
Post Meeting Announcement

Expert Panel for Cosmetic Ingredient Safety 157th Meeting (March 11-12, 2021) - Findings

March 17, 2021

- **Final Safety Assessments**

- Tetrasodium Glutamate Diacetate and Beta-Alanine Diacetic Acid – 2 ingredients – Split (1 safe; 1 insufficient)
- Coconut – 11 ingredients – Split (10 safe; 1 insufficient)
- Basic Brown – 1 ingredient – Mixed (safe with qualifications for hair dye uses; insufficient for other uses)
- Papaya – 5 ingredients – Split (4 safe; 1 insufficient)
- Tris(Tetramethylhydroxypiperidinol) Citrate – 2 ingredients – Safe
- Acetyl Hexapeptide-8 Amide – 1 ingredient - Mixed (safe with qualifications; insufficient)
- Benzophenones – 11 ingredients - Safe

- **Tentative Safety Assessments**

- Sodium Isomerate et al. (previously Saccharide Humectants) – 7 ingredients – Safe
- Levulinic Acid – 2 ingredients – Safe with qualifications
- Red Algae – 60 ingredients – Split (11 safe; 49 insufficient)
- Diacetone Alcohol – 1 ingredient – Safe
- Silicates – 24 ingredients – Split (safe/non-inhalation; safe < 0.1% crystalline silica/inhalation; insufficient/airbrush)
- Tea Tree – 8 ingredients – Safe with qualifications

- **Insufficient Data Announcements**

- Sage – 12 ingredients
- Acryloyloxyethyl Phosphorylcholine Polymers – 8 ingredients

- **157th Meeting Notes**

- Director's Report
- Draft Hair Dye Epidemiology document
- Draft 2022 Priorities
- Scientific Literature Reviews – available or under development
- Next Expert Panel Meeting – Monday and Tuesday, September 13-14, 2021

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 Unpublished data cited as references in CIR safety assessments are available for review.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 Expert Panel for Cosmetic Ingredient Safety (Panel) to amend the safety assessment.

Tetrasodium Glutamate Diacetate and Beta-Alanine Diacetic Acid

The Expert Panel for Cosmetic Ingredient Safety (Panel) issued a final report with the conclusion that Tetrasodium Glutamate Diacetate is safe in cosmetics in the present practices of use and concentration described in this safety assessment. However, the Panel concluded that the data were insufficient to make a determination of safety for Beta-Alanine Diacetic Acid. The additional data needed to determine safety for these cosmetic ingredients are:

- Method of manufacturing
- Composition and impurities
- Concentration of use
- Dermal irritation and sensitization data at maximum use concentration
- 28-d dermal toxicity data
 - o If positive, developmental and reproductive toxicity and genotoxicity data

The Panel found that the systemic toxicity data, including developmental and reproductive toxicity studies, acute and subchronic toxicity studies, and dermal irritation and sensitization studies in this report were sufficient for assessing safety for reported cosmetic uses of Tetrasodium Glutamate Diacetate. The Panel noted that Tetrasodium Glutamate Diacetate is slowly absorbed through the gastrointestinal tract; dermal absorption is likely to be even slower. The Panel also noted the lack of carcinogenicity data and was concerned about the report by a supplier that Tetrasodium Glutamate Diacetate may contain a salt of nitrilotriacetic acid, a 2B carcinogen according to the International Agency for Research on Cancer; however, the concern was mitigated by multiple genotoxicity studies that were negative and the low concentrations of use of this ingredient in leave-on products.

Cocos nucifera (Coconut)-Derived Ingredients

The Panel issued a final report with the conclusion that the following 10 *Cocos nucifera* (coconut)-derived ingredients are safe in the present practices of use and concentration described in the safety assessment:

Coconut Flower Sugar*	Cocos Nucifera (Coconut) Fruit/Fruit Juice Extract*
Cocos Nucifera (Coconut) Flower Extract	Cocos Nucifera (Coconut) Fruit Juice
Cocos Nucifera (Coconut) Flower Nectar Extract*	Cocos Nucifera (Coconut) Fruit Powder
Cocos Nucifera (Coconut) Fruit	Cocos Nucifera (Coconut) Fruit Water
Cocos Nucifera (Coconut) Fruit Extract	Cocos Nucifera (Coconut) Liquid Endosperm

**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 also concluded that the available data are insufficient to make a determination of safety for Cocos Nucifera (Coconut) Shell Powder under the intended conditions of use in cosmetic formulations. The additional data needed for these cosmetic ingredients are:

- Composition and impurities data
- Concentration of use
- Dermal irritation and sensitization data

The Panel noted the lack of toxicity and carcinogenicity data on the coconut flower, fruit, and liquid endosperm ingredients; however, these ingredients are consumed as food, and daily exposure from food use would result in much larger systemic exposures than possible from use in cosmetic products. The Panel also noted the study of estrogen-like property in young coconut juice; however, the developmental and reproductive toxicity studies on coconut liquid endosperm do not implicate any reproductive effects. This, coupled with the very weak estrogenic effects noted in the study that used a concentration greater than that used in cosmetic products, helped mitigate concern.

Basic Brown 17

The Panel issued a final report with the conclusion that Basic Brown 17 is safe for use in hair dye products; however, the data are insufficient to make a determination of safety for use in other cosmetic product types. The additional data needed for these other uses are:

- Concentration of use and reported function for the non-hair coloring product uses that were reported in the Food and Drug Administration (FDA) Voluntary Cosmetic Registration Program (VCRP) database
- Dermal irritation and sensitization data at maximum use concentrations

Basic Brown 17 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 was not a sufficient basis for changing this advice to consumers at this time.

The Panel expressed concern over the mixed results in the genotoxicity studies and the lack of carcinogenicity studies. However, the Panel noted that the toxicokinetic studies show that Basic Brown 17 does not absorb through the skin and that a conservative margin of safety calculation yielded a result of 1000. These findings, coupled with the short exposure time as a rinse-off product, helped mitigate these concerns.

***Carica papaya* (Papaya)-Derived Ingredients**

The Panel issued a final report with the conclusion that *Carica Papaya* (Papaya) Fruit, *Carica Papaya* (Papaya) Fruit Extract, *Carica Papaya* (Papaya) Fruit Juice, and *Carica Papaya* (Papaya) Fruit Water are safe in the present practices of use and concentrations described in the safety assessment. However, the Panel also concluded that the available data are insufficient to make a determination of safety for *Carica Papaya* (Papaya) Leaf Extract. The additional data needed for this ingredient are genotoxicity, irritation, sensitization, and phototoxicity/photosensitization data.

The Panel determined that photosensitization and ultraviolet spectrum data on *Carica Papaya* (Fruit) Extract were sufficient to mitigate concern regarding potential photosensitization of the *Carica papaya* fruit ingredients. Furthermore, the safety of the *Carica papaya* fruit ingredients was supported by historical food use and a lack of clinical case reports involving dermatitis/cheilitis following the handling of *Carica papaya* fruit.

Hydroxy Tetramethylhydroxypiperidine Oxide and Tris(Tetramethylhydroxypiperidinol) Citrate

The Panel issued a final report with the conclusion that Hydroxy Tetramethylhydroxypiperidine Oxide and Tris(Tetramethylhydroxypiperidinol) Citrate are safe in the present practices of use and concentration as described in the safety assessment. Initial concerns about the lack of carcinogenicity data were mitigated by sufficient data supporting a lack of genotoxic potential. Additionally, although the Panel noted very limited information on methods of manufacture and impurities for these ingredients, the description for a general synthesis of Hydroxy Tetramethylpiperidine Oxide and the high purity indicated for Tris(Tetramethyl-hydroxypiperidinol) Citrate (93.64 - 97.3%), in conjunction with the lack of adverse effects in a 90-d dermal toxicity study (in which the no observed adverse effect level was 150 mg/kg bw/d) mitigated this concern. The safe dermal toxicity profile demonstrated in this report, in addition to a log K_{ow} of -0.29, indicating minimal dermal penetration, reassured the Panel of safety.

Acetyl Hexapeptide-8 Amide

The Panel issued a final report with the conclusion that Acetyl Hexapeptide-8 Amide is safe in cosmetics at concentrations $\leq 0.005\%$. The Panel further concluded that the available data are insufficient to make a determination of safety in cosmetic formulations at concentrations $> 0.005\%$. The additional data needed for use at concentrations greater than 0.005% are NOAEL for type I and type III collagen synthesis.

Acetyl Hexapeptide-8 Amide (CAS No. 616204-22-9) is defined as the product obtained by the acetylation of hexapeptide-8 in which the C-terminus is an amide. Acetyl Hexapeptide-8 Amide is synonymous with Acetyl Hexapeptide-8, acetyl hexapeptide-3, Acetyl Hexapeptide-24, and Acetyl Hexapeptide-24 Amide. The sequence for this acetylated and amidated peptide is Ac-Glu-Glu-Met-Gln-Arg-Arg-NH₂.

The Panel noted that the available in vitro and in vivo data indicate that Acetyl Hexapeptide-8 Amide may have drug activity (i.e., anti-wrinkle effect) by exerting an effect on type I and type III collagen in the dermis at a concentration of 10%; however, whether the mechanism of action of this product is via hydration of the skin or a biological effect on collagen synthesis is unclear. The Panel also stated their awareness of a consumer product purported to contain 10 to 30% Acetyl Hexapeptide; however, whether this product is a drug or cosmetic remains unknown. The Panel did recognize, however, that Acetyl Hexapeptide-8 Amide is known to be used in leave-on cosmetic products at concentrations up to 0.005%, based on vetted information sources, and that a drug effect (i.e., anti-wrinkle effect) on the dermis would not be likely at this low concentration.

The Panel noted the absence of systemic toxicity and detailed genotoxicity data on Acetyl Hexapeptide-8 Amide. Still, concern over the lack of these data was mitigated after considering the peptide structure of this ingredient, the associated low partitioning coefficient of -6.3 (i.e., percutaneous absorption unlikely), and the low maximum use concentration of 0.005% in leave-on cosmetic products.

Benzophenones

The Panel issued a final amended report with the conclusion that Benzophenone-1, -2, -3, -4, -5, -6, -8, -9, -10, -11, and -12 are safe in cosmetics in the present practices of use and concentration described in this safety assessment.

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

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

Tentative Safety Assessments

For those tentative safety assessments below to be posted on the CIR website at www.cir-safety.org on or before **March 24, 2021**, interested persons are given 60 days from the posting date to comment, provide information, and/or request an oral hearing before the Expert Panel for Cosmetic Ingredient Safety. 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 **September 13-14, 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 **December 6-7, 2021** meeting.

Anhydrogalactose, Anhydroglucitol, Anhydroxylitol, Arabinose, Psicose, Saccharide Hydrolysate, and Saccharide Isomerate (previously Saccharide Humectants)

The Panel issued a tentative report for public comment with the conclusion that the following ingredients are safe in the present practices of use and concentration described in the safety assessment:

Anhydrogalactose	Psicose
Anhydroglucitol	Saccharide Hydrolysate
Anhydroxylitol	Saccharide Isomerate
Arabinose	

After consideration of the data received and other data included in the safety assessment, the Panel determined that the available data are sufficient for determining the safety of these ingredients. Specifically, the Panel noted that data on Saccharide Isomerate with varying molecular weights (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 molecular weight 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 this toxicity endpoint are mitigated based on this composition. Furthermore, 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.

Levulinic Acid and Sodium Levulinate

The Panel issued a tentative report for public comment 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 did not receive data requested from the previous Insufficient Data Announcement (IDA), namely for impurities, 28-day dermal toxicity data (and, if found to be absorbed other endpoints), and ocular irritation data at, or above, the maximum concentration of use. However, 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, which satisfied cosmetic purity concerns. The Panel considered positive ocular irritation data in the report, in light of the highest reported concentration of use, 0.57%, in eyeshadows. Therefore, in the absence of further ocular toxicity data, these ingredients were deemed to be safe, when formulated to be non-irritating.

Red Algae

The Panel issued a tentative report for public comment with the conclusion that 11 of the 60 red algae-derived cosmetic ingredients reviewed are safe in the present practices of use and concentration described in the safety assessment. However, the Panel also concluded that the data are insufficient to make a determination of safety for the remaining 49 ingredients. The insufficiencies include a lack of systemic toxicity data, sensitization data, and/or sufficient composition 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 is sufficient data to support the safety of one of these ingredients, all related ingredients in the same genus and species would be considered safe.

Ahnfeltiopsis Concinna Extract	Corallina Officinalis Thallus Extract*
Asparagopsis Armata Extract	Cyanidium Caldarium Extract
Betaphycus Gelatinum Extract*	Delesseria Sanguinea Extract
Botryocladia Occidentalis Extract*	Digenea Simplex Extract*
Calliblepharis Ciliata Extract*	Dilsea Carnosa Extract*
Ceramium Kondoi Extract*	Furcellaria Lumbricalis Extract
Ceramium Rubrum Extract*	Gelidiella Acerosa Extract
Chondracanthus Teedei Powder*	Gelidium Amansii Extract
Chondrus Crispus	Gelidium Amansii Oligosaccharides*
Chondrus Crispus Extract	Gelidium Cartilagineum Extract
Chondrus Crispus Powder	Gelidium Pulchrum Protein*
Corallina Officinalis Extract	Gelidium Sesquipedale Extract*
Corallina Officinalis Powder*	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 were considered safe as used by the Expert Panel.

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

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

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

Diacetone Alcohol

The Panel issued a tentative report for public comment with the conclusion that Diacetone Alcohol is safe in cosmetics in the present practices of use and concentration described in the safety assessment.

The Panel found that the systemic toxicity and dermal irritation/sensitization data were sufficient to determine safety for this ingredient. Safety of this ingredient was further supported by low concentrations of use in leave-on products. In addition, because Diacetone Alcohol is used at low concentrations of use, expected amounts of exposure to impurities would be extremely low, mitigating the need for further Diacetone Alcohol impurities data.

Silicates

The Panel issued a tentative amended report for public comment with the conclusion that the following 24 silicate ingredients (previously reviewed ingredients are in red) are safe for use in cosmetics that are not expected to be incidentally inhaled with use, when formulated to be non-irritating. Additionally, the Panel concluded that these ingredients are safe for use in products that may be incidentally inhaled, when the presence of crystalline silica is < 0.1%, OR, the results of a repeated dose inhalation study demonstrate no adverse effects when crystalline silica is present at $\geq 0.1\%$. However, the Panel also concluded that the data are insufficient to make a determination of safety for use of these ingredients with airbrush use.

The additional data needed to determine safety of these ingredients for use in airbrush cosmetics are:

- particle size distribution, present concentrations of use, and if the particles are considered of respirable size, respiratory toxicity data
- information on methods of use, including exposure duration and frequency (e.g., daily, brief foundation application, compared to periodic, but longer suntan spray exposure).

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 about the potential for crystalline silica to be present in products containing silicate ingredients which may be incidentally inhaled. The Panel determined that in the absence of a no observed adverse effect level in repeated dose inhalation studies of the silicate ingredients with the presence of

crystalline silica greater or equal to 0.1%, the presence of crystalline silica should be below this level, which is the level of detection in the current state-of-the-art methodology X-ray diffraction. The Panel emphasized that this qualification is not an endorsement of safety at this level.

Melaleuca alternifolia (Tea Tree-Derived Ingredients)

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

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

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

The Panel noted that although the majority of the data in this report pertained to oil-derived ingredients, it was the opinion of the Panel that constituents of concern are present at the highest levels in oil-derived ingredients, and no signals for additional constituents of concern were noted in the extracts. Therefore, the Panel determined that the data on oil-derived ingredients could be used to evaluate the safety of all ingredients included in this report.

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. For *Melaleuca alternifolia* (tea tree)-derived ingredients, examples of the constituents the Panel was concerned about include 1,8-cineole (also known as eucalyptol), a possible allergen, and terpinolene, α -terpinene, α -phellandrene, and limonene, possible sensitizers. 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 was made aware that some of the *Melaleuca alternifolia* (tea tree)-derived ingredients could be supplied as adulterated ingredients. The Panel acknowledged this concern, and stressed that the cosmetics industry should continue to use current good manufacturing practices (cGMPs) to limit impurities.

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 August 13, 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 September 13-14, 2021 meeting.

Acryloyloxyethyl Phosphorylcholine Polymers

The Panel issued an IDA for the following 8 acryloyloxyethyl phosphorylcholine polymers that are included in this report:

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

The additional data needed for these ingredients are:

- Composition/impurities data on all ingredients
- Molecular weight data (e.g., average, distribution) on all ingredients
- Skin sensitization data on Polyquaternium-51 at the maximum use concentration of use
- Structures for Hydroxyethylcellulose/Phosphorylcholine Glycol Acrylate Copolymer and Polyquaternium-10/Phosphorylcholine Glycol Acrylate Copolymer

Salvia officinalis Sage-Derived Ingredients

The Panel issued an IDA for the following 12 *Salvia officinalis* (sage)-derived ingredients that are included in this report:

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

The additional data needed for these ingredients are:

For all ingredients:

- Composition and impurities data
- Dermal irritation and sensitization data, at the maximum concentration of use

For the Salvia Officinalis (Sage) Leaf Extract

- 28-d dermal toxicity data (if absorbed, other toxicological & genotoxicity endpoints for systemic toxicity)

For the Salvia Officinalis (Sage) Root Extract, the following additional data are needed

- Method of manufacture
- 28-d dermal toxicity data (if absorbed, other toxicological & genotoxicity endpoints for systemic toxicity)

157th Meeting Notes

Director's Report

Dr. Heldreth expressed gratitude for the Panel's and other stakeholders' continued support of the Cosmetic Ingredient Review (CIR) program. He also noted that 2021 looks to be a year of getting back to it. While all of the meetings of the Expert Panel this year will be 100% virtual, it looks likely that the barriers to traveling and meeting together safely in DC will come down this year. Despite the challenges of virtual meetings, this Panel has proceeded unfettered. Indeed, virtual meetings have presented us with certain advantages, including for example, more international participation. Because of that, Dr. Heldreth planned for there to be at least a small virtual component to these meetings, even once we are face-to-face again.

Draft 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 7 reports proposed (2 of the lead ingredients below are proposed to be reviewed together in 1 report) on the 2022 Draft 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 \geq 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	
To be determined – a hair dye	-
Per FOU	
Sodium Acetylated Hyaluronate	305
Hydrolyzed Hyaluronic Acid	269
Polyhydroxystearic Acid	264
Diphenylsiloxy Phenyl Trimethicone	251
Trisodium Ethylenediamine Disuccinate	236
Charcoal Powder	229
Zanthoxylum Piperitum Fruit Extract	217
Pyridoxine HCl	197

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.

Hair Dye Epidemiology Resource Document

The Panel reviewed the latest draft of the Hair Dye Epidemiology Resource Document. The Panel considered the 11 newly added studies as relevant and agreed the inclusion of those studies in the document. The Panel felt the document still substantiates, and supports, the conclusion that the currently available hair dye epidemiology data do not provide sufficient evidence for a causal relationship between personal hair dye use and cancer. The Panel requested Table 1 in the document be reorganized to cover all studies and include more study details. The Panel also requested the quality of individual studies be evaluated by external epidemiologists to better assess the importance of each study contained in the document.

The Panel also suggested some minor reformatting. This document will be brought before the Panel once more before finalization.

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 few meetings.

- | | |
|---------------------------------------|---|
| • Acrylate/Acrylamide Copolymers | • <i>Olea europaea</i> -Derived Ingredients |
| • Basic Yellow 57 | • Radish Root-Derived Ingredients |
| • Diatomaceous Earth | • <i>Rosa centifolia</i> -Derived Ingredients |
| • Fatty Esters End-Capped Alkoxylates | • <i>Rosa damascena</i> -Derived Ingredients |
| • Fatty Ethers | • Starch Phosphates |
| • Glucosamines | • Yeast-derived ingredients |
| • Glyceryl Acrylates | • <i>Zingiber officinale</i> -Derived ingredients |
| • Glycolactones | |
| • Hydroxyacetophenone | |

Next Expert Panel Meeting

Monday and Tuesday, September 13-14, 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 158th meeting page of the CIR website. <https://www.cir-safety.org/>