Post Meeting Announcement

Expert Panel for Cosmetic Ingredient Safety
159th Meeting (December 6-7, 2021) - Findings

December 10, 2021

● Final Safety Assessments

- **Silicates – 24 ingredients – Split (24 safe with qualifications, except insufficient for potential inhalation)**
- **Basic Yellow 57 – 1 ingredient – Safe as a hair dye**
- **Diacetone Alcohol – 1 ingredient – Safe**
- ***Saccharum officinarum* (Sugarcane) – 4 ingredients – Safe**
- ***Equisetum arvense* – 5 ingredients – Safe**

● Tentative Safety Assessments

- **Methicones – 30 ingredients – Safe with qualifications**
- ***Salvia officinalis* (Sage) – 12 ingredients – Split (6 safe with qualifications; 6 insufficient)**
- **Radish Root – 7 ingredients – Safe with qualifications**
- **Acryloyloxyethyl Phosphorylcholine – 8 ingredients – Safe**
- **Acrylamide/Acrylate Copolymers – 16 ingredients – Safe**

● Insufficient Data Announcements

- **Barley – 16 ingredients**
- **Zeolites – 6 ingredients**
- **Fatty Ester End-Capped Alkoxylates 14 – ingredients**
- **Fatty Ethers (e.g., Dicaprylyl Ether) – 8 ingredients**
- ***Portulaca oleracea* – 4 ingredients**
- **Glucosamine – 4 ingredients**
- ***Zingiber officinale* (Ginger) – 9 ingredients**

● 159th Meeting Notes

- **Director's Report**
- **Methacrylate Ester Monomers – Re-Review**
- **Inhalation Document**
- **MCI/MI Request - Response**
- **Scientific Literature Reviews – available or under development**
- **Next Expert Panel Meeting – Monday and Tuesday, March 7-8, 2022**

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 Unpublished data cited as references in CIR safety assessments are available for review.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.

Silicates

The Expert Panel for Cosmetic Ingredient Safety (Panel) issued a Final Amended Report with the conclusion that the following 24 silicate ingredients are safe in cosmetics in the present practices of use and concentration described in the 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.

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 is of the understanding 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 inhalation, in the absence of composition/impurities data or negative repeat-dose inhalation toxicity data.

Basic Yellow 57

The Panel issued a Final 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 described in the safety assessment. 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 absorbs slowly through the skin, is not genotoxic, 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 of use and concentration in hair dye formulations.

Diacetone Alcohol

The Panel issued a Final Report with the conclusion that Diacetone Alcohol is safe in cosmetics in the present practices of use and concentration described in the safety assessment. The safety of this ingredient is supported by the available systemic toxicity and dermal irritation/sensitization data. Safety is further supported by low concentrations of use.

According to 2021 VCRP data, Diacetone Alcohol is reported to be used in 107 nail formulations (uses were not reported in any other product category in the VCRP). However, the results of a concentration of use survey conducted by the Council in 2019 indicate that Diacetone Alcohol is used in several different product categories. The highest leave-on use concentration resulting in dermal contact is reported to be 0.25% in "other" eye makeup preparations, and the highest rinse-off concentration is reported to be 9.2% in rinse-off shaving products.

***Saccharum officinarum* (Sugarcane)**

The Panel issued a Final Report with the conclusion that following 4 ingredients are safe in cosmetics in the present practices of use and concentrations described in the safety assessment. The safety of these ingredients was supported by available oral toxicity, genotoxicity, carcinogenicity, and irritation/sensitization data, as well as low concentrations of use.

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. If this ingredient were 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.*

According to 2021 VCRP data, the ingredient with the most reported uses, Saccharum Officinarum (Sugarcane) Extract, is reported to be used in 211 formulations (121 of which are leave-on formulations). The results of concentration of a use survey conducted by the Council indicate Saccharum Officinarum (Sugarcane) Extract also has the highest concentration of use; it is used at up to 2.4% in foot powders and sprays.

Equisetum arvense

The Panel issued a Final Report with a conclusion stating that the following 5 *Equisetum arvense*-derived ingredients are safe in cosmetics in the present practices of use and concentration described in the safety assessment.

Equisetum Arvense Extract
Equisetum Arvense Juice*

Equisetum Arvense Leaf Extract | Equisetum Arvense Powder
Equisetum Arvense Leaf Powder*

**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.

Tentative Safety Assessments

For the tentative safety assessments listed below, to be posted on the CIR website at www.cir-safety.org in the near future, 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* ***March 7-8, 2022*** *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* ***June 2022*** *meeting.*

Methicones

The Panel issued a Revised Tentative Amended Report, with a split conclusion, for these 30 ingredients. Specifically, the Panel concluded that these ingredients are 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 data are insufficient to support the safety of products containing these ingredients when applied via airbrush technology.

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

At the September 2021 meeting, the Panel was presented with the possibility that other spray products (such as deodorant and hair sprays) may be in the respirable range, and could therefore be incidentally inhaled. At the December 2021 meeting, the Panel felt that these concerns regarding incidental inhalation are mitigated, after considering data on particle size distributions for these products, duration of exposure, updates to the Respiratory Resource document, a lack of toxicity in a short-term inhalation study, and an overall favorable toxicological profile for this ingredient group. However, the Panel noted that, in addition to particle size distribution, other information is still needed to make a determination of safety for the use of these ingredients in products delivered via airbrush technology, including: dose, chemistry, duration of exposure, particle volume and density, and details regarding the mode/device used for application of the cosmetic. Thus, the Panel deemed the available data insufficient to make a determination of safety for this product category.

***Salvia officinalis* (Sage)**

The Panel issued a Tentative Report for public comment with the split conclusion that the following 6 (of 12) *Salvia officinalis* (sage)-derived ingredients are safe in cosmetics in the present practices of use and concentration described in the safety assessment when formulated to be non-sensitizing:

Salvia Officinalis (Sage) Leaf	Salvia Officinalis (Sage) Leaf Oil	Salvia Officinalis (Sage) Leaf Water
Salvia Officinalis (Sage) Leaf Extract	Salvia Officinalis (Sage) Leaf Powder	Salvia Officinalis (Sage) Oil

The Panel discussed that most of these ingredients are derived from the leaf, and subsequently have GRAS status, mitigating systemic toxicity concerns. The Panel acknowledged that constituents with the highest potential for sensitization are found in the leaf and oil ingredients, and accordingly, identified the need for manufacturers and cosmetic formulators to avoid reaching levels of plant constituents that may cause sensitization or adverse aggregate exposures.

However, the Panel also concluded that the available data are insufficient to make a determination that the following 6 *Salvia officinalis* (sage)-derived ingredients are safe under the intended conditions of use in cosmetic formulations:

Salvia Officinalis (Sage) Extract	Salvia Officinalis (Sage) Flower/Leaf/Stem Juice	Salvia Officinalis (Sage) Root Extract
Salvia Officinalis (Sage) Flower/Leaf/Stem Extract	Salvia Officinalis (Sage) Flower/Leaf/Stem Water	Salvia Officinalis (Sage) Water

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

- 28-day dermal toxicity data for the Salvia Officinalis (Sage) Flower/Leaf/Stem Extract, Salvia Officinalis (Sage) Root Extract, or for the whole plant
    - depending on the results of the study, additional toxicity data may be needed

Radish Root

The Panel issued a Tentative Report for public comment with a conclusion that these 7 radish root-derived ingredients are safe in cosmetics in the present practices of use and concentration described in the safety assessment when formulated to be non-sensitizing:

Lactobacillus/Radish Root Ferment Extract Filtrate*
Lactobacillus/Radish Root Ferment Filtrate
Leuconostoc/Radish Root Ferment Filtrate
Leuconostoc/Radish Root Ferment Lysate Filtrate*
Raphanus Sativus (Radish) Root Extract
Raphanus Sativus (Radish) Root Juice*
Raphanus Sativus (Radish) Root Powder*

**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 considered that the root portion of the *Raphanus sativus* plant is consumed as food, and that foods fermented with lactic acid and the Leuconostoc bacterial strains have GRAS status, mitigating any systemic or dermal toxicity concerns. The Panel discussed data suggesting the potential for a root juice and a methanolic root extract of *Raphanus sativus* to cause skin-lightening, and concluded that the use concentrations of these ingredients in cosmetics are too low, and not purified or potent enough to produce a skin-lightening effect; the Panel also acknowledged that skin lightening is considered to be a drug effect, and should not occur during the use of cosmetic products. Additionally, the Panel acknowledged the need for manufacturers and cosmetic formulators to avoid reaching levels of plant constituents that may cause sensitization or adverse aggregate exposures.

Acryloyloxyethyl Phosphorylcholine

The Panel issued a Tentative Report for public comment with a conclusion stating that the following 8 acryloyloxyethyl phosphorylcholine polymers are safe in cosmetics in the present practices of use and concentration described in the safety assessment.

Acrylic Acid/Phosphorylcholine Glycol Acrylate Crosspolymer
C4-18 Alkyl Methacrylate/Methacryloyloxyethyl Phosphorylcholine Copolymer*
Hydroxyethylcellulose/Phosphorylcholine Glycol Acrylate Copolymer*
Phosphorylcholine Glycol Methacrylate/PEG-10 dimethacrylate Crosspolymer*
Polyphosphorylcholine Glycol Acrylate
Polyquaternium-10/Phosphorylcholine Glycol Acrylate Copolymer*
Polyquaternium-51
Polyquaternium-61

**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 considered the available data to be adequate for determining safety. It was noted that the data provided indicate that Phosphorylcholine Glycol Acrylate, Polyquaternium-51, and Polyquaternium-61 are high molecular weight polymers. In the absence of molecular weight data on the remaining 5 acryloyloxyethyl phosphorylcholine polymers in this safety assessment, the expectation is that their molecular weights are comparable. The only skin penetration data in this report (which indicate a lack of penetration) are on poly(2-methacryloyloxyethyl phosphorylcholine-co-n-butyl methacrylate), which is considered by the Panel to be a sufficient read-across source chemical for Polyquaternium-51. Furthermore, the Panel agrees that these skin penetration data essentially eliminate the need for systemic toxicity data (i.e., subchronic/chronic toxicity, carcinogenicity, and reproductive/developmental toxicity data) on the acryloyloxyethyl phosphorylcholine polymers. It was also noted that the absence of structural alerts for genotoxicity in these polymers obviates the need for genotoxicity data.

The chemical characterization data provided include information on the residual monomer content of Polyquaternium-51 (100 ppm max, for butyl methacrylate), and the Panel noted the sensitization potential of butyl methacrylate. However, because the method of manufacture of amphiphilic block copolymers based on poly(2-acryloyloxyethyl phosphorylcholine) involves purification (dialysis and rinsing) of the final product, the Panel agreed that residual monomer content is not a major concern. Additionally, the volatility of acrylate and methacrylate monomers was considered, and supports the lack of concern over monomer content. In addition to the issue of monomer-induced sensitization potential, the issue of skin sensitization potential of acryloyloxyethyl phosphorylcholine polymers was also addressed. The Panel noted that the absence of skin penetration mitigates concern over the skin irritation/sensitization potential of these polymers. Furthermore, the absence of skin sensitization potential was confirmed in a human repeated insult patch test on a serum containing 0.12% Polyquaternium-51, a guinea pig maximization test on Polyquaternium-51 at challenge concentrations up to 100%, and a guinea pig adjuvant and patch test on Polyquaternium-61 at a challenge concentration of 25%.

Acrylamide/Acrylate Copolymers

The Panel issued a Tentative Report for public comment with the conclusion that the following 16 acrylamide/acrylate copolymer ingredients are safe in cosmetics in the present practices of use and concentration described in the safety assessment.

Acrylamide/Ammonium Acrylate Copolymer
Acrylamide/Sodium Acrylate Copolymer
Acrylates/Acrylamide Copolymer
Acrylates/t-Butylacrylamide Copolymer
Acrylates/Methacrylamide Copolymer
Acrylates/Octylacrylamide Copolymer
AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer
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
Corn Starch/Acrylamide/Sodium Acrylate Copolymer
Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer
Dimethylacrylamide/Lauryl Methacrylate Copolymer
Potassium Acrylates/Acrylamide Copolymer
Sodium Acrylate/Hydroxyethyl Acrylamide Copolymer
Starch/Acrylates/Acrylamide Copolymer

Formulators utilizing these ingredients should ensure that the concentration of acrylamide monomer in cosmetic formulations does not exceed 5 ppm. The Panel determined that the available manufacturing, composition and impurities, systemic toxicity, and dermal irritation and sensitization data are sufficient to support the safety of these ingredients. Safety is further supported by the large molecular weights of these ingredients, which precludes dermal absorption. The Panel noted the use of these ingredients in aerosolized and pump spray hair products, and determined that the potential for inhalation toxicity following exposure to these products was unlikely due to low concentrations of use, a lack of systemic toxicity, and large, irrespirable molecule sizes.

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 February 8, 2022, 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* ***March 7-8, 2022*** *meeting.*

Barley

The Panel issued an Insufficient Data Announcement (IDA) for these 16 barley-derived ingredients.

Hordeum Distichon (Barley) Extract	Hordeum Vulgare Leaf Juice	Hordeum Vulgare Seed Flour
Hordeum Distichon (Barley) Seed Flour	Hordeum Vulgare Leaf Powder	Hordeum Vulgare Seed Water
Hordeum Vulgare Extract	Hordeum Vulgare Leaf/Stem Powder	Hordeum Vulgare Sprout Extract
Hordeum Vulgare Flower/Leaf/Stem Juice	Hordeum Vulgare Powder	Hordeum Vulgare Stem Water
Hordeum Vulgare Juice	Hordeum Vulgare Root Extract	
Hordeum Vulgare Leaf Extract	Hordeum Vulgare Seed Extract	

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

- Clarification of the plant parts used to make the whole plant extracts Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract
- Method of manufacturing for Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract
- Composition and impurities data for Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract
- 28-day dermal toxicity data on the whole plant extract Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract
    - If positive, additional data, such as developmental and reproductive toxicity and genotoxicity data, may be needed
    - Alternatively, acceptable evidence of safe use as food for ingredients derived from the flower, leaf, stem, and root
- Dermal irritation and sensitization data for Hordeum Leaf Extract or other leaf ingredients

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:

- Maximum use concentration for both mined and synthetic zeolites
- Method of manufacturing and/or source data for Ammonium Silver Zeolite, Gold Zeolite, Silver Copper Zeolite, Titanium Zeolite, and Zinc Zeolite
- Chemical characterization, including specific framework(s), and composition and impurities data for mined Zeolite, Ammonium Silver Zeolite, Gold Zeolite, Silver Copper Zeolite, Titanium Zeolite, and Zinc Zeolite
    - Depending on composition, additional toxicity data may be needed
- The range of particle sizes that is used in spray and powder formulations
- Human dermal irritation and sensitization data at maximum use concentrations

Fatty Ester End-Capped Alkoxylates

The Panel issued an IDA for these 14 fatty ester end-capped alkoxylates.

PEG/PPG-8/3 Diisostearate	PEG-12 Glyceryl Dimyristate
PEG-15 Butylene Glycol Diisostearate	PEG-12 Glyceryl Dioleate
PEG-10 Glyceryl Diisostearate	PEG-3 Glyceryl Distearate
PEG-15 Glyceryl Diisostearate	PEG-4 Glyceryl Distearate
PEG-20 Glyceryl Diisostearate	PEG-12 Glyceryl Distearate
PEG-30 Glyceryl Diisostearate	PEG-23 Glyceryl Distearate
PEG-60 Glyceryl Diisostearate	PEG-4 Polyglyceryl-2 Distearate

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

- Use concentrations for PEG/PPG-8/3 Diisostearate
- Method and manufacturing for all ingredients except PEG/PPG-8/3 Diisostearate
- Composition and impurities data for all ingredients except PEG/PPG-8/3 Diisostearate

Fatty Ethers (e.g., Dicaprylyl Ether)

The Panel issued an IDA for these 8 fatty ethers.

Cetyl Dimethylbutyl Ether	Didecyl Ether	Dimyristyl Ether
Dicaprylyl Ether	Diisononyl Ether	Distearyl Ether
Dicetyl Ether	Dilauryl Ether	

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

- Method of manufacture data (specific to cosmetic ingredient production) for Dicaprylyl Ether and Distearyl Ether

Portulaca oleracea

The Panel issued an IDA for these 4 *Portulaca oleracea*-derived ingredients:

Portulaca Oleracea Extract	Portulaca Oleracea Juice
Portulaca Oleracea Flower/Leaf/Stem Extract	Portulaca Oleracea Water

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

- 28-day dermal toxicity data at the maximum reported concentration of use for Portulaca Oleracea Extract, preferably in an hydroalcoholic solvent
  - if positive additional toxicity data, such as developmental and reproductive toxicity and genotoxicity data, may be needed
- Clarification on which part(s) of the plant are consumed as a food, and which plant part(s) are used in cosmetics

Glucosamine

The Panel issued an IDA for Acetyl Glucosamine, Glucosamine, Glucosamine HCl, and Glucosamine Sulfate. In order to conclude on safety for these ingredients, the Panel has requested:

- Impurities data on Acetyl Glucosamine
- Dermal irritation and sensitization data on all ingredients at maximum use concentration

The Panel noted the reproductive effects observed in animals following oral ingestion and intraperitoneal injections of Glucosamine, and determined that these effects would not be relevant to cosmetic exposure as these methods of exposure would result in a much higher systemic concentration of Glucosamine compared to dermal cosmetic application. The Panel also noted a lack of inhalation data, but determined that these data are unnecessary as inhalation toxicity following cosmetic exposure to these ingredients would be unlikely due to low concentrations of use and a lack of systemic toxicity. In addition, data included in this report indicate that Acetyl Glucosamine 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. Cosmetic formulators should only use this ingredient in products in a manner that does not cause depigmentation.

***Zingiber officinale* (Ginger)**

The Panel issued an IDA for the following 9 *Zingiber officinale* (ginger)-derived ingredients:

Zingiber Officinale (Ginger) Extract
Zingiber Officinale (Ginger) Leaf Cell Extract
Zingiber Officinale (Ginger) Rhizome Extract
Zingiber Officinale (Ginger) Root
Zingiber Officinale (Ginger) Root Extract
Zingiber Officinale (Ginger) Root Juice
Zingiber Officinale (Ginger) Root Oil
Zingiber Officinale (Ginger) Root Powder
Zingiber Officinale (Ginger) Water

In order to conclude on safety for these ingredients, the Panel requested the following:

- Method of manufacturing, composition, and impurities data on Zingiber Officinale (Ginger) Leaf Cell Extract.
  - if the composition of Zingiber Officinale (Ginger) Leaf Cell Extract notably differs from the composition of the remaining ginger ingredients, systemic toxicity data (28-day dermal toxicity, genotoxicity, developmental/reproductive toxicity, and carcinogenicity data) and dermal irritation/sensitization data would be required
- Dermal irritation and sensitization data on Zingiber Officinale (Ginger) Extract at maximum concentrations of use

The Panel noted that information regarding the specific plant parts (e.g., leaves, rhizome) used in the preparation of the whole plant extract (Zingiber Officinale (Ginger) Extract) would help to inform the safety assessment.

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, sadly, this is the last meeting for long-time Senior Scientific Analyst, Wilbur Johnson Jr. Wilbur is one of the most resolute and polite people. That does not mean he always agrees with you. However, that may be one of the best things about Wilbur; he communicates his position very well.

Wilbur obtained a Bachelor of Science in Biology from Morehouse College, and a Masters of Science in Biology from Florida State University. His only job, outside of working for the Library of Congress (Congressional Research Service, Science Policy Research Division), has been at CIR. In his 37 years of stellar service to CIR, he has seen the progression of technology at CIR, from handing off hand-written research papers to administrative typists and the use of microfiche, to using desktop computers, and now to virtual meetings.

Wilbur will be very happy to be able to spend more time with his wife Sigrid (who retired from being a science teacher last year, after 30 years) and his adult children Jared and Ariana. Dr. Heldreth noted that Wilbur is irreplaceable and that he cannot say enough about how much CIR will miss him.

Nevertheless, the work of CIR and the Panel must march on. To that end, beginning with the new year, Priya Cherian will be promoted to Senior Scientific Analyst, which she so definitely deserves. In addition to Priya's excellent work at CIR, she is working on her Masters of Science in Clinical Toxicology. Also, a new Scientific Analyst, Regina Tucker, will start in the new year. Regina is also working on her Masters of Science, but in Skin Biology.

Methacrylate Ester Monomers

The Panel determined that the published final report on methacrylate ester monomers should not be reopened and that the original conclusion on these ingredients remains valid. It was agreed that an updated search of the published literature did not reveal toxicity data that warrant re-evaluation of the safety of these ingredients in cosmetic products.

Inhalation Document

The Panel reviewed a revised Inhalation Resource Document, and agreed it should replace the current version at the CIR website (https://www.cir-safety.org/cir-findings); the previous version was approved by the Panel at the September 2019 meeting. (This document will replace the 2019 version after a few editorial

changes are made.) The Panel agreed that the CIR Resource Document – Respiratory Exposure to Cosmetic Ingredients would be a living document, that would evolve and incorporate emerging data for evaluating inhalation safety of ingredients.

At the September 2021 meeting, the Panel discussed the particle size distribution of diverse aerosol sprays, in consideration of prolonged duration of nanomaterial exposures in sprayable applications. Per the Panel's request, this resource document has been updated to incorporate new data on characterization of deposited dose of inhalable aerosols released from nano-enabled cosmetics, and consequently, to address the health challenges associated with usage of relevant sprayers.

At this current meeting, the Panel further discussed the potential inhalation risks resulting from the aerosolization of common nano-enabled cosmetics. The Panel re-emphasized that while particle/droplet size is an important parameter, the physicochemical properties of ingredients in a spray formulation, the systemic and local (e.g., lung and skin) toxicity, as well as the realistic exposure factors under in-use conditions (e.g., exposure estimates incorporating spray product use levels and ingredient concentrations, exposure duration and frequency, and adjusted for particle/droplet deposition in human lung airways) also play significant roles in evaluating inhalation safety of ingredients in spray formulations. When spray parameters are insufficient to support a robust inhalation exposure assessment, the Panel would request additional information from Industry and further evaluate the sufficiency of other exposure and toxicity data on a case-by-case basis. The Panel agreed to incorporate sample calculations via a tiered approach to assess inhalation safety of cosmetic products, which were submitted by the CIR Science and Support Committee (CIR SSC) in the memo dated October 30, 2018. In addition, the Panel requested further clarification on current federal regulations regarding the categorization and safety management of consumer products applied with airbrush technologies.

MCI/MI Re-Open Request - Reply

A letter was received from Women's Voices for the Earth (WVE), requesting that the Panel re-open the safety assessment report on the combination use of Methylchloroisothiazolinone/Methylisothiazolinone (MCI/MI). However, this request is denied. The following is the Panel's rationale for not re-opening this report.

First and foremost, it is important to note that there are numerous other sources for sensitization, particularly to these ingredients, like paints and household cleansers and detergents (which are not the purview of this Panel) that are not labeled, and that the WVE is not taking these other sources for sensitization into consideration. Cosmetics are labeled, and consumers allergic to these ingredients can avoid exposure by avoiding products labeled as such. Cosmetic formulators can protect all other consumers from sensitization induction (i.e., becoming allergic) by formulating based on the Panel's most recent conclusions on MCI/MI, and MI by itself. Additionally, while the data submitted by WVE (original data came from North American Contact Dermatitis Group) indicate increasing sensitization incidence in the United States in recent years, it should be noted the incident rates of positive patch test were reported in diseased populations instead of general population, which were subjected to relatively high level of exposure, i.e., 2000 ppm for MI and 200 ppm for MCI/MI.

The Panel agreed that in the last few years, the available data made it apparent that their previous conclusion made in 2005 warranted re-review. Firstly, since that time, it had become apparent that these ingredients are more potent than previously understood. Perhaps more importantly, however, the Panel began to appreciate that induction of sensitization can be very dependent not only on final formulation concentration, but on how that formulation is used (such as on shaved underarms versus palms versus other body sites). Thus, the Quantitative Risk Assessment (QRA) was developed in 2008 and further refined into the QRA 2.0. The Panel chose to follow this plan of assessing risk (and utilizing newer methods for sensitization screening), instead of eliminating another preservative from the ever-shrinking universe of preservatives.

If cosmetics are not preserved, consumers may be put at risk of returning to the dark days when mascaras were causing blindness because of microorganism contamination. Furthermore, when potent preservatives (such as MCI/MI) are removed from the market, less potent ones (such as Phenoxyethanol) must be used instead. Unfortunately, that means these less potent preservatives must be used at much higher concentrations to be effective. At those higher concentrations, those preservatives are much more likely to induce sensitization (and thus, ultimately be banned if a risk-based approach is not taken). Preservatives such as MCI/MI can be safely formulated in finished cosmetic products, by adhering to the Panel's most recent conclusions.

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.

- Basic Yellow 87
- Charcoal ingredients
- Diphenylsiloxy Phenyl Trimethicone
- Hyaluronates
- Hydroxyacetophenone
- *Olea europaea* (Olive)-derived Ingredients
- Phytosteryl Glutamates
- Polyhydroxystearic Acid
- *Rosa centifolia*-derived Ingredients
- Sodium Lauroamphoacetate
- Starch Phosphates
- *Zanthoxylum piperitum* – derived ingredients

Next Expert Panel Meeting

Monday and Tuesday, March 7-8, 2022, 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 160th meeting page of the CIR website. https://www.cir-safety.org/