ADMIN

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EXPERT PANEL MEETING
June 8-9, 2020

Cosmetic Ingredient Review

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MEMORANDUM

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Bart Heldreth, Ph.D., Executive Director, Cosmetic Ingredient Review
Subject: 154th Meeting of the Expert Panel — Monday and Tuesday, June 8-9, 2020
Date: May 15, 2020

Welcome to the first Expert Panel Meeting of 2020! The agenda and accompanying materials for the 154th Expert Panel Meeting to be held on June 8-9, 2020, are now available. The location is ***new*** – 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/154th-expert-panel-meeting

The meeting agenda includes the consideration of 18 reports advancing in the review process, including 5 final reports, 5 tentative reports, and 8 draft reports. Also, on the agenda is the 2021 Draft Priorities Document. All of the report books are essentially unchanged (except for dates and the name of the Expert Panel therein) from those sent prior to the March meeting (which was subsequently cancelled). So, the content and pagination is the same in the report books sent prior to the March meeting and the report books now available on the June meeting page (above). The Wave 2 document that issued prior to the March meeting is also unchanged. **However, this Admin book and a new March-to-June Supplemental document contain substantive data and other information not previously available.** Highlighted below are additional information found in Wave 2 and in the March-to-June Supplement.

Also of significant note, the CIR Expert Panel is hereto renamed the Expert Panel for Cosmetic Ingredient Safety! A description of the Panel, member biographies, and a conflict of interest (COI) statement are now publicly available. Please see here: https://ingredientsafetyexpertpanel.org.

Of paramount importance, CIR is seeking nominations for a new member of the Expert Panel. Specifically, an expert dermatologist is sought to take up the position of a team leader, as Dr. Marks is retiring from the Panel after the September meeting. So, please forward nominations directly to CIR, and such candidates will be considered for appointment by the CIR Steering Committee (per the Procedures: https://www.cir-safety.org/supplementaldoc/cir-procedures).

Team Meetings

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

1. Ascorbyl Glucoside – This is the first time the Panel is reviewing the safety of Ascorbyl Glucoside and Sodium Ascorbyl Glucoside. In addition to information found in the published literature, the report package includes the following unpublished data that were received from the Council:

    - Summary of an HRIPT on a rinse-off product containing 0.1% Ascorbyl Glucoside
    - Summary of an HRIPT on a leave-on product containing 2% Ascorbyl Glucoside

- HRIPT on a10% solution of Ascorbyl Glucoside

According to 2020 VCRP data, Ascorbyl Glucoside is reported to be used in 532 cosmetic products (463 leave-on and 69 rinse-off). The results of a concentration of use survey conducted by the Council in 2018 indicate that Ascorbyl Glucoside is used at concentrations up to 5% (in face and neck skin care preparations, not spray), which is the highest reported maximum use concentration for leave-on formulations. In rinse-off products, Ascorbyl Glucoside is reported to be used at concentrations up to 2% (in paste masks and mud packs). According to VCRP and Council survey data, Sodium Ascorbyl Glucoside is not being used in cosmetic products.

Comments on the Draft Report were received and are available in the March-to-June Supplement.

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. Basic Brown 17 – This is the first time the Panel is reviewing the safety of Basic Brown 17. Basic Brown 17 is reported to function as a hair dye.

   According to 2020 VCRP survey data, Basic Brown 17 is used in a total of 54 formulations. Of these reported uses, 3 are in non-coloring hair products (specifically a shampoo, a conditioner, and an “other” non-coloring hair product) and the remaining 51 are in hair coloring products (specifically, 5 in hair dyes and colors, 22 in coloring rinses, 14 in coloring shampoos, and 10 in “other” hair coloring products). The results of the concentration of use survey conducted by the Council in 2019 indicate that Basic Brown 17 is used at up to 0.66% in hair dyes and colors, up to 0.065% in coloring shampoos, and up to 0.19% in “other” hair coloring products.

   Comments on the Draft Report were received and are available in the March-to-June Supplement.

   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.

3. Methicones – At the December 2019 Panel meeting, the Panel was presented with a re-review of these 20 ingredients to determine whether the safety assessment should be re-opened after 15 years. Due to a significant increase in reported frequency and concentration of use in multiple formulations, especially those that could be inhaled, the Panel decided to reopen this report. The Panel consensus was to seek more data on particle size distribution and inhalation toxicity. To date, additional data have not been received.

   The CIR Science and Support Committee (SSC) has recently sent a memo proposing the addition of Simethicone and 8 other ingredients to this report. This memo was forwarded, ahead of this meeting, to the newly formed Panel Grouping/Clustering Working Group (Working Group) for consideration. Enclosed in the Wave 2 Supplement, are three publicly-accessible materials presented by the Council which may further inform the Working Group’s upcoming decision regarding the addition of Simethicone as an ingredient to this Draft Amended Report. Also included, are US Pharmacopeia monographs (on silicon dioxide and colloidal silicon dioxide, which describe the nature of synthetic amorphous silica) and a recent guidance document from the Silicones Environmental, Health, and Safety Center (SEHSC; 2018; that recommends that any aerosol formulation of a silicone-based material should have an aerodynamic particle size distribution ≥ 30 µm with no more than 1% of the particle mass being ≤ 10 µm).

   Comments on the Draft Amended Report were received and are available in the March-to-June Supplement. Also, concentration of use data were received for Hexyl Methicone, and Simethicone, an ingredient
   being considered for addition. There are no reported concentrations of use for Hexyl Methicone. Simethicone is reported to be used at a maximum concentration of 0.3% (in mascara, deodorant wipes, and “other” hair coloring preparations).

Upon review of this Draft Amended Report, the CIR SSC proposal, and the input of the Working Group, the Panel should determine if the suggested ingredients should be added. If the Panel concludes that these additions are "no-brainers" (i.e. the data currently in the report are sufficient to support the safety of these additions), these ingredients will be added to the next iteration of the report. If, however, the Panel deems that the suggested ingredients need not be added and that the available data are deemed sufficient to make a determination of safety, a Tentative Amended Report with a safe as used, safe with qualifications, or unsafe conclusion should be issued. If the available data are deemed insufficient (for the ingredients in the original report), then the Panel should issue an Insufficient Data Announcement (IDA), specifying the data needs therein.

4. Methylisothiazolinone – At the September 2019 Expert Panel meeting, based upon the adverse events described in the published literature on the inhalation of humidifier disinfectants containing Methylchloroisothiazolinone/Methylisothiazolinone (MCI/MI), the Panel moved to reopen the safety assessment of Methylisothiazolinone. The Panel wanted to further investigate the causes of respiratory issues reported in Korea.

   Enclosed in the Wave 2 supplement, are the concentration of use survey results for Methylisothiazolinone as a stand-alone ingredient. The maximum concentration of use range for Methylisothiazolinone in 2020 is 0.000002% - 0.00975%. The concentration of use for products containing Methylisothiazolinone that may be incidentally inhaled is 0.00095% in hairsprays.

   Comments on the Draft Report were received and are available in the March-to-June Supplement.

   After reviewing this document, if the available data are deemed sufficient to make a determination of safety, the Panel should issue a Tentative Amended 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. Papaya – This is the first time that the Panel is reviewing the safety of these 5 papaya-derived ingredients. In addition to information found in the published literature, the report package includes the following unpublished data that were received from the Council:

   - Manufacturing and impurities data on a Carica Papaya (Papaya) Fruit Extract
   - Physical and chemical properties of a Carica Papaya (Papaya) Fruit Extract

   According to 2020 VCRP survey data, Carica Papaya (Papaya) Fruit Extract has the highest reported frequency of use for the *Carica papaya*-derived ingredients; it is reported to be used in 349 cosmetic products (187 leave-on products, 161 rinse-off products, and 1 diluted for bath use). The results of a concentration of use survey conducted by the Council in 2018 indicate that Carica Papaya (Papaya) Fruit Extract is being used at maximum use concentrations up to 0.25% in rinse-off products and maximum use concentrations up to 0.02% in leave-on products. Concentration of use data were not reported for any of the other ingredients reviewed in this report. Also, according to VCRP and Council survey data, Carica Papaya (Papaya) Fruit Water is not reported to be used in cosmetic products.

   Comments on the Draft Report were received and are available in the March-to-June Supplement.

   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. Quaternium-18 – At the September 2019 meeting, the Panel considered a re-review of Quaternium-18 and Quaternium-18 Bentonite and determined to re-open the safety assessment to evaluate the sufficiency of inhalation data on Quaternium-18 Bentonite.

   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). In that assessment, Quaternium-18 Hectorite was determined to be safe as used in cosmetics in the present practices of use and concentration.

A data supplement regarding an inhalation toxicity study on Quaternium-18 Bentonite was received; please note, this information was previously included in the re-review document reviewed in September 2019.

Comments on the Draft Amended Report were received and are available in the March-to-June Supplement.

The Panel should carefully consider and discuss the data (or lack thereof) 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. Sulfites - At the September 2019 Panel meeting, the Panel considered a re-review of Sulfites and decided to reopen the safety assessment. This decision was based on the following concerns relating to this group of ingredients: 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.

   Comments on the Draft Amended Report were received and are available in the March-to-June Supplement.

   After reviewing these documents, if the available data are deemed sufficient to make a determination of safety, the Panel should issue a Tentative Amended 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. Tris(Tetramethylhydroxypiperidinol) Citrate - This is the first time the Panel is seeing a safety assessment of Tris(Tetramethylhydroxypiperidinol) Citrate. A Scientific Literature Review (SLR) was announced on December 18, 2019.

   According to 2020 VCRP survey data, Tris(Tetramethylhydroxypiperidinol) Citrate is reported to be used in 388 formulations, most of which are leave-on formulations (335 uses). The results of the concentration of use survey conducted by the Council indicate that the maximum use concentration of this ingredient in leave-on dermal products is 0.05% in cologne and toilet waters.

   Comments on the Draft Report were received and are available in the March-to-June Supplement.

   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 5 draft tentative reports.

1. Adenosine – At the September 2019 meeting, the Panel issued an IDA for Adenosine, Adenosine Phosphate, Adenosine Triphosphate, Disodium Adenosine Phosphate, and Disodium Adenosine Triphosphate, and requested impurities data on all of these ingredients. Since the September Panel meeting, unpublished data have been received and incorporated. These data include physical and chemical properties of Adenosine, impurity data on Adenosine Triphosphate, and impurity data on a trade name mixture containing Disodium Adenosine Triphosphate.

   Comments on the Draft Tentative Report were received and are available in the March-to-June Supplement.

   After reviewing these documents, the Panel should issue a Tentative Report with a safe as used, safe with qualifications, unsafe, or insufficient data conclusion (or a split conclusion). Additionally, Discussion items should be identified.

2. Caprylhydroxamic Acid – At the June 2019 meeting, the Panel found that the data were insufficient to determine safety. Although the results for a number of human repeated insult patch tests (HRIPTs) were largely negative, there were some alerts for sensitization in HRIPTs on formulations containing Caprylhydroxamic Acid at less than the maximum reported use concentration. Because 1) the potential for sensitization could not be ruled out completely based on the reactions observed in the HRIPTs; 2) the reported reactions to Caprylhydroxamic Acid in a reformulated moisturizer in Finland; and 3) the absence of a local lymph node assay or guinea pig maximization test to demonstrate a lack of sensitization potential, the following were requested:

    - Human repeated insult patch test at maximum use concentrations
        - the Panel requested that the study include a minimum of 100 subjects, preferably with Fitzpatrick skin types 1-4
    - a quantitative risk assessment (QRA) using an appropriate no-expected-sensitization-induction-level (NESIL)

    At the December 2019 meeting, the Panel was made aware that the requested studies were being conducted, but the results were not available in time for that meeting. Thus, the report was tabled, awaiting the data. These data have now been received, and incorporated into the report:

    - QRA for allergic contact dermatitis
    - HRIPT of 1.9% Caprylhydroxamic Acid
    - HRIPT of 3.8% Caprylhydroxamic Acid
    - summary of an HRIPT of an aqueous formulation containing 0.76% Caprylhydroxamic Acid

    Comments on the Draft Tentative Report were received and are available in the March-to-June Supplement.

    After reviewing these documents, the Panel should issue a Tentative Report with a safe as used, safe with qualifications, unsafe, or insufficient data conclusion. Additionally, Discussion items should be identified.

3. Glycerin Ethoxylates – At the December 2019 meeting, although prior data insufficiencies were met, the Panel deemed that the available HRIPT summaries provided insufficient information, especially in instances of low-level reactions during induction. Thus, the Panel issued a second IDA for full experimental details for each of these summaries, or, newly completed HRIPT experimental data, at or above maximum concentrations of use, 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 IDA, the following data were submitted and have been incorporated:

    - Details for two previously reviewed Glycereth-12 and -26 HRIPTS
    - Summary of results for an HRIPT on a product containing 0.35% Glycereth-12
    - Individual results for an HRIPT on a product containing 5% Glycereth-26
    - HRIPT on a 10% aqueous solution of Glycereth-26

    Comments on the Draft Tentative Report were received and are available in the March-to-June Supplement.

    After reviewing these documents, if the available data are deemed sufficient to make a determination of safety, the Panel should identify matters to be addressed in the Discussion and then issue a Tentative Report with a safe as used, safe with qualifications, or unsafe conclusion. If, however, the available data remain insufficient, the Panel should issue a Tentative Report with a conclusion of insufficient data, discussing the rationale therein.

4. Scutellaria – At the September 2019 meeting, the Panel issued an IDA with the following data requests on this ingredient group.

   For:
   Scutellaria Baicalensis Extract
   Scutellaria Baicalensis Root Extract
   Scutellaria Baicalensis Root Powder
   Scutellaria Baicalensis Sprout Extract

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

   For:
   Scutellaria Baicalensis Root Extract
   Scutellaria Baicalensis Root Powder

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

   For:
   Scutellaria Baicalensis Extract

   - Skin irritation and sensitization
   - 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
   - Skin irritation and sensitization

   To date, the following unpublished data have been received from the Council in response to the IDA, and are incorporated in the Draft Tentative Report text:

   - Method of manufacture of Scutellaria Baicalensis Root Extract (aqueous extract)
   - *in vitro* genotoxicity data on a trade name mixture containing 33.33% Scutellaria Baicalensis Root Extract (aqueous extract)
   - *in vitro* phototoxicity data on a trade name mixture containing 33.33% Scutellaria Baicalensis Root Extract (aqueous extract)
   - HRIPT on a leave-on product containing 0.001% Scutellaria Baicalensis Root Extract

   Additionally, one case report on Scutellaria Baicalensis Extract and two case reports on Scutellaria Baicalensis Root Extract that were identified in the published literature recently, were incorporated into the Draft Tentative Report text as well.

   Comments on the Draft Tentative Report were received and are available in the March-to-June Supplement.

   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. If not, an insufficient data or split conclusion should be issued. Regarding the conclusion that will be determined, Discussion items should be identified.

5. Wheat - In September 2019, the Panel reviewed the safety of the 27 ingredients in this report and issued an IDA with the following data needs:

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

    Since the September Panel meeting, none of the requested data has been received. Additive data on Triticum Vulgare (Wheat) Germ Extract concerning heavy metal and pesticide composition, and summary data on ocular and dermal tolerance in rabbits were received prior to the September Panel meeting and have been incorporated into this draft.

    Comments on the Draft Tentative Report were received and are available in the March-to-June Supplement.

    Based on the proceedings and comments from the September meeting, a draft Discussion with some points for the Panel to consider, including the outstanding data needs, has been included. The Panel should carefully consider and discuss the data (or lack thereof) and the Abstract and draft 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. Honey – The Expert Panel reviewed this report for the first time at the December 2019 meeting, and concluded that these 7 honey ingredients are safe in the present practices of use and concentration described in the safety assessment. The safety of these ingredients is further supported by frequent use in medical wound dressings and historical food use.

    Comments on the Draft Final Report were received and are available in the March-to-June Supplement.

    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. Palm tree – The Panel issued a Revised Tentative Report with the following conclusions at the December 2019 meeting:

    - Euterpe Edulis Fruit Extract, Euterpe Edulis Juice Extract, Euterpe Oleracea Fruit Extract, Euterpe Oleracea Juice, Euterpe Oleracea Pulp Powder, Euterpe Oleracea Seed Powder, and Hydrolyzed Euterpe Oleracea Fruit are safe in cosmetics in the present practices of use and concentration described in the safety assessment.

    - The available data are insufficient to make a determination of safety for Euterpe Oleracea Palm Heart Extract under the intended conditions of use in cosmetic formulations.

    The data needs on this ingredient (previously requested) include:

    - 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

    Comments on the Draft Final Report were received and are available in the March-to-June

Supplement.

To date, there has been no response to this data request. 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. Pomegranate – At the December 2019 meeting, the Panel issued a Revised Tentative Report with the conclusion that the following 8 ingredients are safe in the present practices of use and concentration described in the safety assessment.

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

However, the Panel also concluded that the data were insufficient to make a determination of safety for the following 10 ingredients:

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

The additional data needed for these cosmetic ingredients are:

- Method of manufacture, especially with regard to solvent used for the extracts
- Composition and impurities data
- Systemic toxicity data
- Dermal irritation and sensitization data

Comments on the Draft Final Report, and an unpublished HRIPT study on a product containing 0.4% Pomegranate Flower Extract, were received and are available in the March-to-June Supplement. There were 105 subjects that completed the study. The results indicated that the material was not a dermal irritant or sensitizer.

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.

4. Soy – At the December 2019 meeting, the Panel issued a Tentative 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. However, the Panel determined that there were insufficient data to determine the safety of the remaining 4 ingredients. The insufficiencies include a lack of composition, impurities, method of manufacture, 28-day dermal toxicity, and sensitization/irritation data.

Comments on the Draft Final Report were received and are available in the March-to-June Supplement.

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. Vanilla – At the December 2019 Panel meeting, the Panel issued a Tentative 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 Seed Powder
Vanilla Planifolia Fruit Oil	Vanilla Tahitensis Fruit Extract
Vanilla Planifolia Fruit Water	Vanilla Tahitensis Seed
Vanilla Planifolia Seed	

The Panel also concluded that the available data are insufficient to make a determination that Vanilla Planifolia Flower Extract and Vanilla Planifolia Leaf Cell Extract are safe under the intended conditions of use in cosmetic formulations. The data needed to determine the safety of these 2 ingredients (previously requested) 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)

Comments on the Draft Final Report were received and are available in the March-to-June Supplement.

To date, there has been no response to the above data requests. 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 Item - there is 1 draft priorities document.

1. Priorities – The 2021 Draft 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. This list was forwarded to the Grouping/Clustering Working Group for consideration.

   For organic chemicals, the list of lead ingredients (presented in the initial meeting materials) was forwarded to the newly convened Grouping/Clustering Working Group for consideration. The Working Group has since provided input on such review groupings, which are available in Wave 2.

   Comments on the Draft Priority List were received and are available in the March-to-June Supplement.

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), 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
154th Meeting of the Expert Panel for Cosmetic Ingredient Safety
June 8th - 9th, 2020

Virtual via Microsoft Teams

Monday, June 8th		
8:30 AM	**WELCOME TO THE 154th EXPERT PANEL TEAM MEETINGS**	**Drs. Bergfeld/Heldreth**
8:40 AM	**Presentation: The Expert Panel Grouping/Clustering Working Group**	**Dr. Liebler**
8:50 AM	**TEAM MEETINGS**	**Drs. Marks/Belsito**

Dr. Marks Team		Dr. Belsito Team*	
FR (PC)	Soy	Admin (BH)	Draft Priorities
FR (PC)	Honey	TR (PR)	Glycerin Ethoxylates
TR (PC)	Adenosine	DAR (PR)	Methicones
DAR (PC)	Quaternium-18	DR (PR)	Tris Citrate
DR (PC)	Papaya	FR (CB)	Pomegranate
TR (MF)	Caprylhydroxamic Acid	TR (CB)	Wheat
FR (WJ)	Palm tree	DR (CB)	Basic Brown 17
FR (WJ)	Vanilla	DAR (CB)	MI
TR (WJ)	Scutellaria	FR (PC)	Soy
DR (WJ)	Ascorbyl Glucoside	FR (PC)	Honey
DAR (WJ)	Sulfites	TR (PC)	Adenosine
TR (PR)	Glycerin Ethoxylates	DAR (PC)	Quaternium-18
DAR (PR)	Methicones	DR (PC)	Papaya
DR (PR)	Tris Citrate	FR (WJ)	Palm tree
FR (CB)	Pomegranate	FR (WJ)	Vanilla
TR (CB)	Wheat	TR (WJ)	Scutellaria
DR (CB)	Basic Brown 17	DR (WJ)	Ascorbyl Glucoside
DAR (CB)	MI	DAR (WJ)	Sulfites
Admin (BH)	Draft Priorities	TR (MF)	Caprylhydroxamic Acid

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

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

Tuesday, June 9th			
8:30 am	**WELCOME TO THE 154th FULL EXPERT PANEL MEETING**		**Dr. Bergfeld**
8:45 am	Admin	**MINUTES OF THE DECEMBER 2019 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 (WJ)	Palm tree – *Dr. Belsito Reports*
FR (WJ)	Vanilla – *Dr. Marks Reports*
FR (CB)	Pomegranate – *Dr. Belsito Reports*
FR (PC)	Soy – *Dr. Marks Reports*
FR (PC)	Honey – *Dr. Belsito Reports*

Reports Advancing

DAR (PC)	Quaternium-18 – *Dr. Marks Reports*
TR (PC)	Adenosine – *Dr. Belsito Reports*
DR (PC)	Papaya – *Dr. Marks Reports*
DAR (CB)	MI – *Dr. Belsito Reports*
TR (CB)	Wheat – *Dr. Marks Reports*
DR (CB)	Basic Brown 17 – *Dr. Belsito Reports*
TR (PR)	Glycerin Ethoxylates – *Dr. Marks Reports*
DR (PR)	Tris Citrate – *Dr. Belsito Reports*
DAR (PR)	Methicones – *Dr. Marks Reports*
DAR (WJ)	Sulfites – *Dr. Belsito Reports*
TR (WJ)	Scutellaria – *Dr. Marks Reports*
DR (WJ)	Ascorbyl Glucoside – *Dr. Belsito Reports*
TR (MF)	Caprylhydroxamic Acid – *Dr. Marks Reports*

Other Items

Admin (BH)	Draft Priorities – *Dr. Belsito Reports*

ADJOURN - *Next meeting Monday and Tuesday, September 14-15, 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

Cosmetic Ingredient Review

Commitment & Credibility since 1976

ONE HUNDRED FIFTY-THIRD MEETING

OF THE

EXPERT PANEL

December 9-10, 2019

The Westin Hotel

Washington, D.C.

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

Linda Katz, MD., M.P.H. (absent)

_____
Adopted (Date)

_____
Wilma F. Bergfeld, M.D.

1620 L Street, N.W., Suite 1200, Washington, DC 20036
(Main) 202-331-0651 (Fax) 202-331-0088
(Email) cirinfo@cir-safety.org (CIR Website) www.cir-safety.org
(Expert Panel Website) ingredientsafetyexpertpanel.org

Others Present at the Meeting

Jay Ansell	PCPC
Don Bjerke	P & G
Roshil Budhram	LBrands
Christina Burnett	CIR
Priya Cherian	CIR
Kapel Dewan	FDA
Carol Eisenmann	PCPC
Monice Fiume	CIR
Kevin Fries	CIR
Bart Heldreth	CIR
Carla Jackson	CIR
Wilbur Johnson, Jr.	CIR
Jon Lalko	Estee Lauder
Linda Loretz	PCPC
Preethi Raj	CIR
Teresa Washington	FDA
Michael K.Wyatt	FDA

MINUTES FROM THE 153rd EXPERT PANEL MEETING

CHAIRMAN'S OPENING REMARKS

Dr. Bergfeld welcomed the attendees to the 153rd meeting of the CIR Expert Panel, and thanked the 2 Teams for their work on the preceding day and the CIR staff for their support. She also thanked the CIR Science and Support Committee, industry, and the Personal Care Products Council for supplying information for the Panel's use.

Dr. Bergfeld noted that 15 ingredient reports, one of which is a re-review document on Methicones, are scheduled for review at today's meeting. She also stated that the agenda includes 2 administrative summaries, 1 strategy document on Silicates, and a read-across document that will be changing over time. In response to Dr. Liebler's suggestion, Dr. Bergfeld noted that a CIR workgroup consisting of chemists on the Expert Panel and other Panel members is being assembled today for the purpose of addressing the use of read-across in CIR safety assessments. Another issue that needs to be addressed relates to the abbreviated data summaries, particularly those relating to skin irritation and sensitization potential, and the lack of specific experimental data for review. Dr. Bergfeld remarked that, hopefully, this issue will be resolved at today's meeting. Furthermore, she added that the Panel continues to have a problem relating to the interpretation of botanical ingredients, i.e., whether or not they can be defined as GRAS and how this issue should be dealt with in report discussions.

APPROVAL OF MINUTES

The minutes of the September 16-17, 2019 (152nd) CIR 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 2 new faces participating in these safety assessments. Dr. Lisa Peterson joined the Marks teams at this meeting, filling the vacancy for a chemist. Dr. Peterson is Professor of Environmental Health Sciences and a Co-Leader of Carcinogenesis and the Chemoprevention Program, at the University of Minnesota School of Public Health and Masonic Cancer Center. CIR is thrilled to have this expert join the Panel. This meeting is also the first meeting wherein CIR's newest analyst, Ms. Preethi Raj, participated in the deliberations. Dr. Heldreth noted on what a great addition Preethi has been to the CIR staff.

CIR was invited by the Latin American Cosmetics, Toiletry and Perfumery Association (CASIC) to speak at their international safety symposium in Buenos Aires last month. The symposium was to provide the audience in South America with tools for proper management of cosmetic safety. CIR's Senior Director, Monice Fiume, presented on "Evaluating the Safety of Cosmetics in the US," and was very well received. Her presentation served to inform the audience about the CIR – especially in regard to its mission, this Expert Panel, the CIR process, and conclusions reached thus far. She also clarified some similarities and differences between CIR assessments as compared to our counterparts in Europe.

Also since this Panel's last meeting, 2 commentaries were published, each disparaging the notion that "natural means safe." Each commentary pointed to the importance of scientifically sound safety assessments, regardless of raw material source (e.g., synthetic or botanical). Moreover, in both of the opinions, offered by Dr. Bruce Brod in JAMA Dermatology and by Dr. Mary Beth Genter in the International Journal of Toxicology, this Expert Panel is lauded as the eminent, scientifically-backed, source of cosmetic safety information

Final Reports

Alkyl Amide MIPA

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

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

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

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

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

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

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

Capryloyl Salicylic Acid

The Panel issued a Final Amended Report with the conclusion that the data are insufficient to make a determination that Capryloyl Salicylic Acid is safe under the intended concentrations of use in cosmetic formulations. The data needs are:

- Impurities
- Phototoxicity

The Panel published a safety assessment of Salicylic Acid and 16 salicylates in 2003. That safety assessment included Capryloyl Salicylic Acid, which was included in the grouping because, at the time, it was mischaracterized and defined as an ester. However, it is now known that this ingredient is a ketone; thus, this ingredient was reviewed separately.

The Panel discussed the issue of skin sensitization potential for this ingredient, ultimately noting very little to no concern relating to this endpoint. Capryloyl Salicylic Acid induced skin sensitization in GPMTs at challenge concentrations of 0.5%, 2%, and 5%, but not at 1%. However, in human repeated insult patch tests (HRIPTs), cosmetic products containing 0.5% or 2% Capryloyl Salicylic Acid were classified as non-sensitizing. After reviewing the HRIPT results and considering that the highest reported maximum use concentration of Capryloyl Salicylic Acid is 0.5% in leave-on cosmetic products, the Panel was reassured that the sensitization potential of exposure to this ingredient via cosmetic use is not a risk.

In response to the Panel's data requests, the results of an in vitro 3T3 neutral red uptake (NRU) phototoxicity test were provided by the Council. The study was performed in accordance with the Organization for Economic Co-operation and Development (OECD) Guideline for Testing of Chemicals Draft Proposal for a New Guideline (draft document, dated February 2000). According to the evaluation criteria that were used, a test article was considered to be phototoxic in this assay if a marked decrease in cell viability (as measured by OD340 in the NRU) was observed in the presence of long-wave ultraviolet light (UVA; by comparison with the viability seen in the absence of UVA) such that photo-irritation factors (PIF) of ≥ 5 were obtained. Furthermore, a test article was considered to be non-phototoxic in this assay if there was no marked decrease in cell viability when cells were exposed to the test article in the absence and presence of UVA, or if similar toxic profiles were observed in the absence and presence of UVA (PIF < 5). The test yielded PIF's of 4 and 2.6 - 1.7 in separate experiments that were performed. Based on these PIF values, the author concluded that, according to the proposed OECD

guideline evaluation criteria, Capryloyl Salicylic Acid was not phototoxic in the in vitro 3T3 NRU phototoxicity test. However, the Panel noted that, according to OECD Test Guideline (TG) 432 (adopted April 13, 2004), the results of this test are to be interpreted based on the following criteria: a test substance with a PIF of < 2 predicts "no phototoxicity," a PIF of > 2 and < 5 predicts "probable phototoxicity," and a PIF of > 5 predicts "phototoxicity." Thus, the Panel agreed that Capryloyl Salicylic Acid (PIFs of 4 and 2.6 - 1.7) should have been classified as probably phototoxic in the in vitro 3T3 NRU phototoxicity test. Furthermore, the Panel agreed that because this test is prone to false positives, additional data would be needed in order to evaluate the phototoxicity potential of Capryloyl Salicylic Acid. The reactive oxygen species test for phototoxicity was mentioned as one of the phototoxicity tests that could be performed.

The Panel also noted that impurities data were not provided, and that the need for these data remains.

MCI/MI

The Panel issued a Final Amended Report with the conclusion that the ingredient mixture MCI/MI is safe in cosmetics when formulated to be non-sensitizing, based on the results of a quantitative risk assessment (QRA) or similar methodology. Concentrations of use may not exceed 15 ppm in rinse-off products or 7.5 ppm in leave-on products.

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

The Panel received the requested inhalation study of at least 3 months in duration that is in accordance with the OECD TG 413. This request had been in response to reports of adverse events observed in infants following inhalation exposure to humidifier disinfectants that contained this preservative mixture. The Panel determined that the data sufficiently support safety of the use of this ingredient mixture at the concentrations that could be incidentally inhaled following use in cosmetic products. The concentrations used in the humidifier disinfectant were orders of magnitude greater than those found in cosmetics.

Mannitol, Sorbitol, & Xylitol

The Panel issued a Final Report with the conclusion that Mannitol, Sorbitol, and Xylitol are safe in cosmetics in the present practices of use and concentration described in the safety assessment. The lack of adverse clinical reports after ingestion of foods containing these ingredients, as well as negative sensitization and phototoxicity assays, support the safety of this ingredient group.

According to 2019 VCRP data, Sorbitol, Xylitol, and Mannitol are used in 1976, 472, and 404 formulations, respectively. The results of the concentration of use survey conducted by the Council indicate that Sorbitol has the highest concentration of use; it is used at up to 70% in dentifrices. The highest concentration of use reported for products resulting in leave-on dermal exposure is 60.5% Mannitol in other skin care preparations.

Tentative Reports

Honey

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

Honey	Honey Extract	Hydrolyzed Honey Protein*
Honey Cocoates	Hydrogenated Honey	
Honey Powder	Hydrolyzed Honey*	

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

The Panel noted the lack of sensitization data for six of the seven ingredients, but determined that the available sensitization data on Honey Extract could be used to support safety for the remaining ingredients. The safety of these ingredients was also supported by their frequent medical use in wound dressings and historical food use, without reported adverse events. In

addition, the Panel suggested the inclusion of language suggesting limitations of pesticides and endotoxins, as well as avoiding the use of honey derived from toxic plant sources (e.g., oleander) when formulating with these ingredients.

According to 2019 VCRP survey data, Honey and Honey Extract are reported to be used in 1002 and 359 formulations, respectively. The results of a 2018 concentration of use survey conducted by Council indicate that Honey has the highest reported concentration of use; it is used at up to 22% in rinse-off formulations. The highest concentration of use reported for leave-on products was in formulations containing Honey Extract at up to 7% in body and hand products.

Palm (açai and juçara)-Derived Ingredients

The Panel issued a Revised Tentative Report with the conclusion that the following ingredients are safe in the present practices of use and concentration described in the safety assessment:

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

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

The Panel noted similarities in composition for the two species; accordingly, data on *Euterpe oleracea* was found to be applicable for determining safety of similar *Euterpe edulis* ingredients. This conclusion was found to be applicable to Hydrolyzed Euterpe Oleracea Fruit in the absence of composition data on this ingredient, given the available composition data on Euterpe Oleracea Fruit Extract and *Euterpe oleracea* fruit. Additionally, the Panel concluded that the available data are insufficient to make a determination that Euterpe Oleracea Palm Heart Extract is safe under the intended conditions of use in cosmetic formulations. The data needs to determine the safety of this ingredient are:

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

Pomegranate

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

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

The Panel noted that the available data indicate the potential for extracts of Punica granatum plant parts to cause skin lightening effects. 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, however, the Panel was not concerned that these ingredients would have these effects in cosmetic products under the present practices of use and concentration described in the safety assessment. Nevertheless, cosmetic formulators should only use Punica granatum extracts in products in a manner that does not cause skin depigmentation.

However, the Panel also concluded that the data were insufficient to make a determination of safety for the following 10 ingredients:

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

‡ Ingredient has been deleted from the Dictionary, but uses are currently reported.

**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 additional data needed for these cosmetic ingredients are:

- Method of manufacture, especially with regard to solvent used for the extracts
- Composition and impurities data
- Systemic toxicity data
- Dermal irritation and sensitization data

Soy

The Panel issued a Tentative Report for public comment with the conclusion that the following 24 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.*

However, the Panel determined that there were insufficient data to determine the safety of the following 4 ingredients:

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

None of these 4 ingredients is reported to be in use. The data needs to determine safety of these ingredients comprise:

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

According to 2019 VCRP data, Glycine Max (Soybean) Seed Extract and *Glycine max* (soybean) flour (synonymous with Glycine Soja (Soybean) Flour) are reported to be used in 395 and 66 formulations, respectively. Results of the 2016 concentration of use survey conducted by Council indicate that Glycine Soja (Soybean) Seed Extract has the highest concentration of use; it is used at up to 2% in face and neck products.

Vanilla

The Panel issued a Tentative Report for public comment 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, Vanilla Tahitensis Fruit Extract, and vanilla 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.

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 two 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)

The Panel was not concerned about the positive (++) photopatch test reactions to vanilla extract in a photodermatitis patient, because the strength of the reactions at photoirradiated and non-irradiated sites were the same. Therefore, it was agreed that the observed test results were not due to a photosensitization reaction.

Insufficient Data Announcements

Amino Acid Diacetates

The Panel issued an Insufficient Data Announcement (IDA) for Beta-Alanine Diacetic Acid and Tetrasodium Glutamate Diacetate. The additional data needed to determine safety for these cosmetic ingredients are:

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

Cocos nucifera (Coconut)-Derived Ingredients

The Panel issued an IDA for the following 9 ingredients:

Cocos Nucifera (Coconut) Flower Extract
Cocos Nucifera (Coconut) Fruit
Cocos Nucifera (Coconut) Fruit Extract
Cocos Nucifera (Coconut) Fruit/Fruit Juice Extract
Cocos Nucifera (Coconut) Fruit Juice
Cocos Nucifera (Coconut) Fruit Powder
Cocos Nucifera (Coconut) Fruit Water
Cocos Nucifera (Coconut) Liquid Endosperm
Cocos Nucifera (Coconut) Shell Powder

The additional data needed for these cosmetic ingredients are:

- 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*.

Glycerin Ethoxylates

The Panel reviewed the safety of these 8 glycerin ethoxylate ingredients for the second time and issued a new IDA:

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

The Panel deemed that their previous data insufficiency requests were satisfied because the described method of manufacture addressed the family of ingredients, the received Glycereth-26 certificate of analysis confirmed minimal levels for impurities of concern, and the revised Glycereth-3 inhalation toxicity study reassured the respiratory safety of these ingredients. However, the Panel found the available HRIPT summaries to provide insufficient information. Thus, the Panel has requested full experimental details for each of these summaries, or, newly completed HRIPT experimental data at or above maximum concentrations of use, with $n \geq 100$ 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.

Polysilicone-11

The Panel issued an IDA for Polysilicone-11. The insufficiencies include data regarding impurities, such as residual monomers and other reactants (e.g., polymerization initiators, chain propagators, terminators, and solvents), molecular weight distribution, composition, 28-day dermal toxicity, mammalian genotoxicity, and sensitization/irritation at the current maximum use concentration of 35%.

Tabled Assessment

Caprylhydroxamic Acid

The Panel was informed that the requested HRIPT is underway, but not yet available for review by the Panel. Therefore, discussion of the draft Tentative Report on Caprylhydroxamic Acid was tabled until the March 2020 meeting.

Re-Reviews

Methicones

The Panel first published a review of the safety of these 20 ingredients in 2003. The Panel considered it unlikely for any of these polymers to be absorbed into the skin due to their large molecular weights and low concentrations of use; hence, the Panel concluded that these ingredients are safe as used in cosmetic products. Because it has been at least 15 years since the report was published, in accordance with CIR Procedures, the Panel considered whether the safety assessment of Methicones should be re-opened.

Upon review of the updated frequency and concentration of use data, the Panel determined to re-open this safety assessment. Although Amodimethicone Hydroxystearate, Hydroxypropyldimethicone, and Stearamidopropyl Dimethicone are not reported to be in use, the overall frequency of use for this group of ingredients has increased significantly. The reported frequency of use of Dimethicone has increased from 1659 uses in 1998 to 12,934 uses in 2019, while the reported frequency of use of Methicone increased from 0 in 1998 to 600 in 2019. The reported maximum concentration of use of Dimethicone also increased, from 80% to 85%, with the maximum concentration notably increased for sprays. This dramatic increase, across various product categories and routes of exposure, led to the Panel's concern for potential inhalation toxicity. The Panel noted limited acute inhalation toxicity data in the original report, and acknowledged the need for toxicity data describing ingredient concentration and particle size distribution, especially as it pertains to inhalation toxicity.

Strategy Document

Silicates, Clays, and Zeolites

The Panel considered the proposed groupings of the 38 ingredients that had been previously removed from the Amended Safety Assessment on Silica and Hydrated Silica and a larger re-review package of silicate ingredients. The Panel accepted the groupings proposed by CIR Staff, which will be presented in 3 separate reports at future Panel meetings. The Panel also accepted the proposed addition of the ingredient, Clay, to the reviews. The groups are as follows:

Silicates

Aluminum Silicate
Aluminum Calcium Sodium Silicate
Aluminum Iron Silicates
Aluminum Iron Calcium Magnesium Germanium Silicates
Aluminum Iron Calcium Magnesium Zirconium Silicates
Ammonium Silver Zinc Aluminum Silicate
Calcium Silicate
Calcium Magnesium Silicate
Lithium Magnesium Silicate
Lithium Magnesium Sodium Silicate
Magnesium Aluminometasilicate
Magnesium Aluminum Silicate
Magnesium Silicate
Magnesium Trisilicate
Potassium Silicate
Pyrophyllite
Sodium Magnesium Silicate
Sodium Metasilicate
Sodium Magnesium Aluminum Silicate
Sodium Potassium Aluminum Silicate
Sodium Silver Aluminum Silicate
Sodium Silicate
Tromethamine Magnesium Aluminum Silicate
Zinc Silicate
Zirconium Silicate

Clays

Activated Clay	Bentonite	Fuller's Earth	Kaolin
Attapulgite	Clay	Hectorite	Montmorillonite

Zeolite

Ammonium Silver Zeolite	Silver Copper Zeolite	Zeolite
Gold Zeolite	Titanium Zeolite	Zinc Zeolite

Read-Across Resource Document

At this meeting, a newly prepared draft of a Read-Across Resource Document was presented for Panel review. The Panel consensus was to table this document until further efforts were completed within the Panel processes related to read-across. These further efforts are to include a special working group of the Panel to evaluate grouping/clustering of ingredients and to propose read-across sources where necessary.

Re-Review Summaries

Sodium Naphthalenesulfonate and Sodium Polynaphthalenesulfonate

The Panel approved the re-review summary of Sodium Naphthalenesulfonate and Sodium Polynaphthalenesulfonate, reaffirming that these ingredients are "safe as used in cosmetic formulations intended to be applied to the skin. The available data, however, are insufficient to support the safety for use in cosmetic products which may contact mucous membranes or be ingested." This conclusion was originally published by CIR in 2003. Limited new data that were identified in the published literature, as well as updated information regarding frequencies of use, provided by the FDA, and maximum use concentrations of use, provided by the Council, were reviewed by the Panel.

Isopropyl Lanolate

The Panel approved the re-review summary of Isopropyl Lanolate, reaffirming that this ingredient is "safe as currently used in cosmetic products." This conclusion was originally published by CIR in 1980, and again in 2001. Limited new data identified in the published literature that have become available since the original report was published, as well as updated information regarding frequencies of use (provided by the FDA) and maximum use concentrations of use (provided by the Council), were reviewed by the Panel.

Cosmetic Ingredient Review

Commitment & Credibility since 1976

Memorandum

Date: May 15th, 2020

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

To: All Stakeholders

Re: 2021 Draft Priority List

The CIR Procedures require preparation of the 2021 Draft Priority List for public comment by June 1, 2020. 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 those purely inorganic chemicals (e.g., Magnesium Chloride), no grouping will be proposed (unless the difference between ingredients is merely hydration (e.g., Calcium Sulfate and Calcium Sulfate Hydrate)), as the Panel consensus is that read-across/inference strategies are not amenable for such chemicals. However, for organic chemicals, the list of lead ingredients has been forwarded to the newly convened CIR Grouping/Clustering Working Group for consideration.

There are 13 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.

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

1620 L Street, NW Suite 1200, Washington, DC 20036
(Main) 202-331-0651 (Fax) 202-331-0088
(Email) cirinfo@cir-safety.org (Website) www.cir-safety.org

- 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 Priorities List

Ingredients	Frequency of Use (FOU) Data Year 2020
For cause	
***To be determined* – a hair dye**	-
Per FOU	
Butyl Methoxydibenzoylmethane	5128
Magnesium Chloride	799
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
Calcium Sulfate	331
Zingiber Officinale (Ginger) Root Extract	326
Rosa Centifolia Flower Extract	321
Phytosteryl/Octyldodecyl Lauroyl Glutamate	313

2021 Draft Priorities Groupings for New Reports

Proposed 2021 Report – per cause

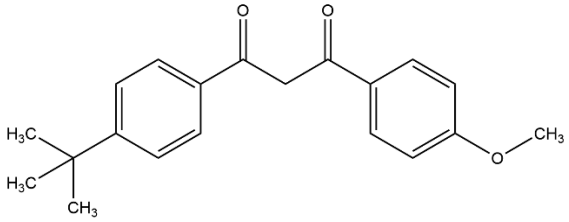
To be determined *– per PCPC Hair Color Technical Committee(HCTC)* **FOU = ___**

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 CIR review. The HCTC typically submits a proposed hair dye ingredient between the 1st and 2nd meetings of the year.*
Grouping proposal: None

Proposed 2021 Reports – per FOU

Butyl Methoxydibenzoylmethane **FOU = 5128**

Definition: Butyl Methoxydibenzoylmethane is the substituted aromatic compound that conforms to the structure:



Reported **Functions**: Light Stabilizers; Sunscreen Agents
Notes: *CAS No. 70356-09-1. While this ingredient is used as an OTC active ingredient (as a sunscreen; drug name = Avobenzone), only 49 uses are reported in the VCRP under its drug name (compared to 5128 uses reported under its cosmetic ingredient name). The Expert Panel has previously assessed the safety of a number of ingredients as light stabilizers (which are also reported as sunscreen agents; e.g., cosmetic ingredient, Benzophenone-3 = OTC sunscreen (drug), oxybenzone).*
Grouping proposal/clustering: *to be determined*

Magnesium Chloride

FOU = 799

Definition: Magnesium Chloride is the inorganic salt that conforms to the formula:

$MgCl_2$

Reported **Functions**: Flavoring Agents; Viscosity Increasing Agents - Aqueous

Notes: While flavoring agents may be excluded from CIR review, this ingredient is also reported to function as a viscosity increasing agent (most reported uses are ***not*** in oral care formulations).

Grouping proposal: *none - inorganic*

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)*

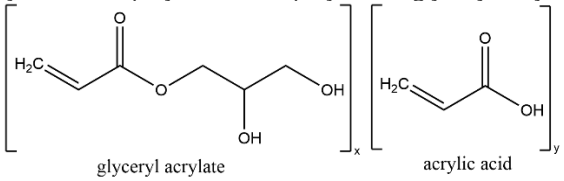
Yeast Extract (FOU priority ingredient)	**736**
Hydrolyzed Yeast Extract	**37**
Hydrolyzed Yeast	**9**
Hydrolyzed Yeast Protein	**103**
Yeast	**6**
Yeast Beta-Glucan	**60**
Yeast Polysaccharides	**7**

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.



glyceryl acrylate acrylic acid

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

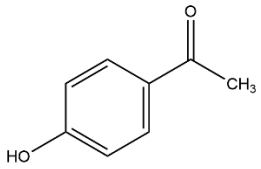
Notes: *The Panel recently (2018) concluded that 126 acrylates copolymers are safe (e.g., Acrylates Copolymer or Ethylene/Acrylic Acid Copolymer).*

Grouping/clustering proposal: *to be determined*

Hydroxyacetophenone

FOU = 409

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



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

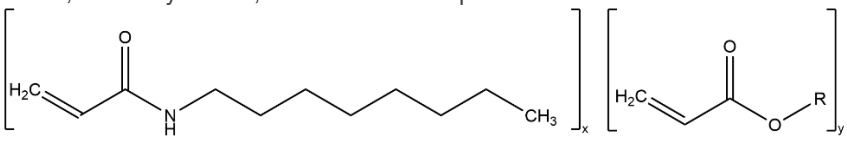
Notes: CAS No. *99-93-4*

Grouping/clustering proposal: *to be determined*

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*.

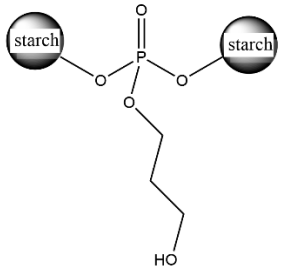
Grouping/clustering proposal: *to be determined*

Other polyacrylamides previously assessed by the Panel *include Polyquaternium-73 (no CAS No.), Polyquaternium-33 (CAS No. 69418-26-4), Polyquaternium-53 (84647-38-1), Polyacrylate-2 (31759-42-9), Polyacrylamide (9003-05-8), Polyquaternium-32 (35429-19-7), Acrylamidopropyltrimonium Chloride/Acrylamide Copolymer (75150-29-7), Polyquaternium-7 (26590-05-6), Acrylamide/Sodium Acryloyldimethyltaurate Copolymer (38193-60-1), Acrylamide/Ethyltrimonium Chloride Acrylate/Ethalkonium Chloride Acrylate Copolymer (no CAS), Polyquaternium-63 (no CAS No.), and Polyquaternium-39 (25136-75-8).*

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

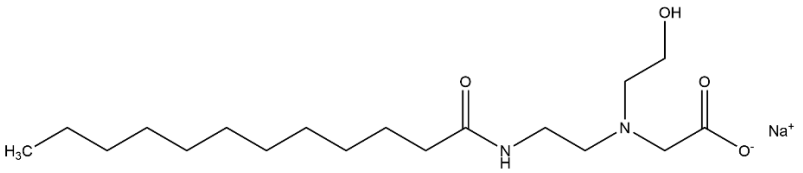
Notes: *CAS Nos. 113894-92-1, 39346-84-4, 53124-00-8. The Panel has previously assessed modified starches (e.g. Starch Hydroxypropyl Trimethylammonium Chloride), but not with phosphate groups.*

Grouping/clustering proposal: *to be determined*

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: *to be determined*

Calcium Sulfate

FOU = 331

Definition: Calcium Sulfate is the inorganic salt that conforms to the formula:

$CaSO_4$

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

Notes: *CAS Nos. 10034-76-1 and 10101-41-4.*

Grouping proposal: *Calcium Sulfate and Calcium Sulfate Hydrate (13397-24-5; FOU=9)*

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)*

Zingiber Officinale (Ginger) Root Extract (FOU priority ingredient)	326
Zingiber Officinale (Ginger) Extract	**-**
Zingiber Officinale (Ginger) Leaf Cell Extract	**-**
Zingiber Officinale (Ginger) Rhizome Extract	-
Zingiber Officinale (Ginger) Root	-
Zingiber Officinale (Ginger) Root Juice	-
Zingiber Officinale (Ginger) Root Oil	171
Zingiber Officinale (Ginger) Root Powder	11
Zingiber Officinale (Ginger) Water	2

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*

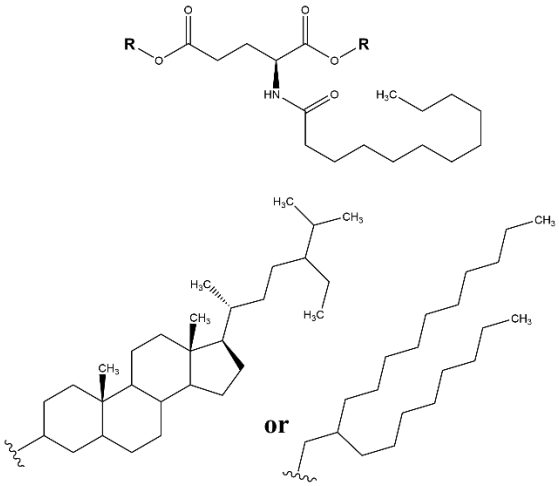
Grouping proposal: *(11 ingredients, 595 sum FOU)*

Rosa Centifolia Flower Extract **(FOU priority ingredient)**	**321**
Rosa Centifolia Bud Extract	**-**
Rosa Centifolia Callus Culture Extract	**-**
Rosa Centifolia Extract	**-**
Rosa Centifolia Flower	**17**
Rosa Centifolia Flower Juice	**3**
Rosa Centifolia Flower Powder	**6**
Rosa Centifolia Flower Water	**220**
Rosa Centifolia Flower Wax	**28**
Rosa Centifolia Leaf Cell Extract	**-**
Rosa Centifolia Stem Extract	**-**

Phytosteryl/Octyldodecyl Lauroyl Glutamate

FOU = 313

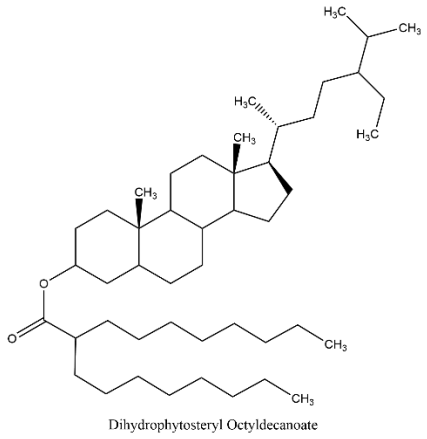
Definition: Phytosteryl/Octyldodecyl Lauroyl Glutamate is the mixed ester of phytosterol and Octyldodecanol with Lauroyl Glutamic Acid.



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: *to be determined*