Post Meeting Announcement

Cosmetic Ingredient Review Expert Panel
152nd Meeting (September 16-17, 2019) - Findings

September 20, 2019

● Final Safety Assessments

- **Silica & Hydrated Silica – 2 ingredients – Safe with qualifications**
- **Parabens – 21 ingredients – Split conclusion (20 safe with qualifications; 1 insufficient)**
- **Brown Algae – 82 ingredients – Split conclusion (68 safe; 14 insufficient)**

● Tentative Safety Assessment

- **Mannitol, Sorbitol, & Xylitol – 3 ingredients – Safe**
- **MCI/MI – 2 ingredients (1 mixture) – Split conclusion (safe with qualifications; insufficient for inhalation)**
- **Pomegranate – 18 ingredients – Insufficient**
- **Alkyl Amide MIPA - 14 ingredients – Safe with qualifications**
- **Capryloyl Salicylic Acid – 1 ingredient – Insufficient**
- **Palm (açaí & juçara) - 8 ingredients – Split conclusion (3 safe with qualifications; 5 insufficient)**

● Insufficient Data Announcements

- **Adenosine – 5 ingredients**
- **Wheat – 27 ingredients**
- **Scutellaria – 4 ingredients**

● Re-Reviews

- **Quaternium-18 & Quaternium-18 Bentonite – re-open**
- **Sodium Naphthalenesulfonate & Sodium Polynaphthalenesulfonate – do not re-open**
- **Isopropyl Lanolate – do not re-open**
- **Sulfites –re-open**

● 152nd Meeting Notes

- **Director's Report**
- **Respiratory Exposure Resource Document**
- **Re-Review Summaries**
  - **Acetyl Trialkyl Citrates**
  - **BHT**
  - **Imidazolidinyl Urea**
  - **EDTA**
- **Scientific Literature Reviews – under development**
- **Next Expert Panel Meeting – Monday and Tuesday, December 9-10, 2019**

Final Safety Assessments

Final safety assessments will be posted on the 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 Unpublished data cited as references in CIR safety assessments are available for review.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 CIR Expert Panel to amend the safety assessment.

Silica & Hydrated Silica

The Panel issued a final amended report with the conclusion that synthetically-manufactured amorphous Silica and Hydrated Silica are safe in the present practices of use and concentration described in the safety assessment when formulated to be non-irritating.

The Panel emphasized that this report applies to the safety of synthetically-manufactured amorphous Silica and Hydrated Silica only. Crystalline silica is not toxicologically similar to synthetically-manufactured amorphous silica and would need to be reviewed separately, if used in cosmetics.

The Panel reviewed the current safety test data on synthetically-manufactured amorphous Silica and Hydrated Silica and determined that these two ingredients do not pose an inhalation risk. The concentrations that were tested in inhalation studies were at much higher concentrations than those found in cosmetics and yet had very few adverse effects. The carcinogenicity study used such high concentrations of Silica that the noted effects on the lymph nodes were due to the load on the animal system; incidental inhalation of Silica in cosmetics is not a concern.

Additionally, the Panel moved 22 silicate ingredients from this report to be reviewed at a later date with other silicate ingredients that are determined to be naturally sourced (i.e. mined), including clay materials, zeolites, and any other similar ingredients that are mined. Currently, the data on those ingredients are insufficient to support the determination of safety. The additional data needed for those ingredients comprise at least:

- Chemical characterization (structure), composition (including degree and % of crystallinity), and impurities data
- Method of manufacturing and/or source data
    - Depending on the information provided, additional data on toxicological endpoints may be needed

Parabens

The Panel issued a final amended report with the conclusion that the following 20 alkyl parabens are safe in the present practices of use and concentration described in the safety assessment when the sum of paraben concentrations in the final formulation does not exceed 0.8%.

Butylparaben	Methylparaben	Potassium Propylparaben*	Sodium Isopropylparaben*
Calcium Paraben*	Potassium Butylparaben*	Propylparaben	Sodium Methylparaben
Ethylparaben	Potassium Ethylparaben*	Sodium Butylparaben	Sodium Paraben
Isobutylparaben	Potassium Methylparaben*	Sodium Ethylparaben	Sodium Propylparaben
Isopropylparaben	Potassium Paraben*	Sodium Isobutylparaben	4-Hydroxybenzoic Acid*

**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.*

However, the Panel concluded that the available data are insufficient to determine the safety of Benzylparaben. (This ingredient is not reported to be in use.) The data needed to determine the safety of this ingredient comprise a no-observed-adverse-effect-level (NOAEL) derived from developmental and reproductive toxicity (DART) studies.

Because of the extensive metabolism of parabens, the Panel determined that safety data for one of these alkyl parabens can be used to support the safety of the other alkyl parabens. Indeed, the Panel clarified that studies appearing to report high levels of paraben dermal penetration were instead demonstrating high levels of a metabolite (4-Hydroxybenzoic Acid (i.e. not an actual paraben)).

The Panel further noted that the constant influx of newly published associative studies seems to indicate that epidemiological research is ongoing, and may be for some time. Thus, the Panel proposed the continued tracking of this research and the formulation of a resource document in which these new studies can be considered periodically.

Brown Algae

The Panel issued a final report with the conclusion that 68 of the 82 brown algae-derived ingredients reviewed are safe in the present practices of use and concentration described in the safety assessment.

Agarum Cribrosum Extract	Himanthalia Elongata Powder*
Alaria Esculenta Extract	Hizikia Fusiforme Extract*
Ascophyllum Nodosum Extract	Hizikia Fusiformis Callus Culture Extract*
Ascophyllum Nodosum Powder	Hizikia Fusiformis Water*
Ascophyllum Nodosum*	Hydrolyzed Ecklonia Cava Extract*
Cladosiphon Okamuranus Extract	Hydrolyzed Fucus Vesiculosus Extract*
Cystoseira Amentacea/Caespitosa/Branchycarpa Extract*	Hydrolyzed Fucus Vesiculosus Protein*
Cystoseira Baccata Extract*	Laminaria Cloustoni Extract
Cystoseira Compressa Extract*	Laminaria Diabolica Extract*
Cystoseira Compressa Powder*	Laminaria Digitata Extract
Cystoseira Tamariscifolia Extract*	Laminaria Digitata Powder
Dictyopteris Polypodioides Extract	Laminaria Japonica Extract
Ecklonia Cava Extract*	Laminaria Hyperborea Extract
Ecklonia Cava Water*	Laminaria Japonica Powder*
Eisenia Arborea Extract*	Laminaria Longissima Extract*
Fucus Serratus Extract	Laminaria Ochroleuca Extract
Fucus Spiralis Extract*	Laminaria Saccharina Extract
Fucus Vesiculosus	Macrocystis Pyrifera (Kelp)
Fucus Vesiculosus Extract	Macrocystis Pyrifera (Kelp) Blade/Pneumatocyst/Stipe Juice Extract*
Fucus Vesiculosus Powder	Macrocystis Pyrifera (Kelp) Extract
Halidrys Siliquosa Extract	Macrocystis Pyrifera (Kelp) Juice*
Halopteris Scoparia Extract*	Macrocystis Pyrifera (Kelp) Protein
Himanthalia Elongata Extract	Nereocystis Luetkeana Extract

Pelvetia Canaliculata Extract
Phyllacantha Fibrosa Extract*
Saccharina Angustata Extract*
Saccharina Japonica Extract*
Saccharina Longicruris Extract
Sargassum Filipendula Extract
Sargassum Muticum Extract
Sargassum Fulvellum Extract
Sargassum Fusiforme Extract
Sargassum Glaucescens Extract*
Sargassum Horneri Extract*
Sargassum Pallidum Extract*
Sargassum Siliquastrum Extract*
Sargassum Thunbergii Extract*
Sargassum Vulgare Extract
Sphacelaria Scoparia Extract
Undaria Peterseniana Extra
Undaria Pinnatifida Cell Culture Extract*
Undaria Pinnatifida Extract
Undaria Pinnatifida Leaf/Stem Extract
Undaria Pinnatifida Powder
Undaria Pinnatifida 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 determined, based on a lack of adverse reactions in their clinical experience and in clinical reports, combined with the historically safe use in foods, that concern for dermal sensitization or irritation resulting from cosmetic exposure to these ingredients is confidently mitigated. In addition, the Panel explained that the compositions of these brown algae are consistent across the different genera, and no allergenic constituents of concern were found therein.

However, the Panel determined there were insufficient data to determine the safety of the remaining 14 ingredients. The insufficiencies include a lack of composition data, use in foods/GRAS status, or sensitization data for these ingredients:

Cladosiphon Novae-Caledoniae Extract**
Cystoseira Balearica Extract**
Cystoseira Caespitosa Extract**
Dictyota Coriacea Extract**
Durvillaea Antarctica Extract
Ecklonia Kurome Extract**
Ecklonia Kurome Powder**
Ecklonia Maxima Extract**
Ecklonia Maxima Powder**
Ecklonia Radiata Extract
Ecklonia/Laminaria Extract**
Lessonia Nigrescens Extract
Lessonia Nigrescens Powder**
Pelvetia Siliquosa Extract**

***Not reported to be in current use.*

Tentative Safety Assessments

*Tentative safety assessments will be posted on the CIR website at www.cir-safety.org on or before **September 27, 2019**. Interested persons are given 60 days from the posting date (**November 26, 2019**) to comment, provide information, and/or request an oral hearing before the CIR Expert 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 26, 2019 for full consideration.** The updated reports may be scheduled for review by the CIR Expert Panel as early as at its **December 9-10, 2019** meeting.*

Mannitol, Sorbitol, & Xylitol

The Panel issued a tentative report for public comment with the conclusion that Mannitol, Sorbitol, and Xylitol are safe in the present practices of use and concentration described in the safety assessment. Positive phototoxicity results were reported for a test material containing Xylitol; however, Xylitol is a chromophorically inert molecule that lacks a UV-visible light-absorbing structure and cannot directly trigger phototoxicity. The Panel noted that it was not clear whether other components of the cream or gel formulations may have contributed to the positive phototoxicity results. In addition, levels of irradiation used in this phototoxicity study were far greater than typical exposure. Two negative phototoxicity results with Mannitol support this interpretation (Mannitol is also void of a chromophore). Thus, the Panel felt that the available data do not indicate a risk of phototoxicity with these ingredients.

The Panel determined, based on a lack of adverse reactions in their clinical experience and in clinical reports, combined with the historically safe use in foods, that irritation data at use concentration were unnecessary to determine safety for this ingredient group. The addition of a negative guinea pig maximization test (GPMT) mitigated the need for sensitization data at maximum use concentrations (as this method of testing utilizes a combination of exposures, including intradermal injections which bypass the stratum corneum). Because the dermal barrier is eliminated in this method of testing, it may be surmised that sensitization studies at higher concentrations would also yield negative results.

Methylchloroisothiazolinone/Methylisothiazolinone (MCI/MI)

The Panel issued a tentative amended report for public comment with the conclusion that the ingredient mixture MCI/MI is safe in cosmetics when formulated to be non-sensitizing, based on the results of a quantitative risk assessment (QRA) or similar methodology; however, at no point should concentrations exceed 7.5 ppm in leave-on products or 15 ppm in rinse-off products. However, the Panel concluded that the data are insufficient to support the safety of MCI/MI in products which may be incidentally inhaled. The Panel requested an inhalation study of at least 3 months in duration that is in accordance with the Organization for Economic Co-operation and Development (OECD) test guideline (TG) 413. This request is in response to reports of adverse events observed in infants following inhalation exposure to humidifier disinfectants that contained this preservative mixture.

The Panel noted the results of a QRA for skin sensitization performed by the CIR Science and Support Committee. The results indicated that some leave-on products comprising MCI/MI at the recommended safe concentration of 7.5 ppm may yet increase the risk of inducing dermal sensitization. In most rinse-off products, 15 ppm MCI/MI was not associated with a potential increased risk of skin sensitization induction. Individuals previously sensitized to MCI/MI should avoid products that contain this ingredient mixture.

Pomegranate

The Panel issued a tentative report for public comment with the conclusion that the data were insufficient to support a determination of safety for the following 18 ingredients:

Punica Granatum Extract
Punica Granatum Bark Extract
Punica Granatum Bark/Fruit Extract
Punica Granatum Callus Culture Extract
Punica Granatum Flower Extract
Punica Granatum Fruit Extract
Punica Granatum Fruit Juice
Punica Granatum Fruit/Root/Stem Powder
Punica Granatum Fruit/Sucrose Ferment Filtrate
Punica Granatum Fruit Water
Punica Granatum Juice Extract
Punica Granatum Leaf Cell Extract
Punica Granatum Peel Extract
Punica Granatum Pericarp Extract
Punica Granatum Seed
Punica Granatum Seed Cell Culture Lysate
Punica Granatum Seed Extract
Punica Granatum Seed Powder

The additional data needed for these cosmetic ingredients are:

- A no-observed-effect-level (NOEL) for skin lightening effects for all ingredients
- Method of manufacturing for the extracts with regard to solvent-type used
- For Punica Granatum Bark Extract, Punica Granatum Bark/Fruit Extract, Punica Granatum Callus Culture Extract, Punica Granatum Flower Extract, Punica Granatum Fruit/Root/Stem Powder, Punica Granatum Leaf Cell Extract, and Punica Granatum Peel Extract
    - Composition and impurities data
    - Systemic toxicity data
    - Dermal irritation and sensitization data

Alkyl Amide MIPA

The Panel issued a tentative report for public comment with the conclusion that the 14 alkyl amide MIPA ingredients named below are safe in cosmetics in the present practices of use and concentration described in the safety assessment when formulated to be non-irritating.

Cocamide MIPA
Coconut Oil MIPA Amides*
Hydroxyethyl Stearamide-MIPA*
Isostearamide MIPA*
Lauramide MIPA
Linoleamide MIPA*
MIPA- Myristate*
Myristamide MIPA*
Oleamide MIPA
Palmamide MIPA*
Palm Kernelamide MIPA*
Peanutamide MIPA*
Ricinoleamide MIPA*
Stearamide MIPA*

**Use not reported in the VCRP and/or concentration of use survey. The expectation is that if used in cosmetic formulations, these ingredients would be used in product categories and at concentrations comparable to those reported for others in this group.*

The ingredients in this group are fatty amides resulting from amidation with MIPA. Accordingly, the Panel specified that these ingredients should not be used in cosmetic products in which *N*-nitroso compounds can be formed.

The alkyl amide MIPA ingredients are primarily used in rinse-off formulations. However, leave-on uses are reported, with 0.4% Oleamide MIPA reported as the highest concentration of use in leave-on formulations. The Panel noted that delayed contact hypersensitivity was reported in a GPMT performed with high concentrations of Oleamide MIPA (75% for topical induction/50% at challenge), but not in GPMTs on Cocamide MIPA (25% at topical induction/5% at challenge) and Isostearamide MIPA (100% at topical induction/1% at challenge). The Panel stated that the sensitization observed with Oleamide MIPA was most likely a result of the high concentrations and a stressing of the system (as this method of testing utilizes a combination of exposures, including intradermal injections which bypass the stratum corneum). Because the Panel felt that it was appropriate to read-across from Cocamide MIPA and Isostearamide MIPA, concern that Oleamide MIPA would be a sensitizer in cosmetic formulations was mitigated. However, the Panel was concerned that the potential exists for dermal or ocular irritation with the use of products formulated with the ingredients named in this assessment. Therefore, the Panel specified that products containing the ingredients listed above must be formulated to be non-irritating.

Published studies were not found, and unpublished data were not submitted, for certain toxicological endpoints on the alkyl amide MIPA ingredients. Nevertheless, because these ingredients are structurally similar to the diethanolamides, the Panel determined that information on diethanolamides of equivalent chain lengths (from a previous CIR report, as well as from European Chemical Agency (ECHA) dossiers) could be used for read-across for the missing data endpoints.

The acyl groups (i.e. fatty acid chain residues) in Peanutamide MIPA are derived from peanut oil. The Panel has previously reviewed the safety of Arachis Hypogaea (Peanut) Oil as used in cosmetics, and discussed therein the relationship between food allergies and exposure to refined oils. Individuals who have food allergies to a plant protein rarely exhibit allergic reactions when exposed to refined oils of the same plant; proteins do not partition into the oil. Additionally, the Panel noted that aflatoxins, which could be associated with peanuts, do not partition into the oil. However, the Panel does caution manufacturers to make certain that Peanutamide MIPA is free from proteins and aflatoxins.

Capryloyl Salicylic Acid

The Panel issued a tentative amended report for public comment with the conclusion that the data are insufficient to support a determination that Capryloyl Salicylic Acid is safe under the intended concentrations of use in cosmetic formulations. The data needs (unchanged from those requested in a June 2019 insufficient data announcement (IDA)) comprise:

- Phototoxicity
- Impurities

Impurities data were not provided; therefore, that data need remains outstanding. Additionally, although phototoxicity data were received, the Panel were not satisfied with the data. In response to the Panel's data requests, the results of an *in vitro* 3T3 neutral red uptake (NRU) phototoxicity test were submitted. The study was performed in accordance with the OECD Guideline for Testing of Chemicals Draft Proposal for a New Guideline (draft document, dated February 2000). According to the evaluation criteria that were used, a test article was considered to be phototoxic in this assay if a marked decrease in cell viability (as measured by

OD540 in the NRU) was observed in the presence of UVA (by comparison with the viability seen in the absence of UVA) such that photo-irritation factors (PIF) values of ≥ 5 were obtained. Furthermore, a test article was considered to be non-phototoxic in this assay if there was no marked decrease in cell viability when cells were exposed to the test article in the absence and presence of UVA, or if similar toxic profiles were observed in the absence and presence of UVA (PIF < 5). The test yielded PIF's of 4 and 2.6 - 1.7 in separate experiments that were performed. Based on these PIF values, the author concluded that, according to the proposed OECD guideline evaluation criteria, Capryloyl Salicylic Acid was not phototoxic in the *in vitro* 3T3 NRU phototoxicity test. However, the Panel noted that, according to OECD Guideline 432 (adopted April 2004), the results of this test are to be interpreted based on the following criteria: a test substance with a PIF of < 2 predicts "no phototoxicity," a PIF of > 2 but < 5 predicts "probable phototoxicity," and a PIF of > 5 predicts "phototoxicity." Thus, the Panel agreed that Capryloyl Salicylic Acid (PIF values of 4 and 2.6 - 1.7) should have been classified as probably phototoxic in the *in vitro* 3T3 NRU phototoxicity test. Furthermore, the Panel agreed that because this test is prone to false positives, additional data would be needed in order to evaluate the phototoxicity potential of Capryloyl Salicylic Acid. The reactive oxygen species test for phototoxicity was mentioned as one of the phototoxicity tests that could be performed to meet this data need.

Additionally, the Panel discussed the issue of skin sensitization potential for this ingredient. Capryloyl Salicylic Acid induced skin sensitization in GPMTs at challenge concentrations of 0.5%, 2%, and 5%, but not at 1%. However, in human repeated insult patch tests (HRIPTs), cosmetic products containing 0.5% or 2% Capryloyl Salicylic Acid were classified as non-sensitizing. After reviewing the HRIPT results, considering that the highest reported maximum use concentration of Capryloyl Salicylic Acid is 0.5% in leave-on cosmetic products, and noting the stressing of the system that occurs in the GPMTs, the Panel concluded that the sensitization potential of exposure to this ingredient via cosmetic use is not a risk.

Palm (açaí & juçara)

The Panel issued a tentative report for public comment with the conclusion that 3 palm tree (açaí)-derived ingredients, Euterpe Oleracea Fruit Extract, Euterpe Oleracea Juice, and Euterpe Oleracea Pulp Powder, are safe in the present practices of use and concentration described in the safety assessment when formulated to be non-sensitizing. The skin sensitization potential of a face and neck product containing 3% Euterpe Oleracea Pulp Powder (the highest maximum use concentration in leave-on products that is reported in this safety assessment) was evaluated in a study involving 214 subjects. Although definite erythema and damage to the epidermis (but no edema) were observed in 1 subject at the 5th induction evaluation, the results were classified as negative. However, 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. Therefore, when formulating products, manufacturers should avoid reaching levels of plant constituents that may cause sensitization or other adverse health effects.

Additionally, the Panel concluded that the available data are insufficient to support a determination that the following 5 palm tree (açaí and jaçara)-derived ingredients are safe under the intended conditions of use in cosmetic formulations:

Euterpe Edulis Fruit Extract	Euterpe Oleracea Palm Heart Extract	Hydrolyzed Euterpe Oleracea Fruit
Euterpe Edulis Juice Extract	Euterpe Oleracea Seed Powder	

The data needs are as follows:

Euterpe Edulis Fruit Extract and Euterpe Edulis Juice Extract

- Method of manufacture
- Skin sensitization

Euterpe Oleracea Seed Powder and Hydrolyzed Euterpe Oleracea Fruit

- Method of Manufacture

Euterpe Oleracea Palm Heart Extract

- Skin irritation and sensitization

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 CIR Expert 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 19, 2019, for full consideration****. These reports may be scheduled for review by the CIR Expert Panel as soon as the* ***December 9-10, 2019*** *meeting.*

Adenosine

The Panel issued an IDA for Adenosine, Adenosine Phosphate, Adenosine Triphosphate, Disodium Adenosine Phosphate, and Disodium Adenosine Triphosphate. In order to conclude on safety, the Panel requested impurities data on all five ingredients. The Panel noted that these ingredients are naturally-occurring, ubiquitous chemicals, but, found impurities data to be necessary as methods of manufacture specific to these cosmetic ingredients are unknown. The Panel also noted the lack of sensitization/irritation data for these ingredients, but decided that the available sensitization/irritation data on Disodium Adenosine Phosphate and Adenosine can be read-across to those ingredients lacking these data.

Wheat

The Panel issued an IDA for the following ingredients:

Triticum Aestivum (Wheat) Flour Lipids	Triticum Spelta Seed Water
Triticum Aestivum (Wheat) Germ Extract	Triticum Turgidum Durum (Wheat) Seed Extract
Triticum Aestivum (Wheat) Leaf Extract	Triticum Vulgare/Aestivum (Wheat) Grain Extract
Triticum Aestivum (Wheat) Peptide	Triticum Vulgare (Wheat) Bran
Triticum Aestivum (Wheat) Seed Extract	Triticum Vulgare (Wheat) Bran Extract
Triticum Monococcum (Wheat) Seed Extract	Triticum Vulgare (Wheat) Bran Lipids
Triticum Monococcum (Wheat) Stem Water	Triticum Vulgare (Wheat) Flour Extract

Triticum Vulgare (Wheat) Flour Lipids
Triticum Vulgare (Wheat) Germ
Triticum Vulgare (Wheat) Germ Extract
Triticum Vulgare (Wheat) Germ Powder
Triticum Vulgare (Wheat) Germ Protein
Triticum Vulgare (Wheat) Gluten
Triticum Vulgare (Wheat) Gluten Extract
Triticum Vulgare (Wheat) Kernel Flour
Triticum Vulgare (Wheat) Protein
Triticum Vulgare (Wheat) Seed Extract
Triticum Vulgare (Wheat) Sprout Extract
Triticum Vulgare (Wheat) Straw Water
Wheat Germ Glycerides

The additional data needed for these cosmetic ingredients are:

- Method of manufacturing, composition, and impurities data for Triticum Aestivum (Wheat) Germ Extract, Triticum Aestivum (Wheat) Seed Extract, Triticum Monococcum (Wheat) Seed Extract, Triticum Turgidum Durum (Wheat) Seed Extract, Triticum Vulgare (Wheat) Germ Extract, Triticum Vulgare (Wheat) Seed Extract, and Triticum Vulgare (Wheat) Sprout Extract
- Dermal irritation and sensitization data at maximum leave-on use concentrations for Triticum Aestivum (Wheat) Germ Extract, Triticum Vulgare (Wheat) Germ Extract, Triticum Vulgare (Wheat) Sprout Extract, and Wheat Germ Glycerides

Scutellaria

The Panel reviewed the safety of the following 4 *Scutellaria baicalensis*-derived ingredients for the first time and issued an IDA.

Scutellaria Baicalensis Extract
Scutellaria Baicalensis Root Extract
Scutellaria Baicalensis Root Powder
Scutellaria Baicalensis Sprout Extract

The following data were requested:

- Genotoxicity (*in vitro* and mammalian); for ingredient extracts, methanol and aqueous extracts should be tested
- Phototoxicity

Scutellaria Baicalensis Root Extract and Scutellaria Baicalensis Root Powder

- An NOAEL for skin pigmentation and anti-inflammatory effects, including the suppression of delayed contact hypersensitivity, is needed

Scutellaria Baicalensis Extract

- Skin irritation and sensitization
- 28-day dermal toxicity; if dermal absorption occurs, additional data may be needed

Scutellaria Baicalensis Sprout Extract

- Method of Manufacture
- Composition
- Impurities
- Dermal absorption; if dermal absorption occurs, additional data may be needed
- Skin irritation and sensitization

The Panel expressed concern over the genotoxicity potential of Scutellaria Baicalensis Root Extract, and possibly other *Scutellaria baicalensis* plant part extracts. In the *Bacillus subtilis* rec-assay (strains H17 Rec+ and M45 Rec-) without metabolic activation, results for the methanol and aqueous extracts of a *Scutellaria baicalensis* root extract were positive and negative, respectively. In the Ames test (*Salmonella typhimurium* strains TA98 and TA100), results for the aqueous extract of a *Scutellaria baicalensis* root extract were positive in strain TA100 with, but not without, metabolic activation. However, results for the methanol extract were negative (with or without metabolic activation) in both bacterial strains in the Ames test. The Panel agreed that the conflicting results for the aqueous and methanol extracts in the 2 *in vitro* assays are inconclusive. Thus, the Panel noted that the *in vitro* assays should be repeated and that genotoxicity should also be evaluated using a mammalian system.

Re-Reviews

Quaternium-18 & Quaternium-18 Bentonite

In 1982, the final report on Quaternium-18 and Quaternium-18 Bentonite was published with the conclusion that these ingredients are safe as cosmetic ingredients in the present practices of use and concentration, as described in that report. In 2003, after considering new studies and updated use data on these ingredients, the Panel published a re-review summary in which it was stated that the Panel determined not to re-open the safety assessment. It should be noted that Quaternium-18 Hectorite, which was included in the 1982 and 2003 documents, was not included in the current re-review because it was recently part of a separate assessment (Safety Assessment of Ammonium Hectorites as used in Cosmetics). The Panel re-opened the safety assessment on Quaternium-18 and Quaternium-18 Bentonite due to a lack of inhalation toxicity data, and requested information on aerosolized Quaternium-18 Bentonite.

Sodium Naphthalenesulfonate and Sodium Polynaphthalenesulfonate

The Panel first reviewed the safety of Sodium Naphthalenesulfonate and Sodium Polynaphthalenesulfonate in a report published in 2003 with the conclusion that these ingredients were “safe as used in cosmetic formulations intended to be applied to the skin. The available data, however, are insufficient to support the safety for use in cosmetic products which may contact mucous membranes or be ingested.” Because it has been at least 15 years since the original review was published, in accord with CIR Procedures, the Panel considered whether the safety assessment of Sodium Naphthalenesulfonate and Sodium Polynaphthalenesulfonate should be re-opened.

The Panel reviewed data that have been published since the original safety assessment, as well as updated frequency and concentration of use data. The frequency of use for Sodium Polynaphthalenesulfonate has decreased since the original review was considered. Uses were neither reported for Sodium Naphthalenesulfonate in the 2003 report, nor in 2019. The Panel determined that there were no new relevant data that informed a new review of this ingredient. Therefore, the Panel reaffirmed the original conclusion, and did not re-open this safety assessment.

Isopropyl Lanolate

The Panel first reviewed the safety of Isopropyl Lanolate in 1980, concluding that "on the basis of the information available, which the Expert Panel believes to have been accumulated in a reasonable manner, it is concluded that Isopropyl Lanolate is safe as currently used in cosmetic products." In 2003, after considering new studies and updated use data, the Panel determined to not re-open the safety assessment. Because it has been at least 15 years since the first re-review summary was published, in accord with CIR Procedures, the Panel again considered whether the safety assessment of Isopropyl Lanolate should be re-opened.

An exhaustive search of the world's literature was performed for studies dated 1995 forward, but no relevant new data were found. The Panel did review updated frequency and concentration of use data. The frequency and maximum concentrations of use have decreased significantly since the initial re-review was considered, and even more so when compared to the use data included in the 1980 assessment. Therefore, the Panel reaffirmed the original conclusion, and did not re-open this safety assessment.

Sulfites

The Panel first reviewed the safety of Sulfites in 2003. The Panel concluded that Ammonium Bisulfite, Ammonium Sulfite, Potassium Metabisulfite, Potassium Sulfite, Sodium Bisulfite, Sodium Metabisulfite, and Sodium Sulfite are safe as used in cosmetic formulations. Because it has been at least 15 years since this report was published, in accordance with CIR Procedures, the Panel considered whether the safety assessment of these 7 ingredients should be reopened. After considering new studies and updated use data on these ingredients, the Panel determined that the safety assessment should be reopened.

The Panel's decision to reopen the safety assessment is based mostly on the following types of toxicity data that have entered the published literature since the final report was issued: genotoxicity (*in vitro* and *in vivo*), dermal sensitization, reproductive toxicity, and enhancement of the allergic response to dust mites. Of particular interest are both the positive *in vivo* and *in vitro* genotoxicity data (mostly on Sodium and Potassium Metabisulfite) that were reviewed. The Panel noted that positive *in vitro*, but not *in vivo*, genotoxicity data are found in the published report.

152nd Meeting Notes

Director's Report

Dr. Heldreth expressed gratitude for the Panel's and other stakeholders' continued support of the Cosmetic Ingredient Review program. He also reported on a vacancy on the CIR Expert Panel and the addition of a new member of the CIR Staff. Regarding the Panel vacancy, CIR is seeking nominations for an expert chemist to join the Marks team as a voting member. In addition to renowned expertise in chemistry and a lack of financial conflicts, nominees should also have expertise in one or more of the following: QSAR, grouping/clustering rationale, read-across, computational predictions, biochemistry (including chemical aspects of ADME), and naturally, synthetic methodology and natural products separations. Nominations may be submitted directly to Dr. Heldreth **no later than the end of this month**. Thereafter, the CIR Steering Committee will select the new Expert Panel member.

Regarding the new staff member at CIR, Dr. Heldreth welcomed Ms. Preethi Raj, CIR's newest Senior Scientific Analyst & Writer. Preethi comes to CIR with some great credentials, including a master's degree in public health from UMass and experience working as an epidemiologist at the National Cancer Institute. Expect to see CIR reports from her starting this December.

Additionally, Dr. Heldreth noted that the CIR Expert Panel, since its inception in 1976, has always comprised a group of world-renowned, independent experts of science and medicine. The CIR Steering Committee recently met to discuss potential steps forward to better highlight, publicly, this Panel's independence. Indeed, the Committee voted and approved a number of advancements, such as a publicly available conflict of interest statement. Dr. Heldreth is working to bring those advancements to bear, in one cohesive package, which will likely be presented sometime in early 2020.

Inhalation – Respiratory Exposure Resource Document

At the December 2018 meeting, the Panel suggested a number of changes to this resource document. At that meeting, the Panel concluded that, while particle/droplet size is an important parameter, the physicochemical properties of ingredients in a spray formulation, as well as the realistic exposure factors under in-use conditions, also play significant roles in evaluating inhalation safety of ingredients in spray formulations. When spray parameters are absent or provide an insufficient basis to support a robust inhalation exposure assessment, the Panel would request additional information from Industry and further evaluate the sufficiency of other exposure data that may be available on a ***case-by-case basis***. All such changes were made to the document, and at this current meeting, the Panel voted to finalize this resource document and publish it to the CIR website. It may now be found under the CIR Findings & Resource Documents tab (https://www.cir-safety.org/cir-findings).

Re-Review Summaries

Acetyl Trialkyl Citrates

The Panel approved the re-review summary of Acetyl Trialkyl Citrates, reaffirming that these ingredients are safe as cosmetic ingredients in the present practices of use and concentration. This conclusion was originally published by CIR in 2002. Limited new data that were identified in the published literature, as well as updated information regarding frequencies of use, provided by the FDA, and maximum use concentrations of use, provided by the Council, were reviewed by the Panel.

BHT

The Panel approved the re-review summary of BHT (Butylated Hydroxytoluene), reaffirming that BHT is safe as used in cosmetic ingredients in the present practices of use and concentration. This conclusion was originally published by CIR in 1999. Limited new data identified in the published literature that have become available since the 1999 report was published, as well as updated information regarding frequencies of use (provided by the FDA) and maximum use concentrations of use (provided by the Council), were reviewed by the Panel.

Imidazolidinyl Urea

The Panel approved the re-review summary of Imidazolidinyl Urea, reaffirming that Imidazolidinyl Urea is safe as used in cosmetic ingredients in the present practices of use and concentration. This conclusion was originally published by CIR in 1980, and reaffirmed in 2001. Limited new data identified in the published literature that have become available since the 2001 re-review, as well as updated information regarding frequencies of use (provided by the FDA) and maximum use concentrations of use (provided by the Council), were reviewed by the Panel.

EDTA

The Panel approved the re-review summary of EDTA and Salts, reaffirming that the following ingredients are safe as cosmetic ingredients in the present practices of use and concentration:

EDTA	TEA-EDTA	HEDTA
Calcium Disodium EDTA	Tetrasodium EDTA	Trisodium HEDTA
Diammonium EDTA	Tripotassium EDTA	
Dipotassium EDTA	Trisodium EDTA	

This conclusion was originally published by CIR in 1998. New data identified in the published literature that have become available since the 1998 report was published, as well as updated information regarding frequencies of use (provided by the FDA) and maximum concentrations of use (provided by the Council), were reviewed by the Panel.

Scientific Literature Reviews

The following Scientific Literature Reviews are posted at the CIR website or are currently under development and may be posted imminently. These may then be presented to the Panel for their review (as Draft Reports) during the next two meetings.

- Acrylate/Acrylamide Copolymers
- Amino Acid Diacetates
- Ascorbyl Glucoside
- Basic Brown 17
- *Carica papaya* (Papaya)-Derived Ingredients
- *Cocos nucifera* (Coconut)-Derived Ingredients
- Diacetone Alcohol
- Honey-Derived Ingredients
- *Hordeum vulgare*-Derived Ingredients
- Levulinic Acid & Sodium Levulinate
- *Melaleuca alternifolia* (Tea Tree)-Derived Ingredients
- Polysilicone-11
- Saccharide Humectants
- Tris(Tetramethylhydroxypiperidinol) Citrate

Next CIR Expert Panel Meeting

Monday and Tuesday, December 9-10, 2019 at the Westin DC City Center Hotel, Washington, DC.
Please contact Carla Jackson (jacksonc@cir-safety.org) before the meeting if you plan to attend.