Post Meeting Announcement

Expert Panel for Cosmetic Ingredient Safety
162nd Meeting (September 26-27, 2022) - Findings

September 30, 2022

● Final Safety Assessments

- **Diatomaceous Earth - 1 ingredient - Safe**
- **Fatty Esters End-Capped Alkoxylates – 14 ingredients – Safe**
- **Glycolactones – 5 ingredients – Split (1 safe; 4 insufficient)**
- **Hydroxyacetophenone – 1 ingredient – Safe**
- ***Portulaca oleracea* – 4 ingredients - Safe with qualifications**
- **Starch Phosphates – 4 ingredients - Safe**

● Tentative Safety Assessments

- **Naturally-Sourced Clays – 8 ingredients – Split (1 safe; 7 safe with qualifications)**
- **Polyhydroxystearic Acid – 3 ingredients – Safe**
- ***Rosa centifolia* – 12 ingredients – Split (9 safe with qualifications; 3 insufficient)**
- **Trisodium Ethylenediamine Disuccinate – 2 ingredients - Safe**

● Insufficient Data Announcement

- **Phenyl-Substituted Methicones – 7 ingredients**

● 162nd Meeting Notes

- **Director's Report**
- **Re-Reviews – 1 re-opened; 7 conclusions reaffirmed**
- **Re-Review summaries – 7 approved**
- **2023 Final Priorities**
- **Strategy Memo – low FOU ingredient re-reviews**
- **Report Format and SOPs**
- **Use Table Format**
- **Presentation and Strategy Memo - Yeast-derived ingredients**
- **Scientific Literature Reviews – available or under development**
- **Next Expert Panel Meeting – Monday and Tuesday, December 5-6, 2022**

Final Safety Assessments

Final safety assessments will be posted on the Cosmetic Ingredient Review (CIR) website at www.cir-safety.org. Unpublished data cited as references in CIR safety assessments are available for review. Any interested person who has sound scientific evidence that a final safety assessment is incorrect may petition the Expert Panel for Cosmetic Ingredient Safety (Panel) to amend the safety assessment.

Diatomaceous Earth

The Panel issued a Final Report with the conclusion that Diatomaceous Earth is safe in cosmetics in the present practices of use and concentration described in the safety assessment. Diatomaceous Earth is a polymorph of silica, or silicon dioxide, and is naturally-occurring. The Panel understands that Diatomaceous Earth, whether unprocessed (natural) or heat-processed (calcined or flux-calcined), can contain crystalline silica, a known respiratory carcinogen. However, the Panel noted that chronic inhalation studies of flux-calcined Diatomaceous Earth (which may comprise up to 60% crystalline silica) were negative for fibrosis or tumors in rats and guinea pigs. These data, coupled with the fact that Diatomaceous Earth is used at relatively low concentrations in cosmetics, mitigated concerns about use in products that may be incidentally inhaled, including face masks which may flake during drying.

Fatty Esters End-Capped Alkoxylates

The Panel issued a Final Report with the conclusion that the following 14 fatty esters end-capped alkoxylates are safe in cosmetics in the present practices of use and concentration described in the safety assessment.

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

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

The Panel noted the lack of developmental and reproductive toxicity data and genotoxicity studies for the fatty ester end-capped alkoxylated ingredients. However, the Panel also noted these ingredients are large molecules (> 1600 Da) and are not likely to absorb readily through the skin. This finding, coupled with the favorable safety profile and lack of structural features associated with genotoxicity, obviated the need for developmental and reproductive toxicity and genotoxicity data.

Glycolactones

The Panel issued a Final Report with the conclusion that Gluconolactone is safe in cosmetics in the present practices of use and concentration described in the safety assessment. The Panel also concluded that the available data are insufficient to make a determination that the following 4 ingredients are safe under the intended conditions of use in cosmetic formulations:

Galactonolactone*
Glucarolactone*
Glucoheptonolactone*
Ribonolactone*

** There are currently no uses reported for these ingredients.*

The insufficiencies include impurities data for all 4 insufficient ingredients, and cosmetic-specific method of manufacturing data for Glucarolactone and Glucoheptonolactone.

Hydroxyacetophenone

The Panel issued a Final Report with the conclusion this ingredient is safe in cosmetics in the present practices of use and concentration described in the safety assessment.

Previously, the Panel noted that Hydroxyacetophenone is conferred a generally recognized as safe (GRAS) status as a food flavoring substance by the Flavoring, Extract, and Manufacturing Association (FEMA). The Panel determined that systemic exposure to Hydroxyacetophenone would be much higher from consumption in food, relative to use in cosmetics. Systemic toxicity concerns were further mitigated by a high reported purity of 99.5%, low concentrations of use in cosmetics, as well as a favorable toxicological profile and lack of chemical structure alerts for this ingredient. The Panel noted the potential for ocular irritation, evidenced by neat application and testing of a granular substance; and thereby stated that manufacturers should be aware of the potential for ocular irritation when formulating products that contain this ingredient for use near the eye, and that measures should be taken to ensure that these products are not irritating.

Portulaca oleracea

The Panel issued a Final Report with the conclusion that the following 4 *Portulaca oleracea*-derived ingredients are safe in cosmetics in the present practices of use and concentration described in the safety assessment when formulated to be non-sensitizing:

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

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

The safety of these ingredients is supported by the available data on food use, limited systemic exposure from dermal absorption, and negative findings in human dermal irritation and sensitization studies on the whole plant extract. The Panel noted the presence of potentially sensitizing constituents (i.e., terpenes) in the composition of these individual ingredients, though at concentrations below concern; accordingly, the Panel stated

that because final product formulations may contain multiple botanicals, each possibly containing the same constituents of concern, formulators are advised to be aware of these constituents and to avoid reaching levels that may be hazardous to consumers.

Starch Phosphates

The Panel issued a Final Report with the conclusion that the following 4 ingredients are safe in cosmetics in the present practices of use and concentrations described in the safety assessment.

Distarch Phosphate
Distarch Phosphate Acetate*
Hydroxypropyl Starch Phosphate
Sodium Hydroxypropyl Starch Phosphate

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

The Panel noted that new data received on Sodium Hydroxypropyl Starch Phosphate. However, this data did not change their conclusion.

Tentative Safety Assessments

For the tentative safety assessments listed below, to be posted on the CIR website (www.cir-safety.org) in the near future, interested persons are given 60 days from the posting date to comment, provide information, and/or request an oral hearing before the Panel. Information may be submitted without identifying the source or the trade name of the cosmetic product containing the ingredient. All unpublished data submitted to CIR will be discussed in open meetings, and are available for review by any interested party. Please submit data and/or comments to CIR ***as soon as possible, but no later than 60 days from the actual posting date of the report, for full consideration. Submissions received thereafter may be in jeopardy of not being considered by the Panel.*** *The updated reports may be scheduled for review by the Expert Panel as early as at its* ***December 5-6, 2022*** *meeting. Of note, Naturally-Sourced Clays will not be scheduled in time for the December 2022 meeting.*

Naturally-Sourced Clays

The Panel issued a Tentative Amended Report for public comment with the conclusion that Kaolin* is safe in cosmetics in the present practices of use and concentration described in the safety assessment. The Panel noted that Kaolin is reported to be used in products which may be incidentally inhaled, including face powders at up to 15%; however, the data available from inhalation studies, including acute, chronic, and carcinogenicity data, suggest little potential for adverse respiratory effects at relevant doses.

The Panel also concluded that the following 7 ingredients are safe in cosmetics in the present practices of use and concentration, with the exception that the available data are insufficient to make a determination that these ingredients are safe in products that may be incidentally inhaled.

Attapulgite*
Bentonite*
Clay
Fuller's Earth*
Hectorite*
Illite
Montmorillonite*

**Previously reviewed by the Panel.*

Because of the potential for crystalline silica to be an impurity and the absence of repeated-dose inhalation data for these 7 ingredients, the additional data needed to determine the safety of the use of these ingredients in formulations that may be incidentally inhaled include:

- Composition and impurities data, specifically, quantification of crystalline silica content
- Chronic inhalation studies

The Panel was also made aware that nanoforms of clay ingredients could potentially be used in cosmetic formulations, including those that could result in incidental ingestion (e.g., lipstick and toothpaste). However, use of nanoform ingredients does not translate into nanoform final formulations. In these formulations, low concentrations of use (e.g., maximum reported use concentration of Kaolin in lipstick is 14.5%) and processing would be expected to result in much larger particle sizes (by, for example, agglomeration) in the consumer product.

Polyhydroxystearic Acid

The Panel issued a Tentative Report for public comment with the conclusion that the following 3 ingredients are safe in cosmetics in the present practices of use and concentration described in the safety assessment:

Polyhydroxystearic Acid Poly(3-Hydroxyoctanoic Acid)* Polylactic Acid

**Not reported to be in current use. Were the ingredient in this group 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.*

According to 2022 Voluntary Cosmetic Registration Program data and the results from a concentration of use survey completed by the Personal Care Products Council in 2021, Polyhydroxystearic Acid has 265 reported uses and is used at up to 14.2% (in lipsticks) and Polylactic Acid has 18 reported uses and is used at up to 5% (in skin cleansing products). The Panel discussed that these are large molecules, which are not likely to be absorbed. Additionally, the Panel considered the prior safety assessments of the corresponding monomers of these ingredients, and surmised that the systemic toxicity of these polymers would not be different. The Panel was further reassured of the dermal safety of these ingredients by the US Food and Drug Administration (FDA)-approved uses of Polylactic Acid in medical devices, as well as the existing American Society for Testing Materials (ASTM) International standard for this ingredient.

Rosa centifolia

The Panel issued a Tentative Report for public comment with the conclusion that the following 9 *Rosa centifolia*-derived ingredients are safe in cosmetics in the present practices of use and concentrations described in the safety assessment when formulated to be non-sensitizing:

Rosa Centifolia Bud Extract*
Rosa Centifolia Juice
Rosa Centifolia Flower Water
Rosa Centifolia Flower
Rosa Centifolia Flower Oil
Rosa Centifolia Flower Wax
Rosa Centifolia Flower Extract
Rosa Centifolia Stem Powder
Rosa Centifolia Stem 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 noted that the flower and bud derived ingredients that are reviewed in this safety assessment are found in foods that are GRAS. Composition and other data on the stem extract denote similarities to both the flower and the bud and obviate the need for additional toxicological data. These findings provided sufficient data for the Panel to conclude on the safety of flower-, bud-, and stem-derived ingredients. The Panel noted the presence of citronellol and geraniol, which are possible sensitizers, though at levels below concern for these individual ingredients. Accordingly, because final product formulations may contain multiple botanicals, each possibly containing the same constituents of concern, formulators are advised to be aware of these constituents and to avoid reaching levels that may be hazardous to consumers.

Additionally, the Panel also concluded the available data are insufficient to make a determination that the following 3 *Rosa centifolia*-derived ingredients are safe under the intended conditions of use in cosmetic formulations:

Rosa Centifolia Callus Culture Extract **
Rosa Centifolia Extract **
Rosa Centifolia Leaf Cell Extract **

***There are currently no uses reported for these ingredients.*

The additional data needed to determine safety for these 3 cosmetic ingredients are:

- Method of manufacture
- Composition and impurities data
- 28-day dermal toxicity data
    - if positive additional toxicological endpoints may be needed
- Dermal irritation and sensitization data.

Trisodium Ethylenediamine Disuccinate

The Panel issued a Tentative Report for public comment with the conclusion that Trisodium Ethylenediamine Disuccinate and Tetrasodium Iminodisuccinate are safe in cosmetics in the present practices of use and concentration as described in the safety assessment. The Panel determined that the available impurities, systemic toxicity, ocular irritation, and dermal irritation/sensitization data were sufficient to support the safety of these ingredients. The Panel noted mutagenicity in an vitro mammalian chromosomal aberration assay performed on Trisodium Ethylenediamine Disuccinate. However, concern for this result was mitigated as mutagenicity was only observed under specific conditions (without metabolic activation, 42-h incubation), and several other in vitro and in vivo genotoxicity assays had negative results.

Insufficient Data Announcement

For this insufficient data announcement, interested persons are given an opportunity to comment, provide information and/or request an oral hearing before the Panel. Information may be submitted without identifying the source or the trade name of the cosmetic product containing the ingredient. All unpublished data submitted to CIR will be discussed in open meetings, and are available for review by any interested party. Please submit data and/or comments to CIR ***as soon as possible, but no later than November 29, 2022, for full consideration****.* ***Submissions received thereafter might not be considered by the Panel at their next meeting.*** *This report may be scheduled for review by the Panel as soon as the* ***March 6-7, 2023*** *meeting.*

Phenyl-Substituted Methicones

The Panel issued an Insufficient Data Announcement (IDA) for these 7 phenyl-substituted methicone ingredients:

Diphenyl Dimethicone
Diphenylsiloxy Phenyl Trimethicone
Diphenylsiloxy Phenyl/Propyl Trimethicone
Phenyl Dimethicone
Phenyl Methicone
Phenyl Trimethicone
Trimethylsiloxyphenyl Dimethicone

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

- Method of manufacture and impurities (specific to cosmetic ingredients) for all ingredients
- Molecular weight ranges for all ingredients

162nd Meeting Notes

Director's Report

Dr. Heldreth noted that CIR is very fortunate to have a new and amazing Panel member join us at this meeting, Dr. Susan Tilton. All agreed that she did a splendid job.

He also noted that when he joined CIR, Dr. Dan Liebler was a rather new addition to the Panel. It is hard to believe that more than a decade has gone by since then, and that Dr. Liebler is now off to run his incorporated proteomics company. Everyone at CIR and on the Expert Panel for Cosmetic Ingredient Safety has greatly appreciated his expertise over the years and has also greatly enjoyed his camaraderie and humor. He will be dearly missed at these meetings.

Dr. Heldreth reiterated his gratitude to each and every one of the members and liaisons for making this Panel what it is. He also remarked about the anticipation to finally see everyone all in-person in December, some of whom it will be the first time in a while and others the very first time ever.

Re-Reviews

In accordance with its Procedures, the Panel evaluates the conclusions of previously-issued safety assessments approximately every 15 years. At this meeting, the Panel considered 7 previous assessments for re-review. The Panel determined that the following report should be reopened; a Draft Amended Report will be presented to the Panel for this safety assessment at a later meeting.

- Octyldodecyl Stearoyl Stearate – 1 ingredient

In contrast, the Panel reaffirmed the conclusions reached for the following 7 safety assessments (choosing to not re-open the original reports). A re-review summary will be presented to the Panel for each of these safety assessments at an upcoming meeting.

- Chloroxylenol – 1 ingredient
- Erythorbic Acid – 2 ingredients
- Glyceryl Diesters – 17 ingredients
- Hexamidine – 2 ingredients
- Mink Oil – 1 ingredient
- Sodium Lauryl Sulfoacetate – 1 ingredient

Additionally, the Panel reconsidered its previous decision to reopen the following safety assessment. A re-review summary will be presented to the Panel for this safety assessment at an upcoming meeting.

- Acid Orange 3 – 1 ingredient

Re-Review Summaries

Once the Panel determines to not reopen a previously-issued safety assessment, thereby reaffirming the existing conclusion, a rereview summary is prepared. The Panel approved the following 7 re-review summaries:

- Amyl Acetate – 2 ingredients
- Cottonseed Glyceride – 2 ingredients
- Glycol Stearate – 2 ingredients
- N,N-Bis(2-Hydroxyethyl-p-Phenylenediamine Sulfate – 1 ingredient
- PEGs Soy Sterol – 6 ingredients
- Polyacrylamide – 1 ingredient
- PPGs Stearyl Ether – 2 ingredients

2023 Priorities

The priority list is typically based on stakeholder requests ("for cause," e.g., a hair dye) and FOU data from FDA's VCRP; this year, VCRP data were received from the FDA on January 11 (in response to a Freedom of Information Act request).

While this list includes only the lead ingredients, groupings of ingredients were drafted in the meeting materials. The Panel considered these groupings and took no issue. These grouping may be found here https://www.cir-safety.org/about

There are 17 reports proposed (2 of the "per FOU" ingredients below are proposed to be reviewed together in 1 report) on the 2023 Final Priorities List. Reports previously prioritized and on the CIR docket at the end of 2022, as well as a significant number of re-reviews of previous assessments, will supplement the total number of reports to be assessed in 2023.

2023 Final Priorities List

Ingredients	Frequency of Use (FOU) Data Year 2022
For cause	
HC Blue No. 15	**22**
Isopropyl Cloprostenate & Ethyl Tafluprostamide	"**3**"
Per FOU	
Sodium Hydrosulfite	**246**
Pelargonium Graveolens Flower Oil	**236**
Phytosteryl/Isostearyl/Cetyl/Stearyl/Behenyl Dimer Dilinoleate	**234**
Diglycerin	**211**
Polyglycerin-3	**208**
Sigesbeckia Orientalis Extract	**202**
Houttuynia Cordata Extract	**201**
Malva Sylvestris (Mallow) Extract	**198**
Palmitoyl Pentapeptide-4	**198**
Salix Alba (Willow) Bark Extract	**197**
Centaurea Cyanus Flower Extract	**196**
Lactobacillus Ferment	**196**
Copper Gluconate	**192**
Inositol	**190**
Paeonia Suffruticosa Root Extract	**189**
Nelumbo Nucifera Flower Extract	**182**

Strategy Memo – rereview of ingredients with no reported use

A strategy memo was presented to the Panel, asking whether no reported frequency of use (FOU = 0) was sufficient reason to not reopen a previously-issued safety assessment that was due for re-review. The Panel stated that it is not, and that all previous safety assessment due for re-review are to be considered by the Panel, regardless of FOU.

Use Table Format

The Panel reviewed proposed changes to the Use Table format that is utilized in each report. Panel members stated that, at this time, they are not inclined to make changes to the existing Use Table format, which employs a summary of frequency and concentration of use based on duration of use and exposure type. Specifically, the Panel finds the summary information delivers a concise summary of this information as they review the report. However, it was requested that the existing format and the proposed format (which would articulate both frequency and concentration of use by individual product category) be provided concurrently in a Draft Report in order for the Panel to consider the functionality of each. Additionally, it has been requested that the journal be queried that, if the existing (summary) use table format is maintained, is it possible for an additional table that describes frequency and concentration of use for each product category be included as a supplement to the report upon publication.

Report Format and SOPs Discussion

The Panel was presented with the report format outline and a compilation of all current and previous boilerplate/guidance documents used as standard operating procedures (SOPs). Changes to some of the boilerplate language were suggested.

Presentation and Strategy Memo – Yeast-derived ingredients

A thorough and insightful presentation on yeast-derived cosmetic ingredients was provided by Dr. Pokrzywa and Dr. Mazalrey, of Silab. The purpose of the presentation was to impart information on the strains of yeast used in cosmetic ingredients, as well as the processes used in manufacturing such ingredients, thereby aiding in the development of the group of ingredients to be reviewed in the resulting safety assessment. This presentation has been added to the meeting page https://www.cir-safety.org/meeting/162nd-expert-panel-meeting.

The Panel discussed the strategy of grouping the yeast-derived ingredients for the safety evaluation by considering the taxonomy, identification and analytical characterization, biosafety level (BSL) classification, as well as the unique cosmetic ingredient manufacturing processes. The Panel further discussed the critical elements that may contribute to the development of the resulting safety assessment, such as VCRP data, marketing information supplemented by industry submissions, and food use data (including GRAS status as determined by FDA), as well as the importance

of distinguishing the pathogenic yeasts of the Saccharomycetes class (which would not be included) and those with BSL-1 confirmation (which would be included).

Scientific Literature Reviews

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

Basic Yellow 87
Charcoal Powder
Diglycerin and Polyglycerins
Hyaluronates
Malva sylvestris (Mallow)-Derived Ingredients
Olea europaea (Olive)-Derived Ingredients
Pyridoxine and Pyridoxine HCl
Sodium Lauroamphoacetate Group
Zanthoxylum piperitum – Derived Ingredients

Next Expert Panel Meeting

Monday and Tuesday, December 5-6, 2022, to be held ***in-person*** at the Melrose Hotel, 2430 Pennsylvania Avenue, NW, Washington, DC.

Please check the CIR website for details as the meeting approaches. The link will be available approximately a month before the meeting and will be found on the 163rd meeting page of the CIR website. https://www.cir-safety.org/