Post Meeting Announcement

Expert Panel for Cosmetic Ingredient Safety
158th Meeting (September 13-14, 2021) - Findings

September 17, 2021

● Final Safety Assessments

- **Red Algae – 60 ingredients – Split (16 safe; 44 insufficient)**
- ***Melaleuca alternifolia* (Tea Tree) – 8 ingredients – Safe with qualifications**
- **Levulinic Acid – 2 ingredients – Safe with qualifications**
- **Polyquaternium-6 – 1 ingredient – Safe**
- **Saccharide Isomerate, et al. – 7 ingredients – Safe**

● Tentative Safety Assessments

- **Barley – 16 ingredients – Split (4 safe; 12 insufficient)**
- ***Equisetum arvense* – 5 ingredients – Safe**
- **Methicones – 30 ingredients – Split (safe; insufficient with incidental inhalation)**
- **Silicates – 24 ingredients – Split (safe; insufficient with incidental inhalation of naturally sourced)**
- ***Saccharum officinarum* (Sugarcane) – 4 ingredients – Safe**
- ***Rosa damascena* – 10 ingredients – Safe with qualifications**
- **Ubiquinone – 4 ingredients – Safe**
- **Basic Yellow 57 – 1 ingredient – Safe in hairdyes**

● Insufficient Data Announcements

- **Diatomaceous Earth – 1 ingredient**
- **Glyceryl Acrylates – 4 ingredients**
- **Glycolactones – 5 ingredients**
- **Yeast – 8 ingredients**
- **Zeolites – 6 ingredients**

● 158th Meeting Notes

- **Director's Report**
- **Final 2022 Priorities**
- **Read-Across Document**
- **Scientific Literature Reviews – available or under development**
- **Next Expert Panel Meeting – Monday and Tuesday, December 6-7, 2021**

Final Safety Assessments

Final safety assessments will be posted on the Cosmetic Ingredient Review (CIR) website at www.cir-safety.org. Unpublished data cited as references in CIR safety assessments are available for review. Any interested person who has sound scientific evidence that a final safety assessment is incorrect may petition the Expert Panel for Cosmetic Ingredient Safety (Panel) to amend the safety assessment.

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
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 Alvarezii 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*

**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) Flower/Leaf/Stem Extract
Melaleuca Alternifolia (Tea Tree) Flower/Leaf/Stem Oil*
Melaleuca Alternifolia (Tea Tree) Leaf
Melaleuca Alternifolia (Tea Tree) Leaf Extract
Melaleuca Alternifolia (Tea Tree) Leaf Oil
Melaleuca Alternifolia (Tea Tree) Leaf Powder*
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, Anhydroxylitol, 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	Anhydroxylitol	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 Assessments

*For the tentative safety assessments listed below, to be posted on the CIR website at www.cir-safety.org on or before **September 24, 2021**, interested persons are given 60 days from the posting date to comment, provide information, and/or request an oral hearing before the Panel. Information may be submitted without identifying the source or the trade name of the cosmetic product containing the ingredient. All unpublished data submitted to CIR will be discussed in open meetings, and are available for review by any interested party. Please submit data and/or comments to CIR **as soon as possible, but no later than 60 days from the actual posting date, for full consideration. Submissions received thereafter may be in jeopardy of not being considered by the Panel.** The updated reports may be scheduled for review by the Expert Panel as early as at its **December 6-7, 2021** meeting. However, some of the tentative safety assessments below may be posted later (with an appropriate 60-day comment period) and likely be scheduled for review by the Panel at its **March 7-8, 2022** meeting.*

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 Extract Hordeum Vulgare Seed Flour 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 Extract	Hordeum Vulgare Powder**
Hordeum Vulgare Extract	Hordeum Vulgare Leaf Juice**	Hordeum Vulgare Root Extract**
Hordeum Vulgare Flower/Leaf/Stem Juice**	Hordeum Vulgare Leaf Powder**	Hordeum Vulgare Sprout Extract**
Hordeum Vulgare Juice**	Hordeum Vulgare Leaf/Stem Powder**	Hordeum Vulgare Stem Water**

***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
Aminopropyl Dimethicone
Amodimethicone
Amodimethicone Hydroxystearate*
Behenoxy Dimethicone
C20-24 Alkyl Dimethicone
C20-24 Alkyl Methicone*
C24-28 Alkyl Dimethicone*
C24-28 Alkyl Methicone
C26-28 Alkyl Dimethicone
C26-28 Alkyl Methicone*
C30-45 Alkyl Dimethicone
C30-45 Alkyl Methicone
C30-60 Alkyl Dimethicone*
C32 Alkyl Dimethicone*
Capryl Dimethicone
Caprylyl Methicone
Cetearyl Methicone
Cetyl Dimethicone
Dimethicone
Dimethoxysilyl Ethylenediaminopropyl Dimethicone
Hexyl Dimethicone
Hexyl Methicone*
Hydroxypropyldimethicone*
Methicone
Stearamidopropyl Dimethicone*
Stearoxy Dimethicone
Stearyl Dimethicone
Stearyl Methicone
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
Aluminum Iron Calcium Magnesium Germanium Silicates*
Aluminum Iron Calcium Magnesium Zirconium Silicates*
Aluminum Iron Silicates*
Aluminum Silicate
Ammonium Silver Zinc Aluminum Silicate
Calcium Magnesium Silicate*
Calcium Silicate
Lithium Magnesium Silicate
Lithium Magnesium Sodium Silicate
Magnesium Aluminometasilicate
Magnesium Aluminum Silicate
Magnesium Silicate
Magnesium Trisilicate*
Potassium Silicate
Pyrophyllite*
Sodium Magnesium Aluminum Silicate*
Sodium Magnesium Silicate
Sodium Metasilicate
Sodium Potassium Aluminum Silicate
Sodium Silicate
Sodium Silver Aluminum Silicate*
Zinc 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) Extract
Saccharum Officinarum (Sugarcane) Juice 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 Bud Extract*
Rosa Damascena Extract
Rosa Damascena Flower
Rosa Damascena Flower Extract
Rosa Damascena Flower Oil
Rosa Damascena Flower Powder
Rosa Damascena Flower Water
Rosa Damascena Flower Water 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 Announcements

For these insufficient data announcements, interested persons are given an opportunity to comment, provide information and/or request an oral hearing before the Panel. Information may be submitted without identifying the source or the trade name of the cosmetic product containing the ingredient. All unpublished data submitted to CIR will be discussed in open meetings, and are available for review by any interested party. Please submit data and/or comments to CIR ***as soon as possible, but no later than November 16, 2021, for full consideration****.* ***Submissions received thereafter might not be considered by the Panel at their next meeting.*** *These reports may be scheduled for review by the Panel as soon as the* ***December 6-7, 2021*** *meeting.*

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

The Panel issued an IDA for these 4 glyceryl acrylate ingredients. (Glyceryl Polyacrylate was added to the original group of 3 glyceryl acrylates on the basis of chemical similarity.)

Glyceryl Acrylate/Acrylic Acid Copolymer	Glyceryl Polyacrylate
Caprylyl Glycol/Glycerin/Polyacrylic Acid Copolymer	Glyceryl Polymethacrylate

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

Glyceryl Acrylate/Acrylic Acid Copolymer, Caprylyl Glycol/Glycerin/Polyacrylic Acid Copolymer, and Glyceryl Polyacrylate

- Method of manufacture

Glyceryl Acrylate/Acrylic Acid Copolymer, Caprylyl Glycol/Glycerin/Polyacrylic Acid Copolymer, Glyceryl Polyacrylate, and Glyceryl Polymethacrylate

- 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 Extract
Hydrolyzed Yeast Protein	Yeast 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	Silver Copper Zeolite	Zeolite
Gold Zeolite	Titanium 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

158th Meeting Notes

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 5500 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 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
For cause	
Basic Yellow 87	**29**
Per FOU	
Sodium Acetylated Hyaluronate	**304**
Hydrolyzed Hyaluronic Acid	**265**
Polyhydroxystearic Acid	**237**
Diphenylsiloxy Phenyl Trimethicone	**234**
Trisodium Ethylenediamine Disuccinate	**202**
Charcoal Powder	**221**
Zanthoxylum Piperitum Fruit Extract	**216**
Pyridoxine HCl	**195**

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.

Scientific Literature Reviews

The following Scientific Literature Reviews(SLRs), and SLR Notices to Proceed (NTP), are posted at the CIR website, or are currently under development and may be posted imminently. (An NTP is prepared when an intensive search of the published information results in insufficient data to justify preparation of a formal SLR.) These may then be presented to the Panel for their review (as Draft Reports) during the next few meetings.

- Acrylamide/Acrylate Copolymers (NTP)
- Charcoal ingredients
- Diphenylsiloxy Phenyl Trimethicone family
- Fatty Esters End-Capped Alkoxylates (NTP)
- Fatty Ethers
- Glucosamines
- Hyaluronates
- Hydroxyacetophenone
- *Olea europaea* (olive)-Derived Ingredients
- Phytosteryl Glutamates
- Polyhydroxystearic Acid
- Radish Root-Derived Ingredients (NTP)
- *Rosa centifolia*-Derived Ingredients
- Sodium Lauroamphoacetate
- Starch Phosphates
- *Zingiber officinale* (ginger)-derived ingredients

Next Expert Panel Meeting

Monday and Tuesday, December 6-7, 2021, to be held virtually via Microsoft Teams.
Please submit a request for an invitation prior to the meeting if you would like to attend. The link will be available approximately a month before the meeting and will be found on the 159th meeting page of the CIR website. https://www.cir-safety.org/