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EXPERT PANEL MEETING
September 14-15, 2020

Cosmetic Ingredient Review

Commitment & Credibility since 1976

MEMORANDUM

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Bart Heldreth, Ph.D., Executive Director, Cosmetic Ingredient Review
Subject: 155th Meeting of the Expert Panel — Monday and Tuesday, September 14-15, 2020
Date: August 21, 2020

Welcome to the second Expert Panel Meeting of 2020! The agenda and accompanying materials for the 155th Expert Panel Meeting to be held on September 14-15, 2020, are now available. The location is the ***same*** – this meeting will be held virtually! Invitations to join the meeting will arrive separately in your email inbox. Please be on the lookout for such regarding the Microsoft Teams virtual meeting platform. Panel members and liaisons will be registered ***automatically***. However, other interested parties may register to attend in advance of the meeting at the meeting page:

https://www.cir-safety.org/meeting/155th-expert-panel-meeting

The meeting agenda includes the consideration of 16 reports advancing in the review process, including 5 final reports, 3 tentative reports, and 8 draft reports. Also, on the agenda are 2 re-review summaries and the 2021 Draft Final Priorities Document.

Sadly, this will be Dr. Marks' final Panel meeting, as he is retiring from the Panel after the September 2020 meeting. Dr. Marks joined the Panel in September 2001. He has provided exemplary service and been an absolute joy to work with. We at CIR will greatly miss Dr. Marks' expertise, leadership, and candor.

Starting with the December 2020 meeting, the Panel will have a new team leader, Dr. David Cohen. Dr. Cohen completed his undergraduate work at the City University of New York, and is a graduate of the State University of New York at Stony Brook, School of Medicine (M.D.) and Columbia University School of Public Health (M.P.H.). He did his dermatology residency at the New York University Medical Center and Columbia University School of Public Health. He joined the NYU School of Medicine in 1994, and is currently Chief - Allergy Section/Contact Dermatitis (among other titles). Dr. Cohen has also served on, and led, numerous professional and scientific associations and committees, including the American Contact Dermatitis Society, the International Eczema Council, the American Dermatological Association, & the American Academy of Dermatology.

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Team Meetings

Draft Reports - there are 8 draft reports for review – Sufficient data to proceed or issue an IDA?

1. Red Algae – DR – This is the first time the Panel is reviewing the safety of these 59 ingredients derived from various species of red algae. In addition to information found in the published literature, the report package includes the following unpublished data that were received from the Council:

- Specifications of a trade name mixture containing 0.75% Ahnfeltiopsis Concinna Extract
- In vitro dermal irritation study on a trade name mixture containing 0.75% Ahnfeltiopsis Concinna Extract
- In vitro ocular irritation study on a trade name mixture containing 0.75% Ahnfeltiopsis Concinna Extract
- Manufacturing data on an Asparagopsis Armata Extract
- Manufacturing data on an Asparagopsis Armata Extract
- Manufacturing data on an Asparagopsis Armata Extract
- Composition of a trade name mixture containing 0.42% Asparagopsis Armata Extract
- Genotoxicity assay on an Asparagopsis Armata Extract containing 8% dry algal matter
- In vitro skin tolerance assay on an Asparagopsis Armata Extract containing 4% dry algal matter
- Human dermal irritation assay on an Asparagopsis Armata Extract containing 4% dry algal matter
- Human dermal irritation assay on a trade name mixture containing 0.5 –2% Asparagopsis Armata Extract, 56 – 62% water, and 38 – 42% propanediol
- HRIPT on a trade name mixture containing 0.5 –2% Asparagopsis Armata Extract, 56 – 62% water, and 38 – 42% propanediol
- HRIPT performed on a product containing 0.325% Asparagopsis Armata Extract
- In vitro ocular tolerance assay on an Asparagopsis Armata Extract containing 4% dry algal matter
- Human dermal irritation assay on an after-shave balm containing 0.8% Chondrus Crispus
- In vitro MatTek EpiOcular™ MTT assay performed on after-shave balm containing 0.8% Chondrus Crispus
- Specifications of a trade name mixture containing 20% Chondrus Crispus Extract
- Specifications of a trade name mixture containing 3.5% Chondrus Crispus Extract
- In vitro MatTek EpiDerm™ MTT assay on a trade name mixture containing 3.5% Chondrus Crispus Extract
- HRIPT performed on a product containing 0.49% Chondrus Crispus Extract
- In vitro MatTek EpiOcular™ MTT assay on a trade name mixture containing 3.5% Chondrus Crispus Extract
- Manufacturing data on a Chondrus Crispus Powder
- Manufacturing data on a Chondrus Crispus Powder
- Human dermal irritation assay on a Chondrus Crispus Powder
- General information on the *Corallina officinalis*
- Composition of a trade name mixture containing Corallina Officinalis Extract (1.5%)
- Method of manufacturing data on a trade name mixture containing Corallina Officinalis Extract
- Metal and mineral analysis for a trade name mixture containing Corallina Officinalis Extract (1.5%)
- Human dermal irritation assay on a trade name mixture containing 1.5% Corallina officinalis Extract
- In vitro ocular irritation assay on a trade name mixture containing 1.5% Corallina officinalis Extract
- Manufacturing information on a trade name mixture containing Chondrus Crispus Extract and Gigartina Stellata Extract (98.10 – 98.95% total extract)
- Composition of a trade name mixture containing Chondrus Crispus Extract and Gigartina Stellata Extract (98.10 – 98.95% total extract)
- Human dermal irritation assay on a trade name mixture containing Chondrus Crispus Extract

and Gigartina Stellata Extract (98.10 – 98.95% total extract)

- Composition of trade name mixture containing Corallina Officinalis Extract, Kappaphycus Alvarezii Extract, and Gigartina Stellata Extract
- Method of manufacture of a trade name mixture containing Corallina Officinalis Extract, Kappaphycus Alvarezii Extract, and Gigartina Stellata Extract
- Genotoxicity assay on a trade name mixture containing Corallina Officinalis Extract, Kappaphycus Alvarezii Extract, and Gigartina Stellata Extract
- Human dermal irritation assay on a trade name mixture containing Corallina Officinalis Extract, Kappaphycus Alvarezii Extract, and Gigartina Stellata Extract
- In vitro ocular irritation assay on a trade name mixture containing Corallina Officinalis Extract, Kappaphycus Alvarezii Extract, and Gigartina Stellata Extract
- HRIPT performed on a product containing 0.0028% Gelidiella Acerosa Extract
- Manufacturing data on a trade name mixture containing Gelidium Cartilagineum Extract
- Composition information on a trade name mixture containing Gelidium Cartilagineum Extract
- Human dermal irritation assay on a trade name mixture consisting of >96% glycerides, mixed decanoyl and octanoyl; <2 % Gelidium Cartilagineum Extract; 1.5-2% 4-cholesten-3-one
- HRIPT on a trade name mixture consisting of >96% glycerides, mixed decanoyl and octanoyl; <2 % Gelidium Cartilagineum Extract; 1.5-2% 4-cholesten-3-one
- Composition of a trade name mixture containing Gelidium Sesquipedale Extract
- Mineral and metal analysis on a trade name mixture containing 4% Gelidium Sesquipedale Extract
- General information on the species Gelidium sesquipedale
- Human dermal irritation assay on a trade name mixture consisting of 48% water; 48% butylene glycol; 4% Gelidium Sesquipedale Extract
- General species information for Gigartina stellate
- Manufacturing information on a trade name mixture containing Hydrolyzed Corallina Officinalis Extract
- Composition information on a trade name mixture containing Hydrolyzed Corallina Officinalis Extract
- Human dermal irritation assay on a trade name mixture consisting of >96% water; 0.5-3% Hydrolyzed Corallina Officinalis Extract; 0.8-1.2% phenoxyethanol
- HIRPT on a trade name mixture consisting of >96% water; 0.5-3% Hydrolyzed Corallina Officinalis Extract; 0.16-0.20% sodium methylparaben
- Manufacturing data on a trade name mixture containing Hypnea Musciformis Extract
- Manufacturing data on a Hypnea Musciformis Extract
- Composition of a trade name mixture containing Hypnea Musciformis Extract
- Composition on a Hypnea Musciformis Extract
- Impurities of a Hypnea Musciformis Extract
- Human dermal irritation assay on a trade name mixture consisting of 72-77% water; 20-70% butylene glycol; 1-3% Hypnea Musciformis Extract; ≤1% potassium gluconate; 0.16-0.2% methylparaben
- Human dermal irritation assay on a Palmaria Palmata Extract
- HRIPT on a Palmaria Palmata Extract
- Manufacturing data on a trade name mixture containing Lithothamnion Calcareum Powder
- Composition of a trade name mixture containing Lithothamnion Calcareum Powder
- Human dermal irritation assay on a trade name mixture consisting of 57-61% Lithothamnion Calcareum Powder. 26-31% mannitol, 9-11% diatomaceous earth, 0.7-1.5% zinc sulfate
- In vitro ocular irritation assay on a trade name mixture consisting of 57-61% Lithothamnion Calcareum Powder. 26-31% mannitol, 9-11% diatomaceous earth, 0.7-1.5% zinc sulfate
- Method of manufacturing information for a Palmaria Palmata Extract
- Composition information on a Palmaria Palmata Extract
- Impurities of a Palmaria Palmata Extract
- Human dermal irritation summary data on a Palmaria Palmata Extract
- HRIPT on a Palmaria Palmata Extract
- Composition information on a trade name mixture containing Polysiphonia Lanosa Extract
- Human dermal irritation assay on a trade name mixture consisting of 67.5% water, 32% Polysiphonia Lanosa Extract
- General information on Porphyra umbilicalis

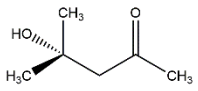
- Method of manufacturing information on a trade name mixture containing Porphyra Umbilicalis Extract
- Method of manufacturing information on a trade name mixture containing Porphyra Umbilicalis Extract
- Composition information on a trade name mixture containing Porphyra Umbilicalis Extract
- Composition information on a trade name mixture containing Porphyra Umbilicalis Extract
- Heavy metal impurities of a trade name mixture consisting of 52% water, 48% Porphyra Umbilicalis Extract
- Genotoxicity data on a trade name mixture consisting of 52% water and 48% Porphyra Umbilicalis Extract
- HRIPT performed on a product containing 0.0004% Porphyra Umbilicalis Extract
- In vitro phototoxicity assay on a trade name mixture consisting of 52% water and 48% Porphyra Umbilicalis Extract
- In vitro ocular irritation study on a trade name mixture consisting of 52% water and 48% Porphyra Umbilicalis Extract
- Human dermal irritation assay on an eye cream containing 0.0375% Rhodymenia Palmata Extract
- In vitro ocular irritation assay on an eye cream containing 0.0375% Rhodymenia Palmata Extract

As it may help the Panel decide on a conclusion of safety for several of these red-algae derived ingredients, a table has been provided presenting each ingredient, as well as a notation of the presence or absence of systemic toxicity data (repeated dose studies or use in food/as a GRAS substance) and sensitization data. This table can be found in the packet as *redalg092020data1*.

According to 2020 VCRP survey data, Chondrus Crispus Extract is reported to be used in 381 formulations (306 leave-on formulations, 74 rinse-off formulations, and 1 formulation diluted for bath). Hypnea Musciformis Extract is reported to be used in 141 formulations, Corallina Officinalis Extract is reported to be used in 96 formulations, and Palmaria Palmata Extract is reported to be used in 83 formulations. All other in-use ingredients are reported to be used in 55 formulations or less. The results of a concentration of use survey conducted by Council in 2020 indicate Corallina Officinalis Extract has the highest reported maximum concentration of use; it is used at up to 2% in blushers, other makeup preparations, and face and neck products. Chondrus Crispus is reported to be used at up to 1.4% in dentifrices. All other ingredients are reported to be used at 0.25% or less.

After reviewing these documents, if the available data are deemed sufficient to make a determination of safety, the Panel should issue a Tentative Report with a safe as used, safe with qualifications, or unsafe conclusion, and Discussion items should be identified. If the available data are insufficient, the Panel should issue an Insufficient Data Announcement (IDA), specifying the data needs therein.

2. Diacetone Alcohol – DR – This is the first time the Panel is reviewing the safety of this ingredient. Diacetone Alcohol is reported to be used in cosmetics as a fragrance ingredient and solvent.



According to 2020 VCRP survey data, Diacetone Alcohol is reported to be used in 239 nail formulations (uses were not reported in any other product category in the VCRP). The results of a concentration of use survey conducted by Council in 2019 indicate Diacetone Alcohol is used at up to 9.2% in rinse-off shaving products (a “razor lube strip”); all other uses are at 0.84% or below. Diacetone Alcohol is used at up to 0.84% in nail polish and enamel formulations, and the highest concentration resulting in leave-on dermal exposure is 0.25% in “other” eye makeup preparations.

If no further data are needed to reach a conclusion of safety, the Panel should formulate a Discussion and issue a Tentative Report. However, if additional data are required, the Panel should be prepared to identify those needs and issue an IDA, specifying the data needs therein.

3. Silicates – DAR – The silicate family includes ingredients from re-opened reports on silicate ingredients that had been published or finalized in 2003, 2005, and 2009, along with additional add-on ingredients. In December 2019, the Panel considered the proposed groupings for 3 different mineral ingredients reports, and accepted the proposed grouping of the 24 silicate ingredients described in this current draft

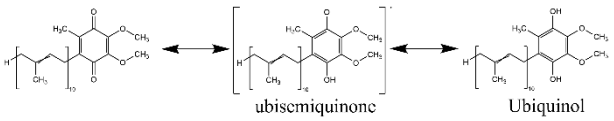
amended safety assessment.

Since the Panel's review last year of these ingredients, data submitted from the Council and the Synthetic Amorphous Silica and Silicate Industry Association have been incorporated into the report. Comments from the Council from December 2019, at which time the Panel reviewed the proposed report groupings, have also been included.

According to 2020 VCRP data, Magnesium Aluminum Silicate has the most reported uses in cosmetic products, with a total of 938; the majority of the uses are in leave-on eye makeup preparations and skin care preparations. Aluminum Calcium Sodium Silicate has the second most reported uses in cosmetic products, with a total of 287; the majority of the uses are in lipsticks. The reported numbers of uses for the remaining ingredients in this report are much lower. The frequencies of use for both of these ingredients have greatly increased since the original safety assessments were finalized: in 1998, Magnesium Aluminum Silicate was reported to have 632 uses, and in 2009, Aluminum Calcium Sodium Silicate was reported to have 7 uses. The results of the concentration of use survey conducted in 2018 by the Council indicate Aluminum Calcium Sodium Silicate has the highest reported maximum concentration of use for leave-on products; it is used at up to 26.3% in eye shadows. Magnesium Silicate is reported to have a maximum concentration of use for leave-on products of 21.6% in eye shadows. According to the original safety assessment, the maximum use concentration in 2008 for Aluminum Calcium Sodium Silicate was 6% in foundations and lipsticks. Additionally, according to 1999 data, there were no reported uses for Magnesium Silicate.

If no further data are needed to reach a conclusion of safety, the Panel should formulate a Discussion and issue a Tentative Amended Report. However, if additional data are required, the Panel should be prepared to identify those needs and issue an IDA, specifying the data needs therein.

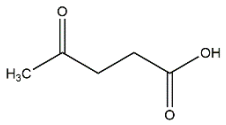
4. Ubiquinone – DR – This is the first time the Panel is reviewing the safety these 4 ingredients. These Ubiquinone ingredients are reported to function in cosmetics as antioxidants; some are also reported to function as skin protectants, skin conditioning agents, and/or hair conditioning agents.



According to 2020 VCRP survey data, Ubiquinone is reported to be used in 421 cosmetic products, of which 387 are leave-on products. The results of a concentration of use survey conducted by the Council in 2018 indicate that the maximum leave-on use concentration in this ingredient group is 0.05% for Ubiquinone, in body and hand products.

After reviewing this document, if the available data are deemed sufficient to make a determination of safety, the Panel should issue a Tentative Report with a safe as used, safe with qualifications, or unsafe conclusion, and Discussion items should be identified. If the available data are insufficient, the Panel should issue an IDA, specifying the data needs therein.

5. Levulinic – DR – This is the first time the Panel is seeing a safety assessment of Levulinic Acid and Sodium Levulinate. Both of these ingredients are reported to function in cosmetics as skin conditioning agents; Levulinic Acid is also reported to function as a fragrance ingredient. In addition to information found in the published literature, the report package includes the following unpublished data that were received from the Council (in addition to concentration of use):

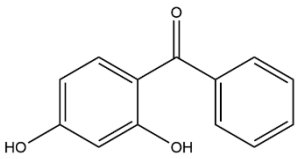


- Essex Testing Clinic, Inc. (2016) Clinical safety evaluation repeated insult patch test of a product containing 0.4011% Sodium Levulinate
- Essex Testing Clinic, Inc. (2016) Clinical safety evaluation repeated insult patch test of a product containing 0.57% Sodium Levulinate

According to 2020 VCRP survey data, Levulinic Acid is reported to be used in 131 cosmetic formulations, and Sodium Levulinate is reported to be used in 402 cosmetic formulations, 293 of which are leave-on products. Results from a 2019 concentration of use survey, conducted by the Council, indicate that Levulinic Acid has the highest maximum concentration of use, at 4.5% in hair dyes, while Sodium Levulinate is used at a maximum concentration of 0.62% in mouthwashes and breath fresheners. The greatest concentrations for leave-on dermal exposure are in foundations containing Levulinic Acid (0.0005%) and eye shadows containing Sodium Levulinate (0.57%).

After reviewing these documents, if the available data are deemed sufficient to make a determination of safety, the Panel should issue a Tentative Report with a safe as used, safe with qualifications, or unsafe conclusion, and Discussion items should be identified. If the available data are insufficient, the Panel should issue an IDA, specifying the data needs therein.

6. Benzophenones – DAR – The Panel first reviewed the safety of benzophenones in 1981. The Panel subsequently published a final report (in 1983) with a conclusion stating that Benzophenones-1, -3, -4, -5, -9, and -11 are safe for topical application to humans in the present practices of use and concentration in cosmetics. In the same year, the Panel published an addendum to the final report, having concluded that Benzophenones-2, -6, and -8 are not mutagenic or genotoxic and that the published conclusion on Benzophenones -1, -3, -4, -5, -9, and -11 is applicable to these 3 ingredients as well.

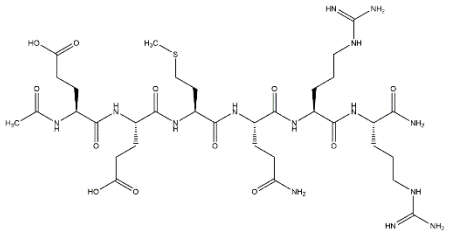


At the September 2002 Panel meeting, the Panel determined to not reopen the 1983 published safety assessment until results from National Toxicology Program (NTP) carcinogenicity studies on benzophenones were available. Because an NTP oral carcinogenicity study on Benzophenone-3 was published earlier this year, the Panel is asked to determine whether the 1983 published safety assessment should be reopened to include these and other current safety test data, and to add Benzophenones-7, -10, and -12, along with any available safety test data on these 3 ingredients.

In the 1983 original report and in 2020, Benzophenone-2 (299 uses then; 103 uses now) and Benzophenone-4 (240 uses then; 2259 uses now) had the highest reported use frequency. Of the ingredients reviewed in the1983 report, Benzophenone-4 had the highest use concentration (≤ 10% in suntan gels, creams, and liquids; leave-on products). In 2020, Benzophenone-4 is the benzophenone with the highest reported use concentration, and is used at substantially lower concentrations of up to 1.6% in other non-coloring hair preparations (leave-on products)

The Panel should carefully consider and discuss the data presented in this report. If the data are sufficient, the Panel should issue a Tentative Amended Report with the appropriate conclusion. If data are insufficient, the Panel should issue an IDA, with the data needs stated therein.

7. Acetyl Hexapeptide-8 – DR – This is the first time the Panel is reviewing the safety assessment on Acetyl Hexapeptide-8 and Acetyl Hexapeptide-8 Amide. Acetyl Hexapeptide-8 is reported to function as a skin-conditioning agent-humectant and Acetyl Hexapeptide-8 Amide is reported to function as a skin-conditioning agent-miscellaneous.

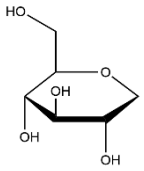


Of note, CIR was made aware, as these reports were going to press, that Acetyl Hexapeptide-8 is synonymous with Acetyl Hexapeptide-8 Amide. Accordingly, all of the data in the literature states Acetyl Hexapeptide-8 as the test material, but is fully applicable to the synonymous ingredient, Acetyl Hexapeptide-8 Amide. The name, Acetyl Hexapeptide-8 Amide, is more accurate, as the ingredient is used as the amidated peptide. Thus, the Amide name is used throughout the report. Furthermore, CIR was just made aware that not only are Acetyl Hexapeptide-8 and Acetyl Hexapeptide-8 Amide synonymous with each other, but are also synonymous with Acetyl Hexapeptide-24 and Acetyl Hexapeptide-24 Amide. Thus, there appears to be 4 ingredient names for 1 chemical. Unless the Panel objects, Acetyl Hexapeptide-24 and Acetyl Hexapeptide-24 Amide will be incorporated into the next iteration of the report.

According to 2020 VCRP data, Acetyl Hexapeptide-8 is reported to be used in 452 cosmetic products (422 leave-on and 30 rinse-off) as Acetyl Hexapeptide-8, and an additional 33 uses are reported with the synonym, acetyl hexapeptide-3 (32 leave-on and 1 rinse-off). The results of a concentration of use survey conducted by the Council in 2019 indicate that Acetyl Hexapeptide-8 is used at concentrations up to 0.005% (in eye lotions and face and neck products; not spray), which is the highest reported maximum use concentration for leave-on formulations. In rinse-off products, Acetyl Hexapeptide-8 is reported to be used at concentrations up to 0.000005% (skin cleansing products). According to VCRP and Council survey data, Acetyl Hexapeptide-8 Amide is not reported to be used in cosmetic products.

After reviewing these documents, if the available data are deemed sufficient to make a determination of safety, the Panel should issue a Tentative Report with a safe as used, safe with qualifications, or unsafe conclusion, and Discussion items should be identified. If the available data are insufficient, the Panel should issue an IDA, specifying the data needs therein.

8. Saccharide Humectants – DR – This is the first time the Panel is seeing a safety assessment of these 7 cosmetic ingredients. All 7 saccharide humectants are reported to function as skin-conditioning agents – humectant in cosmetics. Anhydrogalactose is also reported to function as an antioxidant, and Anhydroglucitol also functions as an oral care agent. In addition to information found in the published literature, the report package includes the following unpublished data that were received from the Council:



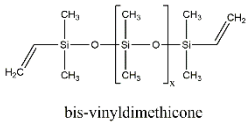
- Use concentration data
- Human ocular irritation data on an eye cream containing 2.75% Saccharide Isomerate
- Human repeated insult patch test on an eye cream containing 2.75% Saccharide Isomerate

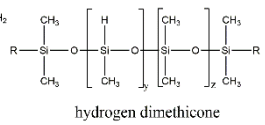
According to 2020 VCRP data, Saccharide Isomerate is reported to be used in 494 cosmetic products (438 leave-on products and 56 rinse-off products). Of the saccharide humectants reviewed in this safety assessment, this is the greatest reported use frequency. The results of a concentration of use survey conducted by the Council in 2018 indicate that Saccharide Hydrolysate is used at maximum use concentrations up to 4.6% in rinse off products (skin cleansing products), and that Saccharide Isomerate is used at maximum use concentrations up to 2.8% in leave-on products (face and neck skin care preparations, not spray).

After reviewing these documents, if the available data are deemed sufficient to make a determination of safety, the Panel should issue a Tentative Report with a safe as used, safe with qualifications, or unsafe conclusion, and Discussion items should be identified. If the available data are insufficient, the Panel should issue an IDA, specifying the data needs therein.

Draft Tentative Reports – there are 3 draft tentative reports for consideration.

1. Polysilicone-11 – TR – At the December 2019 meeting, the Panel issued an insufficient data announcement (IDA) for this ingredient. In order to determine the safety of this ingredient, the following data were requested:


bis-vinyldimethicone


hydrogen dimethicone

- residual monomers and other reactants (e.g., polymerization initiators, chain propagators, terminators, solvents),
- molecular weight distribution
- composition
- impurities
- 28-day dermal toxicity
- mammalian genotoxicity
- sensitization/irritation data at maximum use concentration.

Since the issuing of the IDA, the following unpublished data have been received and highlighted throughout the report:

- Updated method of manufacturing and impurities information
- Data on a cytotoxicity assay on a trade name mixture containing 12 – 16% Polysilicone-11, 43 – 50% dimethicone, and 36 – 42% cyclopentasiloxane
- Summary HRIPT data on a trade name mixture containing 98% Polysilicone-11 and 2% laureth-12

Also included are updated 2020 VCRP data and corrected concentration of use data. Polysilicone-11 is now reported to be used in 440 total formulations (it was previously reported to be used in 420 total formulations). Corrected concentration of use data indicate that the maximum concentration of use reported for Polysilicone-11 is 19.9% in other skin care preparations. The previous maximum concentration of use was reported to be 35% in face and neck preparations; the current maximum concentration of use for this category is reported to be 14.6%.

After reviewing these documents, if the available data are deemed sufficient to make a determination of safety, the Panel should issue a Tentative Report with a safe as used, safe with qualifications, or unsafe conclusion, and Discussion items should be identified. If the available data are still insufficient, the Panel should issue a Tentative Report with an insufficient data conclusion. A split conclusion is also an option.

2. Coconut – TR – At the December 2019 meeting, the Panel issued an IDA for these ingredients. The additional data needed to determine safety were:

   - Method of manufacturing data for Cocos Nucifera (Coconut) Fruit Powder
   - Composition and impurities data for Cocos Nucifera (Coconut) Flower Extract, Cocos Nucifera (Coconut) Fruit Powder, Cocos Nucifera (Coconut) Shell Powder, and Cocos Nucifera (Coconut) Fruit Extract or another Cocos nucifera (coconut) fruit-derived ingredient.
   - Data on Cocos Nucifera (Coconut) Flower Extract and Cocos Nucifera (Coconut) Shell Powder on the following endpoints:
     - 28-day dermal toxicity, and if positive, DART may be needed
     - Genotoxicity
     - Dermal irritation and sensitization
   - Clarification as to whether the data on the trade name mixture containing 20% Cocos Nucifera (Coconut) Fruit Extract and 80% Lactobacillus are actually for a *Lactobacillus* ferment of coconut fruit extract, or for a mixture of the fruit extract and *Lactobacillus*.

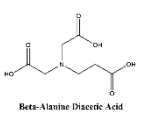
   Since the issuance of the IDA, CIR has received, and incorporated into the report, unpublished data on the composition of Cocos Nucifera (Coconut) Fruit Extract. Per discussions from the December meeting, and because data clarifying the identity of the trade name mixture containing 20% Cocos Nucifera (Coconut) Fruit Extract and 80% *Lactobacillus* were not received, information pertaining to this mixture have been stricken from the safety assessment.

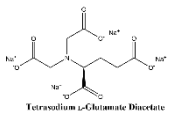
   CIR staff have also received unpublished data submissions for a coconut ingredient identified as Cocos Nucifera (Coconut) Fruit Juice; however, clarification has been requested by staff regarding these data. A memo and the data regarding such are included in this report package. The data will be incorporated into the report once our query has been satisfactorily addressed.

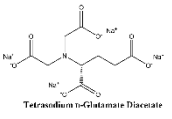
   Also, since December, CIR staff have been made aware that Cocos Nucifera (Coconut) Flower Nectar Extract has been added to the *Dictionary*. This ingredient is defined as the extract of the nectar obtained from the flowers of Cocos nucifera, and it is reported to function as an antimicrobial agent, antioxidant, and pH adjuster in cosmetic products. Currently, there are no reported uses for this ingredient in the VCRP. Would the Panel consider adding this ingredient to this safety assessment at this review stage?

   The Panel should carefully consider and discuss the data (or lack thereof) and the draft Abstract and Discussion presented in this report, and issue a Tentative Report with a safe, safe with qualifications, unsafe, insufficient data, or split conclusion.

3. Amino Acid Diacetates – TR – At the December 2019 meeting, the Panel issued an IDA for these 2 ingredients. The additional data needed to determine safety were:







   - Method of manufacturing, composition, and impurities data
   - Clarification on the status of isomerization of Tetrasodium Glutamate Diacetate

Since the issuance of the IDA, CIR has received unpublished data on Tetrasodium Glutamate Diacetate for the method of manufacturing, composition and impurities data, and information on racemization. These data have been incorporated into the report.

The use information was updated with 2020 VCRP data. Use for Tetrasodium Glutamate Diacetate has increased from 794 total uses to 977; the majority of the uses are in bath soaps and detergents. The number of uses for Beta-Alanine Diacetic Acid remains unchanged: it is reported to be used in only 2 leave-on formulations.

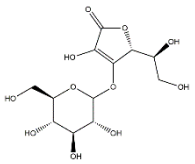
Based on the proceedings and comments from the December 2019 meeting, a draft Discussion has been included. The Panel should carefully consider and discuss the data (or lack thereof) and the draft Abstract and Discussion presented in this report, and issue a Tentative Report with a safe, safe with qualifications, unsafe, insufficient data, or split conclusion.

Draft Final Reports - there are 5 draft final reports for consideration. After reviewing these drafts, especially the rationales provided in the Discussion sections, the Panel should issue these as Final Reports, as appropriate.

1. Scutellaria – FR – At the June 2020 Panel meeting, a tentative report with the following conclusions was issued: 1) Scutellaria Baicalensis Root Extract and Scutellaria Baicalensis Root Powder are safe in cosmetics in the present practices of use and concentration described in the safety assessment, and 2) the available data are insufficient to make a determination that Scutellaria Baicalensis Extract and Scutellaria Baicalensis Sprout Extract are safe under the intended conditions of use in cosmetic formulations.

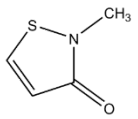
The Panel should carefully consider the Abstract, Discussion, and Conclusion presented in this report. If these are satisfactory, the Panel should issue a Final Report.

2. Ascorbyl Glucoside – FR – At the June 2020 Panel meeting, the Panel concluded that Ascorbyl Glucoside and Sodium Ascorbyl Glucoside are safe in cosmetics in the present practices of use and concentration described in this safety assessment.



The Panel should carefully review the Abstract, Discussion, and Conclusion of this safety assessment. If these are satisfactory, then the Panel should issue a Final Report.

3. MI – FAR – In 2019, the Panel published an amended safety assessment of MI with the conclusion that “MI is safe for use in rinse-off cosmetic products at concentrations up to 100 ppm and safe in leave-on cosmetic products when they are formulated to be non-sensitizing, which may be determined based on a quantitative risk assessment (QRA).” This conclusion superseded the Panel’s original conclusion that was published in 2010.

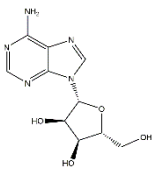


In response to concerns of reports of adverse events observed in infants following inhalation exposure to humidifier disinfectants that contained the preservative mixture Methylchloroisothiazolinone/Methylisothiazolinone (MCI/MI), the Panel moved to reopen the safety assessment of MI in September 2019. A search for inhalation toxicity data regarding MI (separate from the combination of MCI/MI) did not yield any new published literature, aside from the papers already detailed in the MCI/MI report. The Panel reviewed these data as well as the findings of a draft risk assessment for MCI/MI, and a hazard characterization of isothiazolinones produced by the US Environmental Protection Agency, and determined that these data mitigated concern for the use of this ingredient at the reported use and concentrations in cosmetic products that could be incidentally inhaled following use. At the June 2020 Panel meeting, the Panel issued a tentative amended report restating the conclusion that MI is safe for use in rinse-off cosmetic products at concentrations up to 100 ppm and safe in leave-on cosmetic products when formulated to be non-sensitizing, which may be determined based on a QRA or similar methodology.

Since the June 2020 meeting, a published retrospective study indicating the decline of allergy to MI in Europe has been included in the safety assessment. These data are highlighted to aid in the Panel's review. No additional data have been received.

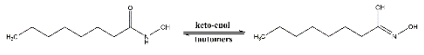
The Panel should carefully consider the Abstract, Discussion, and Conclusion presented in this report. If these are satisfactory, the Panel should issue a Final Amended Report.

4. Adenosine – TR – At the June 2020 meeting, the Expert Panel for Cosmetic Ingredient Safety determined that the data were sufficient to conclude that these 5 ingredients are safe in the present practices of use and concentration as described in the safety assessment.



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

5. Caprylhydroxamic Acid – FR – At the June 2020 meeting, the Panel issued a tentative report for public comment with the conclusion that Caprylhydroxamic Acid is safe in cosmetics in the present practices of use and concentration described in this safety assessment.



The Panel was concerned with inconsistent outcomes regarding dermal sensitization. Upon further review, the Panel determined that studies that had positive sensitization results were those in which the test substance included a penetration enhancer. Additionally, the Panel noted that cases of increased sensitization with use of a moisturizer in Finland, that had been reformulated to include Caprylhydroxamic Acid, appeared to be related to use on damaged skin, and most likely resulted in increased penetration. Therefore, the Panel stated that caution should be taken with use of Caprylhydroxamic Acid in a manner that would result in increased penetration, such as with the inclusion of penetration enhancers in formulations containing Caprylhydroxamic Acid.

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

Administrative Items - there is 1 draft priorities document and 2 re-review summaries.

1. Priorities – The 2021 Draft Final Priority List is based on stakeholder requests; frequency of use data (FOU) from FDA's VCRP January 13th, 2020; and on CIR staff and Panel workflow. The Panel should confirm approval of this list and the associated report groupings.

2. Quaternium-18 – RRsum – At the June 2020 meeting, the Panel determined the data on Quaternium-18 and Quaternium-18 Bentonite were sufficient to re-affirm the original conclusion that these ingredients are safe as cosmetic ingredients in the present practices of use and concentration.

3. Sulfites – RRsum – At the June 2020 meeting, the Panel determined to not reopen this safety assessment, and reaffirmed the original conclusion that these ingredients are safe as used in cosmetic formulations.

Full Panel Meeting

The Panel will consider the 5 reports to be issued as final safety assessments, followed by the remaining reports advancing in the process (including the tentative reports and draft reports), re-review summaries, and a draft priorities document.

Please remember, the meeting starts at 8:30 am on day 1 and on day 2. It is likely that the full Panel session will conclude before lunch on day 2.

Looking forward to seeing you all (virtually)!

Agenda
155th Meeting of the Expert Panel for Cosmetic Ingredient Safety
September 14th - 15th, 2020

Virtual via Microsoft Teams

Monday, September 14th

8:30 AM	**WELCOME TO THE 155th EXPERT PANEL TEAM MEETINGS**	**Drs. Bergfeld/Heldreth**
8:40 AM	**TEAM MEETINGS**	**Drs. Marks/Belsito**

Dr. Marks Team*

FR (PC)	Adenosine
TR (PC)	Polysilicone-11
DR (PC)	Diacetone Alcohol
DR (PC)	Red Algae
RRsum (PC)	Quaternium-18
DR (PR)	Levulinic
DR (PR)	Ubiquinone
Admin (BH)	Final Priorities
FR (MF)	Caprylhydroxamic Acid
FR (WJ)	Ascorbyl Glucoside
FR (WJ)	Scutellaria
DR (WJ)	Saccharide Humectants
DR (WJ)	Acetyl Hexapeptide-8
DAR (WJ)	Benzophenones
RRsum (WJ)	Sulfites
FAR (CB)	MI
TR (CB)	Amino Acid Diacetates
TR (CB)	Coconut
DAR (CB)	Silicates

Dr. Belsito Team

FR (WJ)	Ascorbyl Glucoside
FR (WJ)	Scutellaria
DR (WJ)	Saccharide Humectants
DR (WJ)	Acetyl Hexapeptide-8
DAR (WJ)	Benzophenones
RRsum (WJ)	Sulfites
FAR (CB)	MI
TR (CB)	Amino Acid Diacetates
TR (CB)	Coconut
DAR (CB)	Silicates
FR (MF)	Caprylhydroxamic Acid
Admin (BH)	Final Priorities
FR (PC)	Adenosine
TR (PC)	Polysilicone-11
DR (PC)	Diacetone Alcohol
DR (PC)	Red Algae
RRsum (PC)	Quaternium-18
DR (PR)	Levulinic
DR (PR)	Ubiquinone

The purpose of the Cosmetic Ingredient Review and the Expert Panel for Cosmetic Ingredient Safety is to determine those cosmetic ingredients for which there is a reasonable certainty in the judgment of competent scientists that the ingredients are safe under intended conditions of use.

FR: Final Report // FAR: Final Amended Report // TR: Tentative Report // TAR: Tentative Amended Report // DR: Draft Report // DAR: Draft Amended Report // RR: Re-Review // RRsum: Re-Review Summary // SM: Strategy Memo // Admin: Administrative item

(CB): Christina Burnett || (BH) Bart Heldreth || (MF): Monice Fiume || (PC): Priya Cherian || (WJ): Wilbur Johnson || (PR): Preethi Raj || (JZ): Jinqiu Zhu

*Team moves to breakout room (for a virtual meeting, this means a separate Microsoft Teams meeting).

Tuesday, September 15th			
8:30 am	**WELCOME TO THE 155th FULL EXPERT PANEL MEETING**		**Dr. Bergfeld**
8:45 am	Admin	**MINUTES OF THE JUNE 2020 EXPERT PANEL MEETING**	**Dr. Bergfeld**
9:00 am	**DIRECTOR'S REPORT**		**Dr. Heldreth**
9:10 am	**FINAL REPORTS, REPORTS ADVANCING TO THE NEXT LEVEL, OTHER ITEMS**		

Final Reports

FR (MF)	Caprylhydroxamic Acid – *Dr. Belsito Reports*
FR (PC)	Adenosine – *Dr. Marks Reports*
FAR (CB)	MI – *Dr. Belsito Reports*
FR (WJ)	Ascorbyl Glucoside – *Dr. Marks Reports*
FR (WJ)	Scutellaria – *Dr. Belsito Reports*

Reports Advancing

DR (WJ)	Saccharide Humectants – *Dr. Marks Reports*
DR (WJ)	Acetyl Hexapeptide-8 – *Dr. Belsito Reports*
DAR (WJ)	Benzophenones – *Dr. Marks Reports*
DR (PR)	Levulinic – *Dr. Belsito Reports*
DR (PR)	Ubiquinone – *Dr. Marks Reports*
TR (CB)	Amino Acid Diacetates – *Dr. Belsito Reports*
TR (CB)	Coconut – *Dr. Marks Reports*
DAR (CB)	Silicates – *Dr. Belsito Reports*
TR (PC)	Polysilicone-11 – *Dr. Marks Reports*
DR (PC)	Diacetone Alcohol – *Dr. Belsito Reports*
DR (PC)	Red Algae – *Dr. Marks Reports*

Other Items

RRsum (PC)	Quaternium-18 – *Dr. Belsito Reports*
RRsum (WJ)	Sulfites – *Dr. Marks Reports*
Admin (BH)	Final Priorities – *Dr. Belsito Reports*

ADJOURN - *Next meeting Monday and Tuesday, December 7-8, 2020, will also be held virtually. Please check the CIR website for details as the meeting approaches.*

On the basis of all data and information submitted, and after following all of the Procedures (https://www.cir-safety.org/supplementaldoc/cir-procedures), the Expert Panel shall determine whether each ingredient, under each relevant condition of use, is safe, safe with qualifications, unsafe, or there are insufficient data or information to make a determination of safety. Upon making such a determination, the Expert Panel shall issue a conclusion and/or announcement.

FR: Final Report // FAR: Final Amended Report // TR: Tentative Report // TAR: Tentative Amended Report // DR: Draft Report // DAR: Draft Amended Report // RR: Re-Review // RRsum: Re-Review Summary // SM: Strategy Memo // Admin: Administrative item

(CB): Christina Burnett || (BH) Bart Heldreth || (MF): Monice Fiume || (PC): Priya Cherian || (WJ): Wilbur Johnson || (PR): Preethi Raj || (JZ): Jinqiu Zhu

ONE HUNDRED FIFTY-FOURTH MEETING

OF THE

EXPERT PANEL FOR COSMETIC INGREDIENT SAFETY

June 8-9, 2020

Microsoft Teams - Virtual Meeting

Expert Panel Members

Wilma F. Bergfeld, M.D., Chair

Donald V. Belsito, M.D.

Curtis D. Klaassen, Ph.D.

Daniel C. Liebler, Ph.D.

James G. Marks, Jr., M.D.

Lisa A. Peterson, Ph.D.

Ronald C. Shank, Ph.D.

Thomas J. Slaga, Ph.D.

Paul W. Snyder, D.V.M., Ph.D.

Liaison Representatives

Consumer

Thomas Gremillion, J.D.

Industry

Alex Kowcz, M.B.A.

Government

Nakissa Sadrieh, Ph.D.

_____

Adopted (Date)

_____

Wilma F. Bergfeld, M.D.

Cosmetic Ingredient Review

Commitment & Credibility since 1976

CIR Staff

Administration
Bart Heldreth, Ph.D. - Executive Director

Monice Fiume, M.B.A. - Senior Director

Carla Jackson - Administrative Coordinator

Subject Matter Expertise
Jinqiu Zhu, Ph.D., D.A.B.T, E.R.T. - Toxicologist

Analysis
Christina L. Burnett, M.S.E.S - Senior Scientific Analyst

Wilbur Johnson, Jr., M.S. - Senior Scientific Analyst

Preethi S. Raj, M.S. - Senior Scientific Analyst

Priya Cherian - Scientific Analyst

Information Services
Kevin Stone Fries, M.L.S. - Information Services Manager

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Others Present at the Meeting

Jean Anjos	Presperse Corp.
Jay Ansell	PCPC
Lara Ferreira Azevedo	NATURA COSMÉTICOS S/A, Brazil
Don Bjerke	P & G
Jeffery C Brown	BASF
Kristen Buon	Presperse Corporation
Jens Burfeindt	IKW e. V., Germany
Anne Corriou	Givaudan
Iris Eschenbacher	La Prairie Group AG
Silvia Perez Damonte	CLAIM
Brenda DeShields	Oxiteno
Ana De Sousa	Student
Carol Eisenmann	PCPC
Michael Fevola	INOLEX, Inc.
Marina Filler	BASF Corporation
Nicholas Georges	Household & Commercial Products Assoc.
Dave Gossai	L'Oréal
M. Grothus	IKW
Lipika Hegde	Estee Lauder
Craig Harvey	Colgate-Palmolive
Birgit Huber	IKW
Jon Lalko	Estee Lauder
Jacob Larson	Herbalife Nutrition
Linda Loretz	PCPC
Zydnia Madera	ET Browne Drug Co., Inc
Michael Maynard	Beiersdorf, LLC
Tim McCraw	Skin Science Advisors, LLC
Bhashkar Mukerji	Givaudan Singapore Pte Ltd
Ryan Nelson	HBW Insight
Alexandra O'Brien	TCC
Stefanie O'Neal	Kao USA, Inc.
Petra Osorio	Vogue International – Johnson & Johnson
David Plimpton	INOLEX
Meche Ragland	KDC/One Columbus
Klaus Rettinger	IKW - The German Cosmetic, Toiletry, Perfumery and Detergent Organization
Bridget Salter	L Brands/Mast Global
Jaideep Sarkar	WNS
Alexandra Scranton	Women's Voices for the Earth
Brooke Silvest	Vogue International - Johnson & Johnson
Amrita Sivia	UC Davis
Amy Smith	DuPont Nutrition & Biosciences
Izabela Staniszewska	Presperse Corporation
Matthew Stewart	R. T. Vanderbilt Holding Company, Inc.
Jan Summers	Sanofi
Romain Tempereau	L'Oréal
Suzana Theophilus	Edgewell Personal Care
Christine Thiffault	Edgewell
Donna Webster	Herbalife Nutrition
Kyara Whaley	Liquid Technologies, Inc.
Michael K.Wyatt	FDA

MINUTES FROM THE 154th EXPERT PANEL MEETING

CHAIRMAN'S OPENING REMARKS

Dr. Bergfeld welcomed the attendees to the 154th meeting of the Expert Panel for Cosmetic Ingredient Safety (Panel) and noted that this is the first virtual meeting of the Panel. She stated that vigorous discussions took place at yesterday's Team meetings. The following 18 ingredient reports were reviewed: 5 Draft Final Reports, 5 Draft Tentative Reports, 3 Draft Amended Reports, and 5 Draft Reports. Dr. Bergfeld announced that the Panel's name has been changed to the Expert Panel for Cosmetic Ingredient Safety, and that the Panel now has their own website. Information posted at the website also includes the Panel's biographies and conflict of interest statement.

Dr. Bergfeld also announced the Expert Panel Grouping/Clustering Working Group that has been established. The focus of this group is to inform the Panel of the composition of ingredient groups that are scheduled for initial review, as well as ingredient additions to established groups. Drs. Daniel Liebler and Lisa Peterson are the current members of this working group.

Finally, Dr. Bergfeld thanked the CIR staff for their immense effort in developing comprehensive ingredient reports for review, and the CIR Science and Support Committee for their participation in the review process. She also thanked the Panel for their hard work.

APPROVAL OF MINUTES

The minutes of the December 9-10, 2019 (153rd) Expert Panel meeting were approved.

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 number of firsts for the Panel. Prominently, this was the first ever virtual meeting for the Panel, and it was a complete success.

Secondly, the name of the Panel is henceforth changed from the CIR Expert Panel to the Expert Panel for Cosmetic Ingredient Safety. Much like members of an FDA Advisory Committee for pharmaceutical assessments are not employees of FDA, members of the Panel are not employees of CIR. This change in name was intended to be a first step in clarifying that distinction. Further to that end, a new website has been created exclusively for the Panel: https://ingredientsafetyexpertpanel.org/. Therein, the mission, composition, and an explanation of the Panel's definition of a conflict of interest, are now publicly available.

Sadly, the September 2020 meeting will be the last meeting with Dr. Marks serving as a member of this Panel, as he is retiring therefrom. Accordingly, Dr. Heldreth is seeking nominations to fill this seat on the Panel. Nominees should be experts in dermatology and have no conflicts of interest as defined at https://ingredientsafetyexpertpanel.org/conflict-of-interest-statement/. Nominations may be submitted to https://www.cir-safety.org/, no later than June 26, 2020.

Final Safety Assessments

Palm (açai and juçara)-Derived Ingredients

The Expert Panel for Cosmetic Ingredient Safety (Panel) concluded that the following 8 palm tree (*Euterpe edulis* (juçara) and *Euterpe oleracea* (açaí)-derived) ingredients are safe in cosmetics in the present practices of use and concentration described in the safety assessment, and issued a final report.

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

** 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's conclusion on these ingredients was made by taking into consideration the available toxicity data and similarities in composition. Although there was an absence of compositions data for Hydrolyzed Euterpe Oleracea Fruit, the Panel determined that the available composition data on Euterpe Oleracea Fruit Extract and *Euterpe oleracea* fruit were comparable. It should be noted that, at the December 2019 Panel meeting, the Panel concluded that the available data were insufficient to make a determination that Euterpe Oleracea Palm Heart Extract was safe under the intended conditions of use in cosmetic formulations. The data needs were as follows:

- Composition data
    - If the composition of this ingredient is found to be significantly different from the other ingredients in this group, skin irritation and sensitization data would be needed

The Panel subsequently determined that the need for these data is mitigated, after making the following observations: Palm heart ("hearts of palm") is edible and a commonly consumed part of the palm tree, and there is a lack of consumption-related adverse event reports, such as contact sensitization or colitis, in both the published literature and clinical experience. Additionally, the available data indicate that cosmetic use concentrations of Euterpe Oleracea Palm Heart Extract are rather low, i.e., up to 0.001% in both rinse-off and leave-on products. Therefore, the Panel concluded that Euterpe Oleracea Palm Heart Extract is also safe in the present practices of use and concentration.

Vanilla-Derived Ingredients

The Panel issued a final report with the conclusion that the following 7 vanilla-derived ingredients are safe in the present practices of use and concentration described in the safety assessment when formulated to be non-sensitizing:

Vanilla Planifolia Fruit Extract
Vanilla Planifolia Fruit Oil
Vanilla Planifolia Fruit Water
Vanilla Planifolia Seed*
Vanilla Planifolia Seed Powder
Vanilla Tahitensis Fruit Extract
Vanilla Tahitensis Seed*

**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*.

While the available human skin sensitization data on Vanilla Planifolia Fruit Extract and Vanilla Tahitensis Fruit Extract are negative, final product formulations may contain multiple botanicals, each possibly containing the same constituents of concern. Thus, 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.

Concern was mitigated for the positive (++) photo-patch test reactions to vanilla extract which were observed in a photodermatitis patient, because the strength of the reaction at photo-irradiated and non-irradiated sites was the same. Therefore, it was agreed that the observed test results were not due to a photosensitization reaction.

However, the Panel also concluded that the available data are insufficient to make a determination that the following 2 ingredients are safe under the intended conditions of use in cosmetic formulations:

Vanilla Planifolia Flower Extract
Vanilla Planifolia Leaf Cell Extract

The data needed to determine the safety of these 2 ingredients comprise:

- Method of manufacture and impurities

- Composition
- Concentration of use
- 28-day dermal toxicity
    - Depending on the results, other toxicological endpoints may be needed (e.g., genotoxicity and DART)

***Punica granatum* (Pomegranate)-Derived Ingredients**

The Panel issued a final report with the conclusion that the following 9 ingredients are safe in the present practices of use and concentration described in the safety assessment.

Punica Granatum Flower Extract
Punica Granatum Fruit Extract
Punica Granatum Fruit Juice
Punica Granatum Fruit Water
Punica Granatum Juice Extract
Punica Granatum Pericarp Extract
Punica Granatum Seed
Punica Granatum Seed Extract
Punica Granatum Seed Powder

The Panel noted data that indicate that extracts of parts of *Punica granatum* may have a skin lightening effect. Skin lightening is considered to be a drug effect and should not occur during the use of cosmetic products. Based on the concentration of use of these extracts in cosmetic products, the known mechanism of action, the results of an in vitro study, and clinical experience, the Panel was not concerned that these ingredients would have these effects in cosmetic products, as they are reported to be used in this safety assessment.

The Panel also concluded that the data were insufficient to support a determination of safety for the following 9 ingredients:

Punica Granatum Extract‡
Punica Granatum Bark Extract
Punica Granatum Bark/Fruit Extract*
Punica Granatum Callus Culture Extract*
Punica Granatum Fruit/Root/Stem Powder*
Punica Granatum Fruit/Sucrose Ferment Filtrate*
Punica Granatum Leaf Cell Extract*
Punica Granatum Peel Extract*
Punica Granatum Seed Cell Culture Lysate*

‡ Ingredient has been deleted from the Dictionary, but uses are currently reported to the FDA Voluntary Cosmetic Registration Program (VCRP).
** Uses not reported.*

The additional data needed for these cosmetic ingredients are:

- Method of manufacturing with regard to solvent-type used for the extracts
- Composition and impurities data
- Systemic toxicity data
- Dermal irritation and sensitization data.

Soy-Derived Ingredients

The Panel issued a final report with the conclusion that 24 of the 28 soy-derived ingredients are safe in the present practices of use and concentration described in the safety assessment.

Glycine Max (Soybean) Fiber*
Glycine Max (Soybean) Flower/Leaf/Stem Juice*
Glycine Max (Soybean) Leaf Cell Extract*
Glycine Max (Soybean) Leaf Extract*
Glycine Max (Soybean) Phytoplacenta Extract
Glycine Max (Soybean) Pulp*
Glycine Max (Soybean) Seed Extract
Glycine Max (Soybean) Seedcake Extract*

Glycine Max (Soybean) Seedcoat Extract*
Glycine Max (Soybean) Seed Powder*
Glycine Max (Soybean) Sprout Extract
Glycine Soja (Soybean) Extract
Glycine Soja (Soybean) Fiber*
Glycine Soja (Soybean) Flour
Glycine Soja (Soybean) Germ Extract
Glycine Soja (Soybean) Hull*
Glycine Soja (Soybean) Lipids
Glycine Soja (Soybean) Phytoplacenta Extract*
Glycine Soja (Soybean) Seed
Glycine Soja (Soybean) Seedcake Extract*
Glycine Soja (Soybean) Seed Extract
Glycine Soja (Soybean) Seed Powder*
Glycine Soja (Soybean) Seed Water*
Glycine Soja (Soybean) Sprout Extract

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

The Panel determined that there would be no concern for systemic toxicity, as these ingredients have historical food use, and, exposure via oral ingestion would be much higher than exposure from cosmetics. In addition, the Panel considered the reproductive effects following oral ingestion of soybean and soybean extract; however, the effects were likely attributed to the isoflavone and phytoestrogen content. Concern for these reproductive effects was mitigated considering the total isoflavone and phytoestrogen content would be relatively low in cosmetics, and dermal exposure to these ingredients would be far lower than oral exposure.

However, the Panel determined there were insufficient data to determine the safety of the remaining 4 ingredients.

Glycine Max (Soybean) Callus Culture*
Glycine Max (Soybean) Callus Culture Extract*
Glycine Max (Soybean) Callus Extract*
Glycine Max (Soybean) Phytoplacenta Conditioned Media

The insufficiencies include a lack of:

- Composition
- Impurities
- Method of manufacture
- 28-day dermal toxicity
- Sensitization/irritation data

Honey-Derived Ingredients

The Panel issued a final report with the conclusion that Honey, Honey Cocoates, Honey Powder, Honey Extract, Hydrogenated Honey, Hydrolyzed Honey, and Hydrolyzed Honey Protein are safe in the present practices of use and concentration as described in the safety assessment. The safety of these ingredients is supported by negative sensitization data, historical food use, and use in wound dressings, without adverse effects.

Tentative Safety Assessments

Adenosine Ingredients

The Panel issued a tentative report for public comment with the conclusion that Adenosine, Adenosine Phosphate, Adenosine Triphosphate, Disodium Adenosine Phosphate, and Disodium Adenosine Triphosphate are safe in the present practices of use and concentration described in the safety assessment. The safety of this ingredient group is supported by sufficient impurities data, negative animal oral toxicity assays, negative human dermal irritation/sensitization assays, and low concentrations of use.

According to data received in 2020 from the FDA VCRP, Adenosine, Adenosine Phosphate, Adenosine Triphosphate, and Disodium Adenosine Triphosphate are reported to be used in 905, 96, 42, and 116 formulations, respectively. The results of a concentration of use survey conducted by the Personal Care Products Council (Council) indicate that Adenosine has the highest concentration of use; it is used at up to 1% in body and hand products.

Methylisothiazolinone (MI)

The Panel issued a tentative amended report with the conclusion that MI is safe for use in rinse-off cosmetic products at concentrations up to 100 ppm and safe in leave-on cosmetic products when formulated to be non-sensitizing, which may be determined based on a quantitative risk assessment (QRA) or similar methodology.

The Panel's recommendations for MI in rinse-off and leave-on cosmetic products are intended to prevent the induction of sensitization to MI. The Panel cautioned that following these recommendations may not necessarily prevent the elicitation of allergic reactions in individuals who are already allergic to MI. Individuals sensitized to MI should avoid products that contain MI.

In response to concerns of reports of adverse events observed in infants following inhalation exposure to humidifier disinfectants that contained the preservative mixture Methylchloroisothiazolinone/Methylisothiazolinone (MCI/MI), the Panel moved to reopen the safety assessment of MI in September 2019. A search for inhalation toxicity data regarding MI (separate from the combination of MCI/MI) did not yield any new published literature, aside from the papers already detailed in the MCI/MI report. The Panel reviewed these data as well as the findings of a draft risk assessment for MCI/MI, and a hazard characterization of isothiazolinones produced by the US Environmental Protection Agency, and determined that these data mitigated concern for the use of this ingredient at the reported use and concentrations in cosmetic products that could be incidentally inhaled following use.

Wheat-Derived Ingredients

The Panel issued a tentative report with the conclusion that the data are insufficient to support a determination of safety for the following 27 ingredients:

Triticum Aestivum (Wheat) Flour Lipids
Triticum Aestivum (Wheat) Germ Extract
Triticum Aestivum (Wheat) Leaf Extract
Triticum Aestivum (Wheat) Peptide
Triticum Aestivum (Wheat) Seed Extract
Triticum Monococcum (Wheat) Seed Extract
Triticum Monococcum (Wheat) Stem Water
Triticum Spelta Seed Water
Triticum Turgidum Durum (Wheat) Seed Extract
Triticum Vulgare/Aestivum (Wheat) Grain Extract
Triticum Vulgare (Wheat) Bran
Triticum Vulgare (Wheat) Bran Extract
Triticum Vulgare (Wheat) Bran Lipids
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 data
- Dermal irritation and sensitization data at or above 13% for Triticum Vulgare (Wheat) Sprout Extract.

Glycerin Ethoxylates

The Panel issued a tentative report with the conclusion that the data are insufficient to support a determination of safety for the following 8 glycerin ethoxylate ingredients:

Glycereth-3
Glycereth-7
Glycereth-8
Glycereth-12
Glycereth-18
Glycereth-20
Glycereth-26
Glycereth-31

Previously submitted summary HRIPT data, with test materials 2% Glycereth-7 and 3% Glycereth-26, did not elucidate whether low-level reactions reported during induction and/or challenge occurred repeatedly in the same, or different, participants. Consequently, the Panel issued a second insufficient data announcement (IDA), at the December 2019 meeting, for participant-level, experimental data for these HRIPTs, or, new, complete, experimental data with n ≥ 100 participants. The Panel was especially interested in receiving complete experimental data for an HRIPT done with the maximum reported concentration of use for the ingredient with the highest reported use, namely, 6% Glycereth-26.

In response to the second IDA, the Panel received details for 2 previously submitted 0.35% and 5% Glycereth-26 HRIPT summaries, and a new HRIPT study, with individual-level data for 10% Glycereth-26, in 200 participants, in which there were no positive reactions. However, the Panel concluded that the quality of the existing data still do not fully support the dermal sensitization safety of these ingredients. Hence, the Panel issued a tentative report with an insufficient conclusion for dermal sensitization.

The Panel issued a tentative amended report for public comment with the conclusion that these 30 ingredients are safe when formulated to be non-irritating to the skin and eye.

Stearoxy Dimethicone
Dimethicone
Methicone
Amino Bispropyl Dimethicone
Aminopropyl Dimethicone
Amodimethicone
Amodimethicone Hydroxystearate
Behenoxy Dimethicone
C24-28 Alkyl Methicone
C30-45 Alkyl Methicone
C30-45 Alkyl Dimethicone
Cetearyl Methicone
Cetyl Dimethicone
Dimethoxysilyl Ethylenediaminopropyl Dimethicone
Hexyl Methicone
Hydroxypropyldimethicone
Stearamidopropyl Dimethicone
Stearyl Dimethicone
Stearyl Methicone
Vinyl Dimethicone
Capryl Dimethicone*
Hexyl Dimethicone*
C20-24 Alkyl Dimethicone*
C24-28 Alkyl Dimethicone*
C26-C28 Alkyl Dimethicone*
C30-60 Alkyl Dimethicone*
C32 Alkyl Dimethicone*
Caprylyl Methicone*
C20-24 Alkyl Methicone*
C26-28 Alkyl Methicone*

The Panel first published a review of 20 of these ingredients in 2003, wherein due to large molecular weights and low concentrations of use, this ingredient family was deemed safe as used in cosmetics. In accordance with CIR Procedures, the Panel re-considered these ingredients after 15 years, at the December 2019 meeting. Updated data revealed a dramatic increase in current frequency and concentrations of use, especially in products that might be inhaled, contributing to potential inhalation toxicity concerns. The Panel, therefore, determined to re-open this safety assessment. The CIR Science & Support Committee (SSC) proposed the addition of Simethicone and 10 additional alkyl dimethicone and methicone ingredients (marked with a "*" above). The Panel decided to exclude Simethicone from this review, due to the additional data needs for chemical identity and inhalation toxicity potential of the silica used in cosmetic Simethicone. The Panel's above conclusion on these 30 ingredients is based, in part, upon data suggesting possible ocular irritation resulting from incidental exposure to products used near the eye, especially those containing Dimethicone at concentrations comparable to the maximum reported concentration of use for this category, 37.8%.

Scutellaria baicalensis-Derived Ingredients

The Panel concluded that the following 2 *Scutellaria baicalensis*-derived ingredients are safe in cosmetics in the present practices of use and concentration described in the safety assessment:

Scutellaria Baicalensis Root Extract
Scutellaria Baicalensis Root Powder*

** Not reported to be in current use. Were this ingredient not in current use to be used in the future, the expectation is that it would be used in product categories and at concentrations comparable to the root extract.*

However, the Panel also concluded that the available data are insufficient to make a determination that the following 2 ingredients are safe under the intended conditions of use in cosmetic formulations:

Scutellaria Baicalensis Extract Scutellaria Baicalensis Sprout Extract

The data needed to determine the safety of these 2 ingredients comprise:

- Genotoxicity (in vitro and mammalian); methanol and aqueous extracts should be tested
- Phototoxicity
- Skin irritation and sensitization
- For Scutellaria Baicalensis Extract
    - 28-day dermal toxicity; if dermal absorption occurs, additional data may be needed
- For Scutellaria Baicalensis Sprout Extract
    - Method of Manufacture
    - Composition
    - Impurities
    - Dermal absorption; if dermal absorption occurs, additional data may be needed

In in vitro experiments involving B16F10 mouse melanoma cell cultures, Scutellaria baicalensis root extracts (both the ethanol extract and methanol extract) had an inhibitory effect on melanogenesis. However, in other experiments involving Scutellaria baicalensis root extracts obtained using other extractants (n-hexane, ethyl acetate, and water), an inhibitory effect on melanogenesis in B16F10 mouse melanoma cells was not observed. Given these findings, the Panel noted that if an effect on melanogenesis is observed in a cell culture system only, then a no-effect-level from an in vivo experiment would be needed to determine whether or not Scutellaria Baicalensis Root Extract has any effect on melanogenesis. The Panel also noted that skin lightening is considered to be a drug effect, and should not occur during the use of cosmetic products. Because of that caveat and based on the low concentrations of use of Scutellaria Baicalensis Root Extract in cosmetic products, the results of these in vitro experiments on Scutellaria baicalensis root extracts, and clinical experience of the Panel members, concern for this effect in cosmetics was mitigated.

Ascorbyl Glucoside and Sodium Ascorbyl Glucoside

The Panel concluded that the following ingredients are safe in cosmetics in the present practices of use and concentration described in the safety assessment and issued a tentative report.

Ascorbyl Glucoside Sodium Ascorbyl Glucoside*

* *Not reported to be in current use. Were this ingredient not in current use to be used in the future, the expectation is that it would be used in product categories and at concentrations comparable to Ascorbyl Glucoside.*

The Panel noted the absence of developmental and reproductive toxicity data on Ascorbyl Glucoside and Sodium Ascorbyl Glucoside. However, concern over the lack of these data were mitigated considering that Ascorbyl Glucoside is metabolized to ascorbic acid and glucose in the skin and would not be absorbed in an appreciable quantity.

The Panel also noted the potential for skin lightening effects and that skin lightening is considered to be a drug effect, and should not occur during the use of cosmetic products. Furthermore, based on the low current use concentrations in cosmetic products, the results of an in vitro experiment, and clinical experience, concern for this effect in cosmetics was mitigated.

Caprylhydroxamic Acid

The Panel issued a tentative report for public comment with the conclusion that Caprylhydroxamic Acid is safe in cosmetics in the present practices of use and concentration described in this safety assessment. The Panel was concerned about inconsistent outcomes regarding dermal sensitization. However, upon further review, the Panel determined that studies that had positive sensitization results were those in which the test substance included a

penetration enhancer. Additionally, the Panel noted that cases of increased sensitization with use of a moisturizer in Finland, that had been reformulated to include Caprylhydroxamic Acid, appeared to be related to use on damaged skin, which most likely resulted in increased penetration. Therefore, the Panel stated that caution should be taken with use of Caprylhydroxamic Acid in a manner that would result in increased penetration, such as formulation with penetration enhancers. This is especially important in product types with a margin of safety (MOS), based on an acceptable exposure level/consumer exposure level ratio (AEL/CEL) at or near 1, as calculated in a QRA. According to the results of a QRA 2.0 that was submitted to CIR, product types with an AEL/CEL of 1 include baby lotions, oils, and creams.

Insufficient Data Announcements

Papaya-Derived Ingredients

The Panel issued an insufficient data announcement for the following *Carica papaya* (Papaya) derived ingredients:

Carica Papaya (Papaya) Fruit	Carica Papaya (Papaya) Fruit Juice	Carica Papaya (Papaya) Leaf Extract.
Carica Papaya (Papaya) Fruit Extract	Carica Papaya (Papaya) Fruit Water	

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

- For Carica Papaya (Papaya) Fruit Extract
    - Irritation and sensitization on at the reported maximum use concentration of 0.25%
        - Such data might be applicable as a read-across source for the other Carica papaya fruit ingredients
- For Carica Papaya (Papaya) Leaf Extract
    - Impurities
    - Genotoxicity
    - Irritation/sensitization

Basic Brown 17

The Panel issued an IDA for the hair dye ingredient, Basic Brown 17. The additional data needs for this ingredient are:

- Concentration of use and reported function for the non-coloring hair product uses that were reported in the FDA VCRP database.

Tris(Tetramethylhydroxypiperidinol) Citrate

The Panel issued an IDA for the ingredient Tris(Tetramethylhydroxypiperidinol) Citrate. The additional data need for this ingredient are:

- Method of manufacture
- Impurities

The Council proposed the addition of available data related to the cosmetic ingredient, Hydroxy Tetramethylpiperidine Oxide, and the non-ingredient, 2,2,6,6-tetramethyl-4-piperidine-*N*-oxide, as read-across sources. The Panel noted the analogous structural features and radical scavenging activity of Tris(Tetramethylhydroxypiperidinol) Citrate, Hydroxy Tetramethylpiperidine Oxide, and 2,2,6,6-tetramethyl-4-piperidine-*N*-oxide, and agreed to these additions.

Re-Reviews

Quaternium-18 and Quaternium-18 Bentonite

The Panel concluded that the reopened safety assessment on Quaternium-18 and Quaternium-18 Bentonite should not advance within the CIR review process, and that a re-review summary should be developed, confirming their prior conclusion. The Panel first reviewed the safety of Quaternium-18 and Quaternium-18 Bentonite in 1982 and concluded that these ingredients are safe as used. In 2001, after considering new studies and updated use data on these ingredients, the Panel confirmed the original conclusion. Because it was at least 15 years since the last review, the Panel re-reviewed Quaternium-18 and Quaternium-18 Bentonite at the September 2019 meeting, and determined to re-open the safety assessment to evaluate the sufficiency of inhalation data on Quaternium-18 Bentonite.

After evaluating the new data and original reports, at the June 2020 meeting, the Panel reaffirmed the original conclusion of safe as used for Quaternium-18 and Quaternium-18 Bentonite. The Panel felt the acute inhalation toxicity study was sufficient to support the use of Quaternium-18 Bentonite in cosmetics, as no toxic effects were observed when animals were exposed to a high concentration of the test substance for a prolonged period of time. In cosmetics, exposure to Quaternium-18 Bentonite in potentially inhaled products would be brief and at low concentration. In addition, the concentrations and number of uses for both Quaternium-18 and Quaternium-18 Bentonite have decreased since 2001. Quaternium-18 Bentonite was previously reported to be used at up to 9% in leave-on products, however, according to 2018 concentration of use data, Quaternium-18 Bentonite is reported to be used at up to 2.5% in leave-on products. The Panel considered the concern for developmental/reproductive toxicity or genotoxicity mitigated by the lack of dermal penetration, chronic oral toxicity, and dermal toxicity.

Sulfites

The Panel concluded that the reopened safety assessment on the following 7 sulfites should not advance within the CIR review process, and that a re-review summary should be developed, confirming their prior conclusion.

Ammonium Bisulfite	Potassium Sulfite	Sodium Sulfite
Ammonium Sulfite*	Sodium Bisulfite	
Potassium Metabisulfite	Sodium Metabisulfite	

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

The Panel 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 new studies and updated use data on these ingredients at the September 2019 Panel meeting. Furthermore, the Panel considered the increased ingredient use frequency, reports of dermal sensitization, enhanced asthmatic responses to dust mites, and mutagenic effects in the published literature.

The Panel's concern about sulfite-induced dermal sensitization, following a review of patient studies, was allayed after considering negative results from two HRIPTs on Sodium Sulfite at concentrations greater than 0.25% (the highest reported concentration in leave-on products) in healthy subjects. The Panel noted that results from a patient population are difficult to interpret in terms of their relevance to the general population, and, also, that reactions to sulfites on standard panels used by dermatologists are rare. However, the Panel acknowledged that sulfites may cause hypersensitivity, as evidenced by the enhancement of allergic sensitization (i.e., IgE-mediated allergy) in dust mite allergen-sensitized BALB/c mice. Additionally, the Panel noted that sulfites are associated with IgE-mediated allergic reactions in some individuals, and that individuals with sulfite allergies should exercise caution in using products containing sulfites that may be incidentally inhaled.

After considering that positive genotoxicity results (sister chromatid exchanges) were observed at the highest dose tested, the Panel agreed that such a high dose would not be achieved during cosmetic product use. Furthermore, the Panel noted that the weight of evidence for sulfite-induced carcinogenicity in animal models is negative, and that the

International Agency for Research on Cancer has concluded that there is inadequate evidence for the carcinogenicity of sulfites in experimental animals and humans. The mitigation of concern by the Panel over the potential toxicity of sulfites from cosmetic exposure is also based on the use of these ingredients at low concentrations and the low potential for absorption.

Draft 2021 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 13 (in response to a Freedom of Information Act request).

While this list includes only the lead ingredients, groupings of botanical, or other organism-sourced mixture-type, ingredients (e.g., Rosa Centifolia Flower Extract), were drafted in the meeting materials for potential inference groupings, based on species and plant part(s). However, for organic chemicals, the list of lead ingredients was forwarded to the newly convened CIR Grouping/Clustering Working Group for consideration. The Working Group's input will be incorporated into the Draft Final 2021 Priorities, to be presented at the September 2020 meeting.

There are 11 reports proposed (2 of the lead ingredients below are proposed to be reviewed together in 1 report) on the 2021 Draft Priorities List. Reports previously prioritized and on the CIR docket at the end of 2020, as well as a number of re-reviews of previous assessments, will supplement the total number of reports to be assessed in 2021.

Ingredients	**Frequency of Use (FOU) Data Year 2020**
For cause	
Basic Yellow 57 – a hair dye	45
Per FOU	
Yeast Extract	736
Glyceryl Acrylate/Acrylic Acid Copolymer	519
Hydroxyacetophenone	409
Glyceryl Polymethacrylate	364
Acrylates/Octylacrylamide Copolymer	361
Hydroxypropyl Starch Phosphate	353
Sodium Lauroamphoacetate	344
Zingiber Officinale (Ginger) Root Extract	326
Leuconostoc/Radish Root Ferment Filtrate	322
Rosa Centifolia Flower Extract	321
Phytosteryl/Octyldodecyl Lauroyl Glutamate	313

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
- Toxicokinetics data, specifically dermal absorption and/or penetration
- Repeated-dose toxicity data
- Inhalation toxicity data, if the ingredient is used in a product that can be incidentally inhaled
- Reproductive/developmental 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.

Quaternium-18 and Quaternium-18 Bentonite

The Expert Panel for Cosmetic Ingredient Safety (Panel) first published the safety assessment of Quaternium-18, Quaternium-18 Bentonite, and Quaternium-18 Hectorite in 1982 and concluded that these ingredients are safe as used.[1] In 2003, after considering new studies and updated use data on these ingredients, the Panel determined to not re-open the safety assessment.[2] In 2019, Quaternium-18 and Quaternium-18 Bentonite were again re-reviewed, and it was determined to re-open the safety assessment to evaluate the sufficiency of inhalation data on Quaternium-18 Bentonite. Additionally, an exhaustive search of the world's literature was performed for studies dated 1995 forward. No relevant published data were found; however unpublished data provided by the Personal Care Products Council regarding Quaternium-18 Bentonite were provided.[3] (Some of the data provided were already included in the original report.)

However, at the June 2020 meeting, the Panel determined the data on Quaternium-18 and Quaternium-18 Bentonite was sufficient to re-affirm the original conclusion that these ingredients are safe as cosmetic ingredients in the present practices of use and concentration as given in Table 1. The Panel felt the acute inhalation toxicity study was sufficient to support the use of Quaternium-18 Bentonite in cosmetics, as no toxic effects were observed when animals were exposed to a high concentration of the test substance for a prolonged period of time. In cosmetics, exposure to Quaternium-18 Bentonite in potentially inhaled products would be short, and of a low concentration. In addition, the concentrations and number of uses for both Quaternium-18 and Quaternium-18 Bentonite have decreased since 2001. Quaternium-18 Bentonite was previously reported to be used at up to 9% in leave-on products, however, according to 2018 concentration of use data, Quaternium-18 Bentonite is reported to be used at up to 2.5% in leave-on products. The Panel also mitigated the concern for developmental/reproductive toxicity or genotoxicity, as these ingredients would not result in dermal penetration and have shown no evidence of chronic oral or dermal toxicity.

It should be noted that Quaternium-18 Hectorite was also included in the 1982 safety assessment and 2001 re-review. However, Quaternium-18 Hectorite is not included in the current assessment because it was recently (2013) part of a separate assessment (Safety Assessment of Ammonium Hectorites as Used in Cosmetics).[4] In that assessment, Quaternium-18 Hectorite was determined to be safe as used in cosmetics in the present practices of use and concentration.

Table 1. Current and historical frequency and concentration of use of Quaternium-18 and Quaternium-18 Bentonite

	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	Quaternium-18				**Quaternium-18 Bentonite**			
	2020[5]	**2001[2]**	**2018[6]**	**2001[2]**	**2020[5]**	**2001[2]**	**2018[6]**	**2001[2]**
Totals*	**70**	**90**	**0.46 – 0.95**	**0.1 - 2**	**200**	**221**	**0.15 – 2.5**	**0.8 - 9**
Duration of Use								
Leave-On	*18*	*27*	*0.46*	*0.1 – 2*	*200*	*218*	*0.15 – 2.5*	*0.8 - 9*
Rinse-Off	*53*	*63*	*0.76 – 0.95*	*1 – 2*	*NR*	*3*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	NR	1	NR	NR	72	70	NR	4 – 9
Incidental Ingestion	2	NR	NR	0.7	108	138	NR	5
Incidental Inhalation-Spray	15[a]	1; 3[a]	0.46[a]	0.1 – 2[a]	3[a]; 1[c]	1[a]	2.5[a]	5[a]
Incidental Inhalation-Powder	NR	NR	NR	NR	2	NR	0.29[b]	NR
Dermal Contact	1	16	NR	NR	87	79	0.29 - 1	0.8 – 6
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	0.6[d]	NR
Hair - Non-Coloring	66	68	0.46 – 0.95	0.1 – 2	3	NR	2.5	NR
Hair-Coloring	1	1	NR	NR	NR	NR	NR	NR
Nail	NR	5	NR	NR	2	NR	0.15 – 0.25	NR
Mucous Membrane	2	1	NR	0.7	108	141	NR	5
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

*Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.

[a] It is possible these products are sprays, but it is not specified whether the reported uses are sprays.

[b] It is possible these products are powders, but it is not specified whether the reported uses are powders.

[c] Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, there fore the information is captured in both categories

[d] Formulated as a spray

NR – no reported use

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3. Elementis Specialties. 2015. BENTONE ® (INCI: Quaternium-18 Bentonite): Toxicity dossier. (Unpublished data submitted by the Personal Care Products Council on August 7, 2015.)

4. Becker LC, Bergfeld WF, Belsito DV, et al. Safety Assessment of Ammonium Hectorites as Used in Cosmetics. *International Journal of Toxicology.* 2013;32:33S-40S.

5. U.S. Food and Drug Administration Center for Food Safety & Applied Nutrition (CFSAN). 2020. Voluntary Cosmetic Registration Program - Frequency of Use of Cosmetic Ingredients. College Park, MD. ((Obtained under the Freedom of Information Act from CFSAN; requested as "Frequency of Use Data" January 6, 2020; received January 13, 2020).)

6. Personal Care Products Council. 2018. Council Concentration of Use by FDA Product Category: Quaternium-18 Compounds. *(Unpublished data submitted by the Personal Care Products Council on October 2, 2018)*.

Sulfites

The Expert Panel for Cosmetic Ingredient Safety (Panel) first published the Final Report on the Safety Assessment of Sulfites in 2003.[1] The Panel concluded that "Sodium Sulfite, Potassium Sulfite, Ammonium Sulfite, Sodium Bisulfite, Ammonium Bisulfite, Sodium Metabisulfite, and Potassium Metabisulfite are safe as used in cosmetic formulations." At the September 2019 meeting, the Panel reviewed data identified published since 1998.[2-62] The Panel also considered updated information regarding product types and ingredient use frequencies as reported in the US Food and Drug Administration (FDA) Voluntary Cosmetic Registration Program (VCRP) database,[10] and the maximum use concentrations provided by the Personal Care Products Council (Council).[11] Upon review, the Panel initially determined that the safety assessment should be reopened based on the following concerns: 1) increased ingredient use frequency; 2) reports of contact sensitization; 3) the need for clarification of enhanced asthmatic responses to dust mites; and 4) the need for clarification of mutagenic effects in the published literature.

However, at the June 2020 meeting, the Panel determined to not reopen this safety assessment, and reaffirmed the original conclusion that these ingredients are safe as used in cosmetic formulations, as given in Table 1. Frequency of use has increased substantially for Sodium Sulfite since the original review; in the 2003 report, 911 uses were reported, and in 2020, this ingredient was reported to have 1713 uses.[10] Sodium Metabisulfite also had a substantial increase in reported use frequency, from 348 uses in 2003 to 916 uses in 2020. The maximum concentration of use reported for this family of ingredient has decreased; in the 2003 report, Sodium Metabisulfite had the highest use concentration (14% in rinse-off products);[1] in 2019, this ingredient was reported being used at substantially lower concentrations of up to 0.6% in rinse-off products.[11] The sulfite with the highest reported use concentration in 2019 was Sodium Sulfite, at concentrations up to 3% in rinse-off products. (This is the same use concentration reported for this ingredient in the 2003 report.[1])

The Panel's concern about sulfite-induced contact sensitization, following a review of patient studies, was allayed after considering negative results from two human repeated insult patch tests on Sodium Sulfite at concentrations greater than 0.25% (highest reported use concentration in leave-on products) in normal subjects. The Panel noted that results from a patient population are difficult to interpret in terms of their relevance to the general population, and, also, that few reactions to sulfites on standard panels used by dermatologists are being reported. However, they acknowledged that sulfites can cause hypersensitivity, as evidenced by the enhancement of allergic sensitization in dust mite allergen-sensitized BALB/c mice. Additionally, the Panel noted that sulfites are associated with IgE-mediated allergic reactions in some individuals, and that individuals with sulfite allergies should exercise caution in using products containing sulfites that may be incidentally inhaled. The lack of awareness of asthmatic responses to topical cosmetics was also acknowledged by the Panel.

After considering that positive genotoxicity results (sister chromatid exchanges) were observed at the highest dose tested, the Panel agreed that such a high dose would not be achieved during cosmetic product use. Furthermore, the Panel noted that the weight of evidence for sulfite-induced carcinogenicity in animal models is negative, and that the International Agency for Research on Cancer has concluded that there is inadequate evidence for the carcinogenicity of sulfites, bisulfites, and metabisulfites in experimental animals and humans. The minimal concern by the Panel over the potential toxicity of sulfites from cosmetic exposure is also based on the use of these ingredients at low concentrations and the low potential for absorption.

Table 1. Current and historical frequency and concentration of use of Sulfites according to duration and exposure.

	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	Ammonium Bisulfite				**Potassium Metabisulfite**			
	2020[10]	**2003[1]**	**2019[11]**	**2003[1]**	**2020[10]**	**2003[1]**	**2019[11]**	**2003[1]**
Totals*	**1**	**NR**	**NR**	**32**	**NR**	**1**	**0.35**	**NR**
Duration of Use								
Leave-On	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Rinse-Off	*1*	*NR*	*NR*	*32*	*NR*	*1*	*0.35*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Powder	NR	NR	NR	NR	NR	NR	NR	NR
Dermal Contact	NR	NR	NR	NR	NR	NR	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	1	NR	NR	32	NR	1	0.35	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR
	Potassium Sulfite				**Sodium Bisulfite**			
	2020[10]	**2003[1]**	**2019[11]**	**2003[1]**	**2020[10]**	**2003[1]**	**2019[11]**	**2003[1]**
Totals*	**2**	**1**	**NR**	**NR**	**74**	**58**	**0.0013-0.1**	**0.03-0.7**
Duration of Use								
Leave-On	*2*	*NR*	*NR*	*NR*	*50*	*6*	*0.0013-0.1*	*0.03-0.3*
Rinse-Off	*NR*	*1*	*NR*	*NR*	*24*	*51*	*0.013*	*0.1-0.7*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*1*	*NR*	*NR*
Exposure Type								
Eye Area	NR	NR	NR	NR	8	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	1[a]	NR	NR	NR	11[a];24[c]	1[a]	0.0013[a]	0.03[a];0.05[c]
Incidental Inhalation-Powder	NR	NR	NR	NR	24[c]	NR	0.02[b]	0.05[c]
Dermal Contact	2	NR	NR	NR	69	7	0.02	0.05-0.3
Deodorant (underarm)	1[a]	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	1	NR	NR	5	2	0.0013-0.1	0.03
Hair-Coloring	NR	NR	NR	NR	NR	49	NR	0.7
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	15	1	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR
	Sodium Metabisulfite				**Sodium Sulfite**			
	2020[10]	**2003[1]**	**2019[11]**	**2003[1]**	**2020[10]**	**2003[1]**	**2019[11]**	**2003[1]**
Totals*	**916**	**348**	**0.000005-0.6**	**0.003-14**	**1713**	**911**	**0.000001-3**	**0.01-3**
Duration of Use								
Leave-On	*326*	*28*	*0.0001-0.25*	*0.003-0.4*	*129*	*3*	*0.0000051-0.12*	*0.1-0.4*
Rinse-Off	*590*	*312*	*0.000005-0.6*	*0.1-14*	*1583*	*906*	*0.000001-3*	*0.01-3*
Diluted for (Bath) Use	*NR*	*8*	*NR*	*NR*	*1*	*2*	*NR*	*NR*
Exposure Type								
Eye Area	28	1	0.003-0.03	NR	12	NR	0.03	NR
Incidental Ingestion	NR	NR	0.003	NR	NR	NR	0.0015	NR
Incidental Inhalation-Spray	125[a];115[c]	12[a];2[c]	0.02-0.25	0.003-0.3[a];0.003[c]	45[a];41[c]	NR	0.0000051-0.002[a]	0.1[a]
Incidental Inhalation-Powder	115[c]	2[c]	0.0001;0.001-0.12[b]	0.003[c]	41[c]	NR	0.00001-0.12[b]	NR
Dermal Contact	324	34	0.0001-0.25	0.003-0.4	170	5	0.00001-3	0.1-0.4
Deodorant (underarm)	NR	7[a]	0.04	0.1[a]	6	NR	NR	NR
Hair - Non-Coloring	8	3	0.000005-0.00011	0.1-14	16	12	0.000001-0.35	0.01
Hair-Coloring	537	310	0.29-0.6	NR	1525	893	0.05-1.1	0.5-3
Nail	1	1	NR	NR	1	1	NR	NR
Mucous Membrane	24	8	0.00041-0.1	NR	40	3	0.00005-0.0015	0.2
Baby Products	1	NR	NR	NR	NR	NR	0.00001	NR

*Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.

[a] It is possible these products are sprays, but it is not specified whether the reported uses are sprays.

[b] It is possible these products are powders, but it is not specified whether the reported uses are powders.

[c] Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories

NR – no reported use

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Cosmetic Ingredient Review

Commitment & Credibility since 1976

Memorandum

Date: August 21st, 2020

From: Bart Heldreth, Ph.D., Executive Director, Cosmetic Ingredient Review

To: All Stakeholders

Re: 2021 Draft Final Priority List

The CIR Procedures require preparation of the 2021 Draft Priority List for public comment by June 1, 2020. This list was provided to the Panel and reviewed at the June 2020 meeting; comments made at the June meeting have been considered and incorporated into this 2021 Draft Final Priority List. The priority list is typically based on stakeholder requests (e.g., a hair dye) and frequency of use (FOU) data from FDA's Voluntary Cosmetic Registration Program (VCRP); this year, VCRP data were received from the FDA on January 13 (in response to a Freedom of Information Act request).

While this list includes only the lead ingredients, groupings of botanical or other organism-sourced mixture-type ingredients (e.g., Rosa Centifolia Flower Extract), are drafted on the following pages for potential inference groupings, based on species and plant part(s). For organic chemicals, the list of lead ingredients was forwarded to the newly convened Expert Panel Grouping/Clustering Working Group for consideration; the Working Group's comments have been considered and are incorporated herein, where appropriate.

There are 11 reports proposed (2 of the 12 lead ingredients below are proposed to be reviewed together in 1 report) on the 2021 Draft Final Priorities List. Reports previously prioritized and on the CIR docket at the end of 2020, as well as a number of re-reviews of previous assessments, will supplement the total number of reports to be assessed in 2021.

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
- Toxicokinetics data, specifically dermal absorption and/or penetration

- Repeated-dose toxicity data
- Inhalation toxicity data, if the ingredient is used in a product that can be incidentally inhaled
- Reproductive/developmental 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.

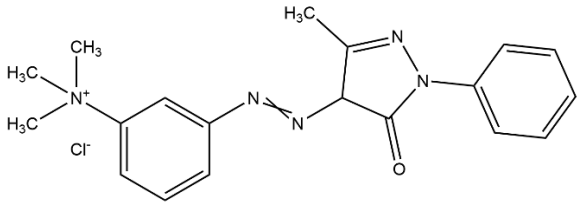
2021 Draft Final Priorities List

Ingredients	Frequency of Use (FOU) Data Year 2020
For cause	
Basic Yellow 57	45
Per FOU	
Yeast Extract	736
Glyceryl Acrylate/Acrylic Acid Copolymer	519
Hydroxyacetophenone	409
Glyceryl Polymethacrylate	364
Acrylates/Octylacrylamide Copolymer	361
Hydroxypropyl Starch Phosphate	353
Sodium Lauroamphoacetate	344
Zingiber Officinale (Ginger) Root Extract	326
Leuconostoc/Radish Root Ferment Filtrate	322
Rosa Centifolia Flower Extract	321
Phytosteryl/Octyldodecyl Lauroyl Glutamate	313

2021 Draft Final Priorities Groupings for New Reports

Proposed 2021 Report – per cause

Basic Yellow 57 *– per PCPC Hair Color Technical Committee(HCTC)* **FOU = 45**



Reported **Function**: Hair Colorant

Notes: *Since FOU might not be a very accurate surrogate for exposure, with regard to hair dyes, the PCPC HCTC proposes one hair dye ingredient annually for Panel review. Basic Yellow 57 is the mono-azo color that conforms to the above structure.*

Grouping proposal: None

Proposed 2021 Reports – per FOU

Yeast Extract **FOU = 736**

Definition: Yeast Extract is the extract of Yeast. (Yeast is a class of microorganisms (Hemiascomycetes) characterized by their lack of photosynthetic ability, existence as unicellular or simple irregular filaments, and reproduction by budding or direct division.)

Reported **Functions**: Skin Protectants; Skin-Conditioning Agents - Miscellaneous

Notes: *This ingredient group was presented for priorities consideration in 2014 (for 2015 priorities). However, we were asked to wait, as this name would soon be retired and ingredients would be reassigned to species specific names. This renaming has not occurred and this ingredient has a very high FOU.*

Grouping proposal: *Yeast-Derived Ingredients (7 ingredients, 958 summed FOU)*

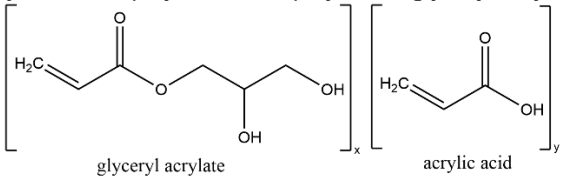
1. Hydrolyzed Yeast Extract	37
2. Hydrolyzed Yeast	9
3. Hydrolyzed Yeast Protein	103
4. Yeast	6
5. Yeast Beta-Glucan	60
6. Yeast Polysaccharides	7

Glyceryl Acrylate/Acrylic Acid Copolymer & Glyceryl Polymethacrylate

FOU = 519

FOU = 364

Definition: Glyceryl Acrylate/Acrylic Acid Copolymer is a copolymer of glyceryl acrylate and Acrylic Acid.



Reported **Functions**: Humectant; Viscosity Increasing Agents – Aqueous; Film Formers

Notes: *The Panel recently (2018) concluded that 126 acrylates copolymers are safe (e.g., Acrylates Copolymer or Ethylene/Acrylic Acid Copolymer).*

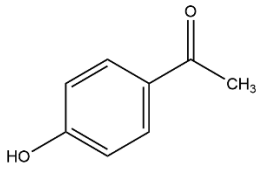
Grouping/clustering proposal: *Glyceryl Acrylates (3 ingredients (2 above); sum FOU =883)*

1. *Caprylyl Glycol/Glycerin/Polyacrylic Acid Copolymer* -

Hydroxyacetophenone

FOU = 409

Definition: Hydroxyacetophenone is the organic compound that conforms to the formula:



Reported **Functions**: Antioxidants; Skin-Conditioning Agents - Miscellaneous

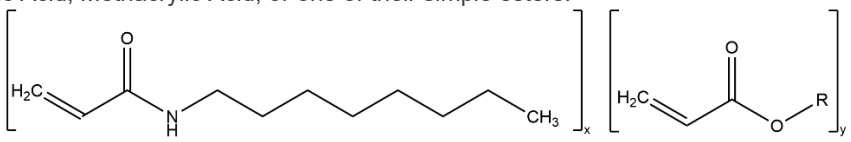
Notes: *CAS No. 99-93-4*

Grouping/clustering proposal: *None*

Acrylates/Octylacrylamide Copolymer

FOU = 361

Definition: Acrylates/Octylacrylamide Copolymer is a copolymer of octylacrylamide and one or more monomers consisting of Acrylic Acid, Methacrylic Acid, or one of their simple esters.



Octylacrylamide "Acrylates"

wherein "R" is hydrogen, methyl, ethyl, propyl, or butyl

Reported **Functions**: Film Formers; Hair Fixatives

Notes: *CAS No. 129702-02-9. The Panel has previously assessed the safety of some acrylamide copolymers and found them to be safe or safe with qualifications*.

Grouping/clustering proposal: *Acrylamide Acrylate Copolymers (16 ingredients; sum FOU = 442)*

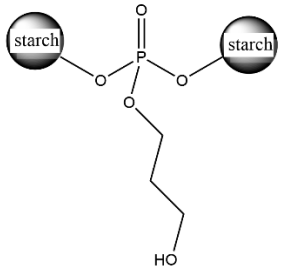
1. Acrylamide/Ammonium Acrylate Copolymer (26100-47-0)	**14**
2. Acrylamide/Sodium Acrylate Copolymer (25085-02-3; 25987-30-8)	**36**
3. Acrylates/Acrylamide Copolymer (9003-06-9)	**3**
4. Acrylates/t-Butylacrylamide Copolymer	**11**
5. Acrylates/Methacrylamide Copolymer	**1**
6. AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer	**2**
7. AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide/Hydroxyethylacrylate Copolymer	**-**
8. t-Butylacrylamide/Dimethylacrylamide/PEG-14 Diacrylate Crosspolymer	**-**
9. Butyl Acrylate/Isopropylacrylamide/PEG-18 Dimethacrylate Crosspolymer	**-**
10. Corn Starch/Acrylamide/Sodium Acrylate Copolymer	**8**
11. Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer	**6**
12. Dimethyl Acrylamide/Lauryl Methacrylate Copolymer (103479-14-7)	**-**
13. Potassium Acrylates/Acrylamide Copolymer	**-**
14. Sodium Acrylate/Hydroxyethyl Acrylamide Copolymer	**-**
15. Starch/Acrylates/Acrylamide Copolymer	**-**

Other polyacrylamides previously assessed by the Panel include*: Polyacrylate-2 (31759-42-9), Polyacrylamide (9003-05-8), and Acrylamide/Sodium Acryloyldimethyltaurate Copolymer (38193-60-1).*

Hydroxypropyl Starch Phosphate

FOU = 353

Definition: Hydroxypropyl Starch Phosphate is the hydroxypropyl ether of Distarch Phosphate.



Reported **Functions**: Antiacne Agents; Chelating Agents; Skin-Conditioning Agents - Miscellaneous

Notes: *CAS Nos. 113894-92-1, 39346-84-4, 53124-00-8. The Panel has previously assessed modified starches (e.g. Starch Hydroxypropyl Trimethylammonium Chloride), but not with phosphate groups.*

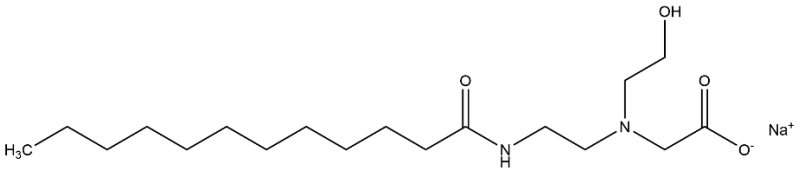
Grouping/clustering proposal: *Starch Phosphates (5 ingredients; sum FOU = 511)*

1. Sodium Hydroxypropyl Starch Phosphate	*33*
2. Distarch Phosphate	*125*
3. Distarch Phosphate Acetate	*-*
4. Sodium Dimaltodextrin Phosphate	*-*

Sodium Lauroamphoacetate

FOU = 344

Definition: Sodium Lauroamphoacetate is the amphoteric organic compound that conforms generally to the structure:



Reported **Functions**: Hair Conditioning Agents; Surfactants - Cleansing Agents; Surfactants - Foam Boosters

Notes: *CAS Nos. 68608-66-2, 156028-14-7, 66161-62-4. The Panel previously assessed the safety of the sodium salts of Cocoamphoacetate, Cocoamphopropionate, Cocoamphodiacetate, and Cocoamphodipropionate, and, found these to be safe as used. The only structural difference between Sodium Cocoamphoacetate and Sodium Lauroamphoacetate is the length(s) of the amide chain. The amide chain-lengths in Sodium Cocoamphoacetate are the results of derivation from coconut fats (i.e. a mixture of lengths, 6 – 18 carbons long; only the even numbers), while the amide chain for Sodium Lauroamphoacetate is lauramide (12 carbons).*

Grouping/clustering proposal: *None*

Zingiber Officinale (Ginger) Root Extract

FOU = 326

Definition: Zingiber Officinale (Ginger) Root Extract is the extract of the roots of the ginger, *Zingiber officinale*.

***Reported* Functions**: Fragrance Ingredients; Skin-Conditioning Agents - Miscellaneous

Notes: *CAS No. 84696-15-1*

Grouping proposal: *Ginger-derived ingredients (9 ingredients; sum FOU = 510)*

1. Zingiber Officinale (Ginger) Extract	-
2. Zingiber Officinale (Ginger) Leaf Cell Extract	-
3. Zingiber Officinale (Ginger) Rhizome Extract	-
4. Zingiber Officinale (Ginger) Root	-
5. Zingiber Officinale (Ginger) Root Juice	-
6. Zingiber Officinale (Ginger) Root Oil	171
7. Zingiber Officinale (Ginger) Root Powder	11
8. Zingiber Officinale (Ginger) Water	2

Leuconostoc/Radish Root Ferment Filtrate

FOU = 322

Definition: Leuconostoc/Radish Root Ferment Filtrate is a filtrate of the product obtained by the fermentation of *Raphanus sativus* roots by the microorganism, Leuconostoc.

***Reported* Functions**: Antifungal Agents; Antimicrobial Agents; Hair Conditioning Agents; Skin-Conditioning Agents - Miscellaneous

Notes: *UNII: D2QHA03458*

Grouping proposal: *Radish Root Derived-Ingredients (7 ingredients; sum FOU = 327)*

1. Leuconostoc/Radish Root Ferment Lysate Filtrate	-
2. Lactobacillus/Radish Root Ferment Filtrate	2
3. Lactobacillus/Radish Root Ferment Extract Filtrate	-
4. Raphanus Sativus (Radish) Root Extract	3
5. Raphanus Sativus (Radish) Root Juice	-
6. Raphanus Sativus (Radish) Root Powder	-

Rosa Centifolia Flower Extract

FOU = 321

Definition: Rosa Centifolia Flower Extract is the extract of the flowers of *Rosa centifolia.* The accepted scientific name for *Rosa centifolia* is *Rosa* x *centifolia.*

Reported **Functions**: Abrasives; Bulking Agents; Opacifying Agents

Notes: *CAS No. 84604-12-6*

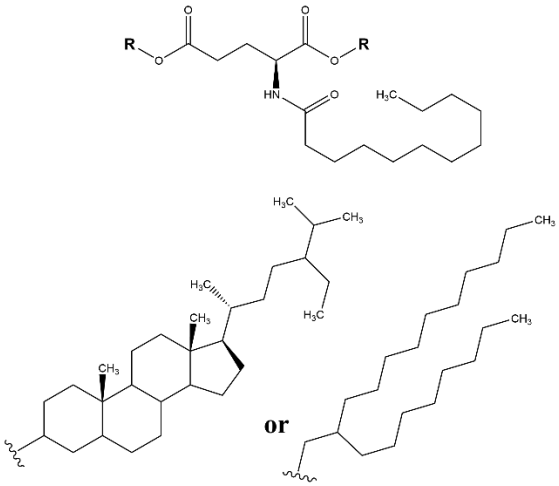
Grouping proposal: *Rosa centifolia Derived-Ingredients (11 ingredients; sum FOU = 595)*

1. *Rosa Centifolia Bud Extract*	**-**
2. *Rosa Centifolia Callus Culture Extract*	**-**
3. *Rosa Centifolia Extract*	**-**
4. *Rosa Centifolia Flower*	**17**
5. *Rosa Centifolia Flower Juice*	**3**
6. *Rosa Centifolia Flower Powder*	**6**
7. *Rosa Centifolia Flower Water*	**220**
8. *Rosa Centifolia Flower Wax*	**28**
9. *Rosa Centifolia Leaf Cell Extract*	**-**
10. *Rosa Centifolia Stem Extract*	**-**

Phytosteryl/Octyldodecyl Lauroyl Glutamate

FOU = 313

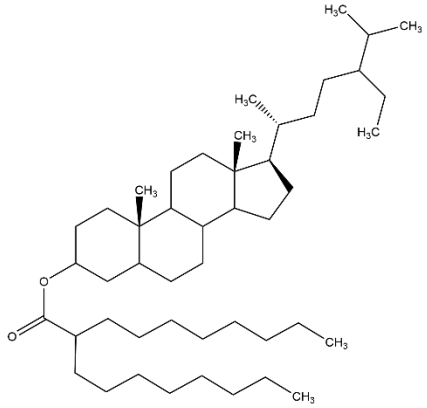
Definition: Phytosteryl/Octyldodecyl Lauroyl Glutamate is the mixed ester of phytosterol and Octyldodecanol with Lauroyl Glutamic Acid.



Reported **Functions**: Skin-Conditioning Agents - Occlusive

Notes: *CAS No. 220465-88-3. The Panel has previously assessed the safety of phytosterols (e.g., Dihydrophytosteryl Octyldecanoate) and found such ingredients to be safe as used. The Panel has also previously assessed the safety of sodium lauroyl glutamate, and found it to be safe when formulated to be non-irritating.*

Dihydrophytosteryl Octodecanoate:



Dihydrophytosteryl Octyldecanoate

Grouping proposal: *Phytosteryl Glutamates (3 ingredients; sum FOU = 395)*

1. Phytosteryl/Behenyl/ Octyldodecyl/Isostearyl Lauroyl Glutamate	*5*
2. Phytosteryl/Behenyl/Octyldodecyl Lauroyl Glutamate	*77*

Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director – Cosmetic Ingredient Review (CIR)

FROM: Hair Coloring Technical Committee (HCTC) of the Personal Care Products Council

DATE: June 5, 2020

SUBJECT: Hair Dye Ingredient Recommended for Inclusion in the 2021 CIR Priority List of Ingredients

The Hair Coloring Technical Committee (HCTC) recommends that the hair dye Basic Yellow 57 be included as the hair dye ingredient in the 2021 priority list of ingredients for review by CIR. Basic Yellow 57 has 45 uses reported in the 2020 FDA Voluntary Cosmetic Registration Program (VCRP). This hair dye ingredient has been reviewed by the European Scientific Committee on Consumer Safety (SCCS). The opinion is available at:
https://ec.europa.eu/health/sites/health/files/scientific_committees/consumer_safety/docs/sccs_o_020.pdf