report with the conclusion that 16 of the 60 distinct red algae-derived ingredients reviewed are safe in the present practices of use and concentration described in the safety assessment. Recent reported use of *Corallina officinalis* as an emulsifier in food products was sufficient to alleviate systemic toxicity concerns regarding the *Corallina officinalis*-derived ingredients. Therefore, coupled with negative sensitization data, Corallina Officinalis Extract, Corallina Officinalis Powder, Corallina Officinalis Thallus Extract, Hydrolyzed Corallina Officinalis, and Hydrolyzed Corallina Officinalis Extract, are considered safe as used in cosmetics. The Panel determined that there are insufficient data to determine the safety of the remaining 44 ingredients. The insufficiencies include a lack of systemic toxicity data (via use in food, GRAS status, or oral toxicity) and/or sensitization data. As for those ingredients that are formulated differently, but are derived from the same genus and species, and would be similar in composition (e.g., Chondrus Crispus Extract and Chondrus Crispus Powder), the Panel confirmed that if there are sufficient data to support the safety of one of these ingredients, all related ingredients in the same genus and species are considered safe.

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

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



**Ingredients in black type are considered safe as used by the Panel.**

**Ingredients in blue type are considered sufficient in systemic toxicity data, however, sensitization data or composition data are required by the Panel to determine safety.**

**Ingredients in green type are considered sufficient in sensitization data, however, systemic toxicity data are required by the Panel to determine safety.**

**Ingredients in red type are considered insufficient in both systemic toxicity and sensitization data.**

#### **Melaleuca alternifolia (Tea Tree)-Derived Ingredients**

The Panel issued a Final Report with the conclusion that the following 8 *Melaleuca alternifolia* (tea tree)-derived ingredients are safe in cosmetics in the present practices of use and concentration described in this safety assessment when formulated to be non-sensitizing.

|  |  |
|--|--|
| Melaleuca Alternifolia (Tea Tree) Extract                  | Melaleuca Alternifolia (Tea Tree) Leaf Extract |
| Melaleuca Alternifolia (Tea Tree) Flower/Leaf/Stem Extract | Melaleuca Alternifolia (Tea Tree) Leaf Oil     |
| Melaleuca Alternifolia (Tea Tree) Flower/Leaf/Stem Oil*    | Melaleuca Alternifolia (Tea Tree) Leaf Powder* |
| Melaleuca Alternifolia (Tea Tree) Leaf                     | Melaleuca Alternifolia (Tea Tree) Leaf Water   |

*\* 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 stated that because final product formulations may contain multiple botanicals, each possibly containing the same constituents of concern, formulators are advised to be aware of these constituents and to avoid reaching levels that may be hazardous to consumers. Additionally, the Panel was aware that variances in the composition of tea tree oil based on a geographical or geological difference in growth have been reported, which could also affect the potential for sensitization. Therefore, when formulating products, manufacturers should avoid reaching levels of plant constituents that may cause sensitization or other adverse health effects. Furthermore, the Panel noted that oxidized tea tree oil has the potential to be a sensitizer, and stated that methods should be employed to minimize oxidation of the oil in the final cosmetic formulation.

The Panel expressed concern about pesticide residues, heavy metals, and other plant species that may be present in botanical ingredients, and acknowledged *Melaleuca alternifolia* (tea tree)-derived ingredients could be supplied as adulterated products. For these reasons, the Panel stressed that the cosmetics industry should continue to use current good manufacturing practices (cGMPs) to limit impurities.

#### **Levulinic Acid and Sodium Levulinate**

The Panel issued a Final Report with the conclusion that Levulinic Acid and Sodium Levulinate are safe in cosmetics in the present practices of use and concentration described in the safety assessment when formulated to be non-irritating.

The Panel noted that Levulinic Acid has been approved by the FDA as a food additive and that food-grade Levulinic Acid is manufactured at no lower than 97% purity. Duly, the Panel discussed that systemic exposure to Levulinic Acid would be much higher via food consumption relative to cosmetics. The Panel agreed that these considerations mitigate cosmetic purity and systemic toxicity concerns. The Panel also considered positive ocular irritation data in the report, in light of the highest reported concentration of use in eye product formulations (0.57% in eyeshadows). In the absence of further ocular toxicity data, these ingredients are deemed to be safe when formulated to be non-irritating.

#### **Polyquaternium-6**

The Panel issued a Final Report with the conclusion that Polyquaternium-6 is safe in cosmetics in the present practices of use and concentration described in the safety assessment.

It was noted that most of the safety test data in this report are on high molecular weight (MW) Polyquaternium-6 (42%, MW 150,000 Da, 6.5% monomer content). The Panel agreed that concern over the DADMAC residual monomer content is mitigated, in part, because this monomer is non-reactive to proteins. They also noted that, overall, the available data are not indicative of any safety concerns relating to skin sensitization, systemic toxicity, or other toxicity endpoints. More specifically, the Panel considered the limited negative skin sensitization/photosensitization data in this safety assessment, but noted that potential concerns relating to systemic exposure, in the absence of additional data, are mitigated due to lack of percutaneous absorption.

The Panel discussed the issue of incidental inhalation exposure from the use of Polyquaternium-6 in hair sprays (pump sprays) at maximum use concentrations up to 0.5%. The Panel stated that droplets/particles deposited in the nasopharyngeal or bronchial regions of the respiratory tract present no toxicological concerns based on the chemical and toxicological properties of Polyquaternium-6. Finally, though the presence of nitrosamines in Polyquaternium-6 has not been determined, it was noted that polyquaterniums have the potential to be N-nitrosated. Thus, the Panel cautions that products containing Polyquaternium-6 should be formulated to avoid the formation of nitrosamines.

#### **Anhydrogalactose, Anhydroglucitol, Anhydroxylytol, Arabinose, Psicose, Saccharide Hydrolysate, and Saccharide Isomerate**

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

|                  |                |                        |                      |
|------------------|----------------|------------------------|----------------------|
| Anhydrogalactose | Anhydroxylytol | Psicose                | Saccharide Isomerate |
| Anhydroglucitol  | Arabinose      | Saccharide Hydrolysate |                      |

After consideration of the data received and other data included in the safety assessment, the Panel determined that these are sufficient for determining the safety of these ingredients. Specifically, the Panel noted that data on Saccharide Isomerate with varying MW (lower MW range: 120 to 400 Da; higher MW of 15,000 Da, 20,000 Da, or > 1.4 MDa) are among the data that have been reviewed. The lower MW Saccharide Isomerate consists mostly of glucose and fructose, and, in the absence of developmental and reproductive toxicity data in the safety assessment, the Panel noted that concerns relating to the lack of this toxicity data for this endpoint are mitigated based on this composition. The Panel agreed that concerns relating to this endpoint are also mitigated for the higher MW Saccharide Isomerate, as it would not be percutaneously absorbed. Moreover, the Panel felt that these data for Saccharide Isomerate mitigated the concern over data gaps for the other ingredients in this report.

### **Tentative Safety Assessment**

#### **Barley-Derived Ingredients**

The Panel issued a Tentative Report for public comment with the conclusion that the following 4 barley-derived ingredients are safe in cosmetics in the present practices of use and concentrations described in this safety assessment:

|  |                             |
|--|-----------------------------|
| Hordeum Distichon (Barley) Seed Flour* | Hordeum Vulgare Seed Flour  |
| Hordeum Vulgare Seed Extract           | Hordeum Vulgare Seed Water* |

*\*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 that the barley seed-derived ingredients that are reviewed in this safety assessment are found in foods that are consumed daily, and daily exposure from food use would result in much larger systemic exposures than those from use in cosmetic products. The potential for systemic exposure from the absorption of these ingredients through the skin is much less than the potential for systemic exposure from absorption through oral exposures. This fact, coupled with negative findings in human dermal irritation and sensitization studies on whole plant extracts and seed extracts, led the Panel to determine that barley seed-derived ingredients are safe for use in cosmetic products.

However, the Panel also concluded that the available data are insufficient to make a determination of safety on the following 12 barley-derived ingredients:

|  |                                    |                                  |
|--|------------------------------------|----------------------------------|
| Hordeum Distichon (Barley) Extract       | Hordeum Vulgare Leaf Juice**       | Hordeum Vulgare Sprout Extract** |
| Hordeum Vulgare Extract                  | Hordeum Vulgare Leaf Powder**      | Hordeum Vulgare Stem Water**     |
| Hordeum Vulgare Flower/Leaf/Stem Juice** | Hordeum Vulgare Leaf/Stem Powder** |                                  |
| Hordeum Vulgare Juice**                  | Hordeum Vulgare Powder**           |                                  |
| Hordeum Vulgare Leaf Extract             | Hordeum Vulgare Root Extract**     |                                  |

*\*\*There are currently no uses reported for these ingredients.*

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

- 28-day dermal toxicity data on the whole plant extracts Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract
  - If positive, developmental and reproductive toxicity and genotoxicity data
  - Alternatively, acceptable evidence of safe use as food for ingredients derived from the flower, leaf, stem, and root.

#### **Equisetum arvense-Derived Ingredients**

The Panel issued a Tentative Report for public comment with the conclusion that the following 5 Equisetum arvense-derived ingredients are safe in the present practices of use and concentration described in the safety assessment.

|                                |                                |
|--------------------------------|--------------------------------|
| Equisetum Arvense Extract      | Equisetum Arvense Leaf Powder* |
| Equisetum Arvense Juice*       | Equisetum Arvense Powder       |
| Equisetum Arvense Leaf Extract |                                |

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

The Panel noted that non-specific ulcerative dermatitis was observed in an oral dosing study in which Sprague-Dawley rats were fed a 4% Equisetum arvense powder in a cholesterol diet for 14 d. However, they also noted no obvious clinical signs in another study in which F344 rats were fed Equisetum arvense (hot water extract of powder) at concentrations up to 3% in a basal diet for 13 wk. Based on negative HRIPT data on products containing 0.000049% (209 subjects) and 0.6% (100 subjects) Equisetum Arvense Extract and a negative in-use safety evaluation (31 subjects) on nail products containing 0.000049% Equisetum Arvense Extract, the Panel agreed that the skin irritation and sensitization potential of this ingredient at the maximum reported use concentration of 0.4% in cosmetics is mitigated. Slight ocular irritation was observed in a study in which Equisetum Arvense Extract (hydroglycolic extract containing ~2% dry extract) was instilled into the eyes of rabbits. However, the Panel noted that this test concentration is greater than the maximum reported use concentration of 0.4% for Equisetum arvense-derived ingredients in cosmetics. Furthermore, the Panel stated that, in the absence of a no-observable adverse effect level (NOAEL) for ocular irritation and use concentration data on products applied near the eye, manufacturers should assure that these products are non-irritating.

Additionally, because final product formulations may contain multiple botanicals, each possibly containing the same constituents of concern, formulators are advised to be aware of these constituents and to avoid reaching levels that may be hazardous to consumers. Additionally, the Panel was aware that variances in the composition of Equisetum arvense, based on the geographical area of plant growth (i.e., Asia and North America vs. Europe), have been reported. Therefore, when formulating products, manufacturers should avoid reaching levels of plant constituents that may cause sensitization or other adverse health effects.

### Methicones

The Panel issued a Revised Tentative Amended Report for the following 30 ingredients. The Panel concluded that these ingredients are safe as used in the present practices of use and concentration as described in the safety assessment when formulated to be non-irritating; however, the Panel also concluded that the data are insufficient to support the safety of products that may be incidentally inhaled.

|                                 |  |
|---------------------------------|--|
| Amino Bispropyl Dimethicone     | Capryl Dimethicone                               |
| Aminopropyl Dimethicone         | Caprylyl Methicone                               |
| Amodimethicone                  | Cetearyl Methicone                               |
| Amodimethicone Hydroxystearate* | Cetyl Dimethicone                                |
| Behenoxy Dimethicone            | Dimethicone                                      |
| C20-24 Alkyl Dimethicone        | Dimethoxysilyl Ethylenediaminopropyl Dimethicone |
| C20-24 Alkyl Methicone*         | Hexyl Dimethicone                                |
| C24-28 Alkyl Dimethicone*       | Hexyl Methicone*                                 |
| C24-28 Alkyl Methicone          | Hydroxypropyldimethicone*                        |
| C26-28 Alkyl Dimethicone        | Methicone  |
| C26-28 Alkyl Methicone*         | Stearamidopropyl Dimethicone*                    |
| C30-45 Alkyl Dimethicone        | Stearoxy Dimethicone                             |
| C30-45 Alkyl Methicone          | Stearyl Dimethicone                              |
| C30-60 Alkyl Dimethicone*       | Stearyl Methicone                                |
| C32 Alkyl Dimethicone*          | Vinyl Dimethicone                                |

*\*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 was concerned that the potential exists for dermal irritation with the use of products formulated using Dimethicone, Methicone, and substituted-methicone polymers. The Panel specified that products containing these ingredients should be formulated to be non-irritating. Additionally, the Panel asserted the need for more data on current uses and concentrations of these ingredients in products that could be incidentally inhaled. Additionally, with the rise of non-professional, personal use, the Panel requested more information on the relevant parameters of devices used to apply cosmetics via airbrush, and other technologies creating potentially respirable particles. Thus, the Panel reasoned that these additional data are necessary to make a determination of safety for this product category.

### Silicates

The Panel issued a Revised Tentative Amended Report for public comment with the conclusion that the following 24 silicate ingredients are safe as used in the present practices of use and concentration described in the safety assessment when formulated to be non-irritating. However, the Panel also

concluded that the data are insufficient to make a determination of safety on naturally-sourced (e.g., mined) silicate ingredients for use in products that may be incidentally inhaled.

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

*\*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 the potential exists for dermal irritation with the use of products formulated using silicate ingredients. Therefore, the Panel specified that products containing these ingredients must be formulated to be non-irritating. Silicates used in cosmetics may be either naturally-sourced or synthetically derived. The Panel understands that only naturally sourced silicates can contain crystalline silica, a known cause of significant lung diseases including cancer. The available data are insufficient for determining safety of formulations containing naturally-sourced silicate used under consumer conditions wherein there is the potential for incidental respiration, in the absence of use concentration or negative repeat-dose inhalation safety data.

#### **Saccharum officinarum (Sugarcane)-Derived Ingredients**

The Panel issued a Tentative Report for public comment with the conclusion that these 4 Saccharum officinarum-derived ingredients are safe in the present practices of use and concentrations described in the safety assessment:

|  |   |
|--|---|
| Saccharum Officinarum, (Sugarcane) Bagasse Powder* | Saccharum Officinarum (Sugarcane) Juice Extract |
| Saccharum Officinarum (Sugarcane) Extract          | Saccharum Officinarum (Sugarcane) Wax           |

*\*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 determined that the data on Saccharum Officinarum (Sugarcane) Extract, particularly an HRIPT performed on 105 subjects using Saccharum Officinarum (Sugarcane) Extract at 2.7%, are sufficient to mitigate concern regarding the sensitization potential of the Saccharum Officinarum (Sugarcane) Bagasse Powder and Saccharum Officinarum (Sugarcane) Juice Extract. The need for systemic toxicity data and sensitization/irritation data on Saccharum Officinarum (Sugarcane) Wax is mitigated due to low concentration of use, use in rinse-off formulations only, and lack of potential dermal penetration. The safety of these ingredients is further supported by a lack of toxicity in available oral toxicity, genotoxicity, and carcinogenicity assays.

#### **Rosa damascena-Derived Ingredients**

The Panel issued a Tentative Report for public comment with the conclusion that these ingredients are safe as used in the present practices of use and concentration described in the safety assessment when formulated to be non-sensitizing.

|   |                                     |
|---|-------------------------------------|
| Hydrolyzed Rosa Damascena Flower Extract* | Rosa Damascena Flower Oil           |
| Rosa Damascena Bud Extract*               | Rosa Damascena Flower Powder        |
| Rosa Damascena Extract                    | Rosa Damascena Flower Water         |
| Rosa Damascena Flower                     | Rosa Damascena Flower Water Extract |
| Rosa Damascena Flower Extract             | Rosa Damascena Flower Wax           |

*\*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 discussed that most of these ingredients are derived from the flower, which is a GRAS food additive, according to the US FDA. Subsequently, concerns regarding the potential for systemic toxicity were mitigated. The Panel acknowledged the presence of potentially sensitizing constituents in the composition of these ingredients; accordingly, the Panel stated that because final product formulations may contain multiple botanicals, each possibly containing the same constituents of concern, formulators are advised to be aware of these constituents and to avoid reaching levels that may be hazardous to consumers. According to 2021 Voluntary Cosmetic Registration Program (VCRP) data, Rosa Damascena Flower Oil and Rosa Damascena Flower Water have the highest reported uses, in 223 and 308 formulations, respectively. Results from the 2019 Council survey also indicate that these ingredients have the highest reported maximum concentrations of use, with Rosa Damascena Flower Oil used at up to 10.8% in skincare preparations and Rosa Damascena Flower Water used at up to 32.7% in face and neck products. Confirmation of these use concentrations is corrected, in that they are much greater than all other reported maximum concentrations of use.

### **Ubiquinone**

The Panel issued a Tentative Report for public comment with the conclusion that the following 4 Ubiquinone-derived ingredients are safe in cosmetics in the present practices of use and concentrations described in the safety assessment:

|                      |                           |           |            |
|----------------------|---------------------------|-----------|------------|
| Disodium Ubiquinone* | Hydroxydecyl Ubiquinone** | Ubiquinol | Ubiquinone |
|----------------------|---------------------------|-----------|------------|

*\*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.*

*\*\*Maximum concentrations of use not reported. The expectation is that this ingredient would be used in product categories and at concentrations comparable to others in this group.*

The Panel stated that although Hydroxydecyl Ubiquinone is a synthetic analog of Ubiquinone with a shorter chain structure, it could reasonably be grouped with the other ingredients because of its shared bioactive ring structure. The Panel also discussed that the inefficiency and expense of extracting these ingredients from biological tissues would most likely make either chemical synthesis or microbial fermentation the primary means of production. In the absence of method of manufacture, impurities, and concentration of use data for Hydroxydecyl Ubiquinone and Ubiquinol, the Panel's safety concerns were mitigated due to the natural occurrence of Ubiquinone in living tissues, use as a food additive and nutritional supplement, as well as the abundance of negative results for developmental and genetic toxicity, and sensitization.

Data included in this report indicate that Ubiquinone may have a skin lightening effect. The Panel noted that skin lightening is considered to be a drug effect, and should not occur during the use of cosmetic products.

### **Basic Yellow 57**

The Panel issued a Tentative Report for public comment with the conclusion that Basic Yellow 57 is safe for use in hair dye products.

Basic Yellow 57 is reported to function as a direct, non-oxidative hair dye in hair coloring products. The Panel recognizes that hair dyes containing this ingredient, as coal tar hair dye products, are exempt from certain adulteration and color additive provisions of the Federal Food, Drug, and Cosmetic Act, when the label bears a caution statement and patch test instructions for determining whether the product causes skin irritation. The Panel expects that following this procedure will identify prospective individuals who would have an irritation/sensitization reaction and allow them to avoid significant exposures. The Panel considered concerns that such self-testing might induce sensitization, but agreed that there is not a sufficient basis for changing this advice to consumers at this time.

The Panel noted that the available toxicokinetic studies show that Basic Yellow 57 has low dermal penetration, has low concentrations of use, and is not sensitizing in animal studies. The Panel considered these findings, coupled with the short exposure time as a rinse-off product, and determined that the data are sufficient to conclude that Basic Yellow 57 is safe in the present practices and concentrations of use in hair dye formulations.

## **Insufficient Data Announcement**

### **Diatomaceous Earth**

The Panel issued an Insufficient Data Announcement (IDA) for Diatomaceous Earth. The additional data needed to determine safety for this cosmetic ingredient are:

- Clarification on the type(s) of Diatomaceous Earth that is used in cosmetic products (i.e., natural, calcined, and/or flux-calcined)
- Method of manufacturing for the type(s) of Diatomaceous Earth that is used in cosmetic products
- Composition and impurities data (including crystalline silicate content) on the type(s) of Diatomaceous Earth that is used in cosmetic products

### **Glyceryl Acrylates**

- Molecular weights and impurities, including residual monomers
  - Depending on the data received (especially residual monomer content), 28-d dermal toxicity, skin penetration data, and other toxicity endpoints may be needed
- Genotoxicity data
- Skin irritation and sensitization data at maximum use concentration in cosmetics

### **Glycolactones**

The Panel issued an IDA for these 5 glycolactones.

|                  |                     |               |
|------------------|---------------------|---------------|
| Galactonolactone | Glucoheptonolactone | Ribonolactone |
| Glucarolactone   | Gluconolactone      |               |

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

- Method of manufacturing data for Glucarolactone and Glucoheptonolactone
- Impurities data on Galactonolactone, Glucarolactone, Glucoheptonolactone, and Ribonolactone
- Irritation and sensitization data at maximum concentrations of use

### **Yeast**

The Panel issued an IDA for these 8 yeast-derived ingredients.

|                          |                   |                          |
|--------------------------|-------------------|--------------------------|
| Hydrolyzed Yeast         | Yeast             | Yeast Polysaccharides    |
| Hydrolyzed Yeast Extract | Yeast Beta-Glucan | Saccharomyces Cerevisiae |
| Hydrolyzed Yeast Protein | Yeast Extract     | Extract                  |

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

- Clarification regarding which species of yeast are used in the manufacturing of these cosmetic ingredients
  - Once these specific species are clarified, associated method of manufacturing, composition, impurities, sensitization, and irritation data may also be needed for these ingredients based upon the clarified species
  - If GRAS status/food use is not indicated for these species, systemic toxicity data are requested (28-d dermal toxicity, genotoxicity, and reproductive/developmental toxicity)
- Method of manufacturing and composition data for the hydrolyzed yeast ingredients (i.e., Hydrolyzed Yeast, Hydrolyzed Yeast Extract, and Hydrolyzed Yeast Protein)

### **Zeolites**

The Panel issued an IDA for these 6 zeolite ingredients.

|                         |                  |
|-------------------------|------------------|
| Ammonium Silver Zeolite | Titanium Zeolite |
| Gold Zeolite            | Zeolite          |
| Silver Copper Zeolite   | Zinc Zeolite     |

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

- Method of manufacturing and/or source data

- Chemical characterization, including specific framework(s), and composition and impurities data
  - Depending on the composition, additional toxicity data as needed
- The range of particle sizes that is used in spray and powder formulations
- Dermal irritation and sensitization data at maximum use concentrations

#### Final 2022 Priorities

The priority list is typically based on stakeholder requests (“for cause,” e.g., a hair dye) and frequency of use (FOU) data from FDA’s VCRP; this year, VCRP data were received from the FDA on January 21 (in response to a Freedom of Information Act request).

While this list includes only the lead ingredients, groupings of ingredients were drafted in the meeting materials. The Grouping/Clustering Working Group considered these groupings and took no issue.

There are 8 reports proposed (2 of the lead ingredients below are proposed to be reviewed together in 1 report) on the 2022 Final Priorities List. Reports previously prioritized and on the CIR docket at the end of 2021, as well as a significant number of re-reviews of previous assessments, will supplement the total number of reports to be assessed in 2022. In addition to the regularly scheduled re-reviews (i.e., those reports ≥ 15 years since publication), the Panel agreed to the acceleration of the re-review of DMDM Hydantoin.

| Ingredients                                  | Frequency of Use (FOU) Data Year 2021 |
|--|---------------------------------------|
| <b><i>For cause</i></b>                      |                                       |
| <b>Basic Yellow 87</b>                       | <b>29</b>                             |
| <b><i>Per FOU</i></b>                        |                                       |
| <b>Sodium Acetylated Hyaluronate</b>         | <b>304</b>                            |
| <b>Hydrolyzed Hyaluronic Acid</b>            | <b>265</b>                            |
| <b>Polyhydroxystearic Acid</b>               | <b>237</b>                            |
| <b>Diphenylsiloxy Phenyl Trimethicone</b>    | <b>234</b>                            |
| <b>Trisodium Ethylenediamine Disuccinate</b> | <b>202</b>                            |
| <b>Charcoal Powder</b>                       | <b>221</b>                            |
| <b>Zanthoxylum Piperitum Fruit Extract</b>   | <b>216</b>                            |
| <b>Pyridoxine HCl</b>                        | <b>195</b>                            |

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, specific to the ingredients as used in cosmetic formulations
- Toxicokinetics data, specifically dermal absorption and/or penetration
- Repeated-dose toxicity data
- Inhalation toxicity data, particularly if the ingredient is used in a product that can be incidentally inhaled
- Developmental and reproductive 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, the additional data needed include species, plant part, extraction method, solvent, and data on component chemical characterization. It is important that these data are specific for the ingredient(s) as used in cosmetics.

### **Read-Across Document**

The Panel reviewed a revised draft of the Read-Across Document. They agreed that it is a great start to outline a framework, which articulates the initial phase and step processes of measuring and layering chemical and toxicological similarities, to systematically identify potential read-across analog candidates for the Panel's consideration, by utilizing currently available public databases enriched with cosmetics-related chemicals. Also included therein, are a variety of computational tools as well as expert judgement in chemical clustering, subcategorization, and property profiling. The Panel also discussed the cautionary issues of using read-across and its inherent risks corresponding to different safety evaluation scenarios. The Panel agreed that this document would be a living document that needs to change and harmonize with developing technologies to improve the feasibility of read-across approach in the assessment of cosmetic ingredient safety.