ADMIN

Memo

Agenda

Minutes

Rereview Summary: Methacrylate Ester Monomers

EXPERT PANEL MEETING
March 7-8, 2022

Cosmetic Ingredient Review

Commitment & Credibility since 1976

MEMORANDUM

To: The Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Bart Heldreth, Ph.D., Executive Director, Cosmetic Ingredient Review
Subject: 160th Meeting of the Expert Panel — Monday and Tuesday, March 7-8, 2022
Date: February 11, 2022

Welcome to the first Panel Meeting of 2022! The agenda and accompanying materials for the 160th Expert Panel Meeting, to be held on March 7-8, 2022, are now available. The location is the ***same*** – this meeting will be held virtually! Invitations (3 of them) to join the meeting will arrive separately in your email inbox. 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/160th-expert-panel-meeting

The meeting agenda includes the consideration of 15 reports advancing in the review process, including 4 final reports, 7 tentative reports, and 4 draft reports. Also on the agenda are 3 administrative items: a re-review summary for Methacrylate Ester Monomers, a strategy memo regarding the report on yeast ingredients, and Draft 2023 Priorities. Also, before we split-off for team meetings, we will have a presentation from Dr. Don Bjerke regarding alternative methods for the assessment of dermal sensitization potential.

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Team Meetings

Draft Reports - there are 4 draft reports for review – Sufficient data to proceed, or issue an IDA?

1. Clays – DAR (Christina) – ***Dr. Belsito reports on day 2*** - In 2018, the Panel voted to re-open the 2003 safety assessment on several silicates, clays, and zeolites to include additional ingredients. At the April 2019 meeting, the Panel decided to split the clay ingredients into a separate report. At that meeting, the Panel also determined that the data were insufficient to support safety of the 8 clay ingredients.

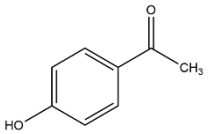
   The additional data needs are:
   a) The mean and range of particle sizes (and corresponding sizes of final formulation particles) that are used in spray and powder formulations
   b) Chemical characterization, composition, and impurities data
   c) Method of manufacturing and/or source data.

   Since the issuance of the Insufficient Data Announcement (IDA), CIR has not received any of the requested data. Since the re-review was initiated, the unpublished data that CIR has received from the Council are concentration of use data and method of manufacturing and particle size distribution for Bentonite.

   According to the 2022 VCRP survey data, Kaolin has the most reported uses in cosmetic products, with a total of 1046; the majority of uses are in leave-on formulations. Bentonite has the second most reported uses in cosmetic products, with a total of 262; a little more than half are reported in leave-on formulations. The frequencies of use for both of these ingredients have greatly changed since the original safety assessment was finalized; in 1998, Kaolin was reported to have 509 uses and Bentonite was reported to have 94. The results of concentration of use surveys conducted by the Council indicate Kaolin also has the highest concentration of use in a leave-on formulation; it is used at up to 53% in manicuring preparations. Bentonite is reported to have a maximum concentration of use for leave-on products of 15% in skin care preparations. According to the original safety assessment, the maximum leave-on use concentration in 1999 for Kaolin was 100% in skin care preparations; the maximum leave-on use concentration for Bentonite was 8% in makeup foundations.

   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, unsafe, insufficient data, or split conclusion, and Discussion items should be identified. If the available data are still insufficient, the Panel should issue an IDA if the needs are new, specifying the data needs therein.

2. Hydroxyacetophenone – DR (Preethi) – ***Dr. Cohen reports on day 2*** - This is the first time the Panel is reviewing the safety of this ingredients. A Scientific Literature Review (SLR) was announced on April 26, 2021. Comments on the SLR that were received from the Council have been addressed. Following the announcement of the SLR, the following were received:



   - Human patch test of a SPF product containing 0.05% Hydroxyacetophenone
   - 21-Day cumulative irritation assay of a SPF 70 cream containing 0.05% Hydroxyacetophenone
   - Repeated insult patch test of a SPF 70 cream containing 0.5% Hydroxyacetophenone
   - Delayed contact hypersensitivity in guinea pigs (Buehler test) of Parahydroxyacetophenone
   - Rabbit closed patch study of Parahydroxyacetophenone
   - Correspondence from a supplier providing permission for use of these data was received
     - Certificate of analysis of Hydroxyacetophenone
     - Production flow chart of Hydroxyacetophenone
     - Summary of a dermal irritation study of Hydroxyacetophenone
     - Summary of an HRIPT of Hydroxyacetophenone

   According to 2022 VCRP survey data, Hydroxyacetophenone is reported to be used in 791 formulations, of which 671 are leave-on products; there are 236 reported uses in moisturizing products and 202 reported uses in face and neck products. Results from a 2020 concentration of use survey conducted by the Council indicate that the highest concentration of use reported for Hydroxyacetophenone is 5%,

in non-spray night products and in paste masks and mud packs; the night product use represents the greatest maximum concentration of use for leave-on dermal exposure.

This ingredient has been reported to be used in products that may come into contact with the eyes; for example, Hydroxyacetophenone is reported to be used at up to 0.23% in eye lotions and eye makeup removers. Reported use of Hydroxyacetophenone in lipsticks also indicates the possibility for incidental ingestion. Hydroxyacetophenone is also reported to be used at up to 0.6% in formulations that could come in contact with mucous membranes, such as bath soaps and detergents. Hydroxyacetophenone is reported to be used in 7 baby products; concentration of use data were not provided for this type of exposure.

Hydroxyacetophenone is reported to be used in cosmetic formulations that could be incidentally inhaled. For example, it is reported to be used in aerosol hair sprays (at up to 0.5%) and in face powder (concentration of use not reported). Additionally, Hydroxyacetophenone is reported to be used in moisturizing spray (at up to 0.3%).

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, unsafe, or split conclusion, and Discussion items should be identified. If the available data are insufficient, the Panel should issue an IDA, specifying the data needs therein.

3. *Rosa centifolia* – DR (Regina) – ***Dr. Cohen reports on day 2*** - This is the first time the Panel is reviewing these ingredients. An SLR on 12 *Rosa centifolia*-derived ingredients was issued on May 4, 2021. Comments were received on the SLR and addressed.

The following unpublished data have been added to the draft report that is included for the Panel's review:

- Unpublished irritation and sensitization data submitted by the Research Institute for Fragrance Materials (RIFM)
- Manufacturing, safety, and specification data on Rosa Centifolia Flower Extract, Flower Juice, and Flower Water
- Chemical characterization and method of manufacture data specific to Rosa Centifolia Flower Extract and Rosa Centifolia Flower Water as used in a cosmetic formulation
- Use concentration data
- Human maximization and skin irritation test on a face mask containing 0.8% Rosa Centifolia Flower; also, additional summary information for this HRIPT

According to 2022 VCRP data, Rosa Centifolia Flower Extract has the greatest frequency of use; it is reported to be used in 174 cosmetic products, 150 of which are leave-on formulations. The results of a concentration of use survey conducted by the Council in 2021 indicate that Rosa Centifolia Flower Water has the highest concentration of use; it is used at maximum use concentrations up to 0.096%. According to both VCRP and Council survey data, 5 of the 12 *Rosa centifolia*-derived ingredients reviewed in this safety assessment are not currently in use in cosmetic products.

Cosmetic products containing *Rosa centifolia*-derived ingredients may incidentally come in contact with the eyes (e.g., Rosa Centifolia Flower Extract is used in mascaras at up to 0.02%). *Rosa centifolia*-derived ingredients are also being used in cosmetic products that may be incidentally ingested (e.g., Rosa Centifolia Flower Extract is used at up to 0.002% in lipstick formulations).

Some of these ingredients are reported to be used in cosmetic products that could possibly be inhaled. For example, Rosa Centifolia Flower Extract is reported to be used at up to 0.025% in spray fragrance preparations and at up to 0.0001% in face powders.

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, unsafe, or split conclusion, and Discussion items should be identified. If the available data are insufficient, the Panel should issue an IDA, specifying the data needs therein.

4. Starch Phosphates – DR (Regina) – ***Dr. Belsito reports on day 2*** – An SLR on these 5 starch phosphates as used in cosmetic ingredients was issued on April 29, 2021. Comments on the SLR and the following unpublished data, all received from the Council, have been added to the draft report that is included for the Panel's review:

    - Use concentration data
    - An evaluation of the contact-sensitizing potential of an eyeliner containing 7.181% Distarch Phosphate in human skin by means of the maximization assay.
    - Clinical evaluation report: Human patch test of a conditioner containing 2% Hydroxypropyl Starch Phosphate.
    - Repeated insult patch test of a conditioner containing 2% Hydroxypropyl Starch Phosphate.

    According to 2022 VCRP data, Hydroxypropyl Starch Phosphate is reported to have the greatest frequency of use; it is reported to be used in 261 cosmetic products, 193 of which are rinse-offs. The results of a concentration of use survey, conducted by the Council in 2020 and provided to CIR in 2021, indicate that Distarch Phosphate has the highest concentration of use; it is reported to be used at maximum use concentrations up to 7.5% in leave-on products (eyeliners). According to VCRP and Council survey data, 2 of the starch phosphates reviewed in this safety assessment (Distarch Phosphate Acetate and Sodium Dimaltodextrin Phosphate) are not currently in use in cosmetic products.

    Cosmetic products containing starch phosphates may incidentally come in contact with the eyes (e.g., Distarch Phosphate in eyeliners at concentrations up to 7.5%). Additionally, Distarch Phosphate (at up to 0.5% in lipstick) and Hydroxypropyl Starch Phosphate (at up to 0.88% in bath soaps and detergents) are used in products that come in contact with mucous membranes.

    Distarch Phosphate is used in cosmetic products that could possibly be inhaled. It is reported to be used in hair sprays (aerosols) at concentrations up to 5.3%, and in face powders (concentrations not reported).

    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, unsafe, or split 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 7 draft tentative reports for consideration.

1. Barley – TR (Christina) – ***Dr. Belsito reports on day 2*** – At the December 2021 meeting, the Panel issued a new IDA. The additional data needed to determine safety of these ingredients as used in cosmetics are:

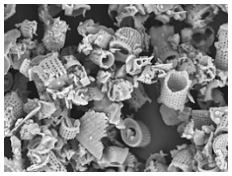
    a. Clarification of the plant parts used to make the whole plant extracts Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract
    b. Method of manufacturing for Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract
    c. Composition and impurities data for Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract
    d. 28-day dermal toxicity data on the whole plant extract Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract
        i. If positive, additional data, such as developmental and reproductive toxicity and genotoxicity data, may be needed
        ii. Alternatively, acceptable evidence of safe use as food for ingredients derived from the flower, leaf, stem, and root
    e. Dermal irritation and sensitization data for Hordeum Leaf Extract or other leaf ingredients

Since the issuance of the second IDA, CIR has received unpublished method of manufacturing and impurities information on barley seed extracts from suppliers that use the names Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract ("b" above). These data are on an extract of the grain; these names may be artifacts of a time where ingredients were named for the plants of origin and not the specific plant parts. Council is working to clarify this issue. Additionally, recently published genotoxicity data on the polysaccharide fraction of young Hordeum vulgare leaves was found in an updated literature search. All of these data have been incorporated into the report and are highlighted to aid in the Panel's review.

The Use Table has been updated with the 2022 VCRP data. Uses for Hordeum Vulgare Extract increased from 167 to 174. The majority of the uses are in leave-on makeup preparations and skin care products. Minor changes in use were observed for Hordeum Distichon (Barley) Extract (an increase of 1 to 31 total formulations) and Hordeum Vulgare Leaf Extract (a decrease from 36 formulations to 33 formulations). Additionally, use has now been reported for Hordeum Vulgare Leaf Juice (a total of 2 leave-on formulations) and Hordeum Vulgare Root Extract (1 leave-on formulation).

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

2. Diatomaceous Earth – TR (Christina) – ***Dr. Belsito reports on day 2*** – At the September 2021 meeting, the Panel issued an IDA. The additional data needed to determine safety for this cosmetic ingredient are:



   a. Clarification on the type(s) of Diatomaceous Earth that is used in cosmetic products (i.e., natural, calcined, and/or flux-calcined)
   b. Method of manufacturing for the type(s) of Diatomaceous Earth that is used in cosmetic products
   c. Composition and impurities data (including crystalline silicate content) on the type(s) of Diatomaceous Earth that is used in cosmetic products

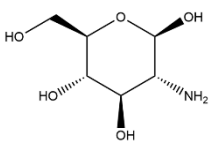
Since the issuance of the IDA, CIR has received information from a supplier providing information on the type of Diatomaceous Earth used in cosmetics (soda ash flux-calcined; "a" from above), method of manufacturing ("b" from above), and composition and impurities data ("c" from above). CIR also received an in vitro ocular study on a formulation containing 9% - 11% soda ash flux-calcined Diatomaceous Earth (diluted at 2%, 5%, and 10%), and information that clarified that some of the previous safety test data that are summarized in the report are on soda ash flux-calcined Diatomaceous Earth. Additional data on the composition of Diatomaceous Earth from the published literature have also been identified.

CIR also received comments and information from the International Diatomite Producers Association (IDPA) for the Panel's consideration. The comments were accompanied by a few published documents that can be furnished to the Panel, upon request. IDPA reports that its member companies only supply natural Diatomaceous Earth for use in cosmetics.

The Use Table has been updated with 2022 VCRP data and with new concentration of use data from the Council. Uses for Diatomaceous Earth increased from 116 to 135. The most notable change is that the number of uses in nail polish and enamel increased from 15 uses to 49. Currently, more than half of the uses for Diatomaceous Earth reported in the VCRP are in leave-on formulations. The results of the updated concentration of use survey conducted by the Council in 2021 indicate that Diatomaceous Earth is now used at up to 2% in rinse-off products (paste masks, which were previously reported to be used at up to 62.2%), and up to 0.01% in leave-on products (nail polish and enamel). Uses are reported in face powders in the VCRP, but no concentrations of use are reported. No other confirmed uses in products which may be incidentally inhaled are reported.

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, unsafe, or split conclusion, and Discussion items should be identified. If the available data remain insufficient, the Panel should issue a tentative report with an insufficient data conclusion, specifying the data needs in the report Discussion.

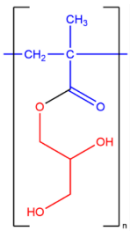
3. Glucosamine – TR (Priya) – ***Dr. Belsito reports on day 2*** – The 4 ingredients reviewed in this report include Acetyl Glucosamine, Glucosamine, Glucosamine HCl, and Glucosamine Sulfate. At the December 2021 meeting, the Panel issued an IDA for this ingredient group. In order to conclude on safety, the Panel requested impurities data on Acetyl Glucosamine, and irritation and sensitization data on all ingredients at the maximum concentration of use. Since the previous review of this report, the following unpublished data were received, incorporated into the text, and highlighted:



- HRIPT performed on 105 subjects using a liquid foundation containing 2% Acetyl Glucosamine
- 21-d cumulative irritation assay performed on 12 subjects using an eye cream containing 2% Acetyl Glucosamine
- In vitro ocular irritation assay performed using a face serum containing 2% Acetyl Glucosamine

The Panel should carefully consider and discuss the data (or lack thereof), and the draft Abstract and draft Discussion presented in this report. A tentative report with a safe, safe with qualifications, unsafe, insufficient data, or split conclusion should then be issued.

4. Glyceryl Acrylates – TR (Regina) - ***Dr. Cohen reports on day 2*** –Upon initial review, at the September 2021 meeting, this report included 3 ingredients. However, at that meeting, the Panel determined that it was appropriate to consider a 4th ingredient, Glyceryl Polyacrylate; consequently, this ingredient has been added to the safety assessment. After reviewing the draft report at the September 2021 meeting, the Panel issued an IDA, with the following data needs:



For all, except Glyceryl Polymethacrylate:

- Method of manufacture data

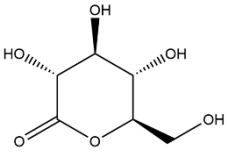
For all 4 ingredients:

- Molecular weights and impurities, including residual monomers
  - Depending on the data received (especially residual monomer content), 28-d dermal toxicity, skin penetration data, and other toxicity endpoints may be needed
- Genotoxicity data
- Skin irritation and sensitization data at maximum use concentration

Following the IDA, CIR received data on concentration of use; a toxicology summary on Glyceryl Acrylate/Acrylic Acid Copolymer (impurities, acute oral toxicity, skin, ocular, and mucosal membrane irritation; summary data on Glyceryl Polyacrylate (molecular weight and impurities, genotoxicity, and skin irritation and sensitization); and various dermal irritation sensitization studies. Additionally, updated VCRP (2022) data have been received, and are updated within the report. No significant changes in frequency of use were noted.

The Panel should carefully consider and discuss the data (or lack thereof), and the draft Abstract and draft Discussion presented in this report. A tentative report with a safe, safe with qualifications, unsafe, insufficient data, or split conclusion should then be issued.

5. Glycolactones – TR (Priya) – ***Dr. Cohen reports on day 2*** – The ingredients reviewed in this report include Galactonolactone, Glucarolactone, Glucoheptonolactone, Gluconolactone, and Ribonolactone. At the September 2021 meeting, the Panel issued an IDA for this ingredient group. In order to determine the safety of these ingredients, the Panel requested the following data:



- Method of manufacturing data for Glucarolactone and Glucoheptonolactone
- Impurities data on Galactonolactone, Glucarolactone, Glucoheptonolactone, and Ribonolactone
- Irritation and sensitization data at maximum concentrations of use

Since the issuing of the IDA, an HRIPT performed in 106 subjects using a product containing 15% Gluconolactone was received. The test substance was considered to be non-irritating and non-sensitizing.

The Panel should carefully consider and discuss the data (or lack thereof), and the draft Abstract and draft Discussion presented in this report. A tentative report with a safe, safe with qualifications, unsafe, insufficient data, or split conclusion should then be issued.

6. *Portulaca oleracea* – TR (Preethi) – ***Dr. Belsito reports on day 2*** – This is the 3rd time the Panel is seeing a safety assessment on these 4 cosmetic ingredients. At the December 2021 meeting, a draft tentative report was presented to the Panel. Upon review, the Panel issued a 2nd IDA for:

- 28-d dermal toxicity study for Portulaca Oleracea Extract, at the maximum concentration of use, preferably with the ingredient in an hydroalcoholic solvent
    - if positive, additional toxicity data, such as developmental and reproductive toxicity and genotoxicity data, may be needed
- Clarification on which part(s) of the plant are consumed as a food, and which plant part(s) are used in cosmetics

As of the date of this memo, no data have been received in response to the IDA. Updated (2022) VCRP data were received from the FDA, and have been incorporated. No significant changes in reported use categories or frequencies occurred.

The Panel should carefully consider and discuss the data (or lack thereof), and the draft Abstract and draft Discussion presented in this report. A tentative report with a safe, safe with qualifications, unsafe, insufficient data, or split conclusion should then be issued.

7. Zeolites – TAR (Christina) – ***Dr. Cohen reports on day 2*** – At the December 2021 meeting, the Panel issued a new IDA on the 6 zeolite ingredients. The additional data needs are:

- Maximum use concentration for both mined and synthetic zeolites
- Method of manufacturing and/or source data for Ammonium Silver Zeolite, Gold Zeolite, Silver Copper Zeolite, Titanium Zeolite, and Zinc Zeolite
- Chemical characterization, including specific framework(s), and composition and impurities data for mined Zeolite, Ammonium Silver Zeolite, Gold Zeolite, Silver Copper Zeolite, Titanium Zeolite, and Zinc Zeolite
    - Depending on composition, additional toxicity data may be needed
- The range of particle sizes that is used in spray and powder formulations
- Human dermal irritation and sensitization data at maximum use concentrations

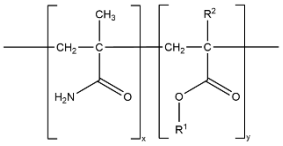
None of the requested data has been received. Since the last meeting, additional published data regarding erionite and its relationship to natural zeolites have been added to the Composition/Impurities section of the report. Council comments on the previous draft tentative amended report have been addressed.

CIR has received 2022 FDA VCRP data, and the Use Table has been updated. Uses for Zeolite have increased from 28 formulations to 33, with new uses mainly reported in leave-on products. No changes were reported for Zinc Zeolite and no uses were reported for the remaining zeolite ingredients. The table has also been updated with the concentration of use data that were received prior to the December 2021 meeting; these data are not included in this submission because they were provided to the Panel in the Wave 2 package for that meeting. According to that data, the maximum concentration of use for synthetic Zeolite is 0.9% in aerosol hair sprays. The maximum concentration of use for natural Zeolite is 0.6% in face powders and foundations. However, at the December 2021 meeting, an industry representative indicated that Zeolite is used at concentrations of greater than 35% in self-heating masks. Official documentation of this information has not yet been received.

The Panel should carefully consider and discuss the data (or lack thereof), and issue a tentative amended report with a safe, safe with qualifications, insufficient data, unsafe, or split conclusion.

Draft Final Reports - there are 4 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.

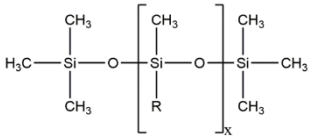
1. Acrylamide/Acrylate Copolymers – FR (Priya) – ***Dr. Belsito reports on day 2*** – At the December 2021 meeting, the Panel issued a Tentative Report for public comment with the conclusion that the acrylamide/acrylate copolymer ingredients reviewed in the safety assessment are safe in the present practices of use and concentration.



Updated 2022 FDA VCRP data were received and incorporated into the report. These data were similar to 2021 FDA VCRP data; however, Potassium Acrylates/Acrylamide Copolymer is now reported to be in use. It should also be noted that 3 of the 8 uses for this ingredient are reported to be in baby products.

Comments that were received from the Council have been addressed. After carefully reviewing the Abstract, Discussion, and Conclusion, the Panel should be prepared to issue a final report.

2. Methicones – FAR (Preethi) – ***Dr. Cohen reports on day 2*** – At the December 2021 meeting, a draft final amended report on the 30 ingredients included in this assessment was presented to the Panel for the 3rd time. Concurrently, the Inhalation Resource Document was revised by CIR Staff to further clarify issues raises by these concerns. In response, the Panel felt that incidental inhalation-related concerns were mitigated, after considering data on particle size distributions for these products, duration of exposure, updates to the Respiratory Resource document, a lack of toxicity in a short-term inhalation study, and an overall favorable toxicological profile for this ingredient group.



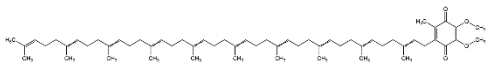
However, the Panel asserted that, in addition to particle size distribution, other information is still needed to make a determination of safety for the use of these ingredients in products delivered via airbrush technology, including dose, chemistry, duration of exposure, particle volume and density, and details regarding the mode/device used for application of the cosmetic. Consequently, the Panel issued a Revised Tentative Amended Report with a split conclusion. Specifically, the Panel concluded that all of these ingredients are safe in cosmetics in the present practices of use and concentration described in the safety assessment when formulated to be non-irritating, with the exception that the available data are insufficient to make a determination of safety in products that may be incidentally inhaled when applied via airbrush devices.

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

3. *Rosa damascena* – FR (Preethi) – ***Dr. Belsito reports on day 2*** – At the September 2021 Panel meeting, the Panel issued a tentative report for public comment with the conclusion that these ingredients are safe as used in the present practices of use and concentration described in the safety assessment when formulated to be non-sensitizing.

Data from 2022 VCRP were received and have been incorporated. Of note in the newly reported uses, is the increase from 22 to 74 reported used for Rosa Damascena Flower Extract in lipsticks. Also, updated concentration of use data were received from the Council in September 2021, and have been incorporated in the report. This updated submission was prompted by the Panel's request to clarify the maximum use concentration reported for Rosa Damascena Flower Water at 32.7% in face and neck, non-spray, products (which was verified to be 0.94%). Additionally, a supplier confirmed that the ingredient with the highest reported concentration of use for these ingredients, Rosa Damascena Flower Oil (at up to 10.8% in other skincare preparations) is an essential oil which is sold with instructions to dilute before use. The second highest reported concentration of use is now Rosa Damascena Flower Water, at up to 1.9% in foundations.

The Panel should carefully consider the newly added data, the Abstract, Discussion, and Conclusion, and be prepared to issue a final report.

4. Ubiquinone – FR (Preethi) – ***Dr. Cohen reports on day 2*** – At the September 2021 meeting, the Panel considered  the available data and issued a tentative report for public comment with the conclusion that the 4 Ubiquinone ingredients are safe in cosmetics in the present practices of use and concentrations described in the safety assessment.

   Since September, published data on ex vivo Ubiquinone dermal penetration, as well as the photostability, and radical formation potential of Ubiquinone and Ubiquinol were found and have been added to the report. The latter study has been placed in the chemistry section; we request the Panel's opinion of whether it is useful. Data from 2022 VCRP were also received and have been incorporated. Use categories have remained the same, with negligible changes in the reported uses compared to the previous year. Total reported uses of Ubiquinone decreased from 231 to 221 formulations, while Hydroxydecyl Ubiquinone and Ubiquinol use remained mostly the same.

   The Panel should carefully consider the newly added data, the Abstract, Discussion, and Conclusion, and be prepared to issue a final report.

Administrative Items - there is 1 rereview summary, 1 strategy memo, and the Draft 2023 Priorities Document.

1. Methacrylate Ester Monomers– RRsum – separate book – (Regina) – ***Dr. Cohen reports on day 2*** – The Panel first published the Final Report on the Safety Assessment of Methacrylate Ester Monomers Used in Nail Enhancement Products in 2005. The Panel concluded that the 22 methacrylate ester monomers therein are safe as used in nail enhancement products when skin contact is avoided. The conclusion also states that products containing these ingredients should be accompanied with directions to avoid skin contact, because of the sensitizing potential of methacrylates. In December 2021, the Panel confirmed this conclusion. The Panel should carefully consider the rereview summary and finalize it.

2. Yeast – SM (PC) – ***Dr. Cohen reports on day 2*** – The CIR staff is asking the Panel for guidance; in light of the data that have been received:

   - should this report continue to only review the safety of *Saccharomyces cerevisiae*-derived yeast ingredients, which would be explained in the document, and only data on *Saccharomyces cerevisiae*-derived ingredients be included.
     Or
   - should data on yeast ingredients derived from other species of yeast of the class Saccharomycetes be included in the document. And if so, should the related yeast cosmetic ingredients (e.g., Pichia Anomala Extract) also be included in this assessment.

3. Draft 2023 Priorities – Admin – (Bart/Monice) – ***Dr. Belsito reports on day 2*** – The CIR Procedures require preparation of the 2023 Draft Priority List for public comment by June 1, 2022. However, it is advantageous for the 2023 Draft Priority List to be issued for public comment earlier (March 2022) in the process to allow more time for the acquisition of data. 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 11 (in response to a Freedom of Information Act request).

   While this list includes only the lead ingredients, groupings of ingredients, drafted by CIR Staff, can be found on the following pages. There are 15 reports proposed, covering 60 ingredients, on the 2023 Draft Priorities List (2 of the ingredients on this list are proposed to be grouped together in 1 report). Once a proposal of a hair dye for assessment has been received from the PCPC Hair Color Technical Committee, 16 new reports in total will be proposed for the 2023 docket. Reports previously prioritized and on the CIR docket at the end of 2022, as well as an extensive number of re-reviews of previous assessments, will supplement the total number of reports to be assessed in 2023. Additionally, if the prostaglandin analogs are considered to be with the Panel's purview, those will constitute at least 1 additional assessment.

   The Panel should carefully consider these ingredients and ingredient groupings.

Full Panel Meeting

The Panel will consider the 4 reports to be issued as final safety assessments, followed by the remaining reports advancing in the process (including the tentative reports and draft reports). In addition, a consensus should be reached for the 3 administrative items.

Please remember, the meeting starts at 8:30 am on day 1 and 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
160th Meeting of the Expert Panel for Cosmetic Ingredient Safety
March 7th - 8th, 2022

Virtual via Microsoft Teams

Monday, March 7th		
8:30 AM	**WELCOME TO THE 160th EXPERT PANEL TEAM MEETINGS**	**Drs. Bergfeld/Heldreth**
8:40 AM	**PRESENTATION - alternative methods for the assessment of sensitization potential**	**Dr. Bjerke**
9:45 AM	**TEAM MEETINGS**	**Drs. Cohen/Belsito**

Dr. Cohen's Team	
TAR (CB)	Zeolites
TR (CB)	Diatomaceous Earth
DAR (CB)	Clays
TR (CB)	Barley
TR (RT)	Glyceryl Acrylates
DR (RT)	*Rosa centifolia*
DR (RT)	Starch Phosphates
RRsum (RT)	Methacrylate Ester Monomers
Admin (BH/MF)	Priorities
FAR (PR)	Methicones
FR (PR)	*Rosa damascena*
FR (PR)	Ubiquinone
TR (PR)	*Portulaca oleracea*
DR (PR)	Hydroxyacetophenone
FR (PC)	Acrylamide/Acrylate Copolymers
TR (PC)	Glucosamine
TR (PC)	Glycolactones
SM (PC)	Yeast-derived ingredients

Dr. Belsito's Team*	
FAR (PR)	Methicones
FR (PR)	*Rosa damascena*
FR (PR)	Ubiquinone
TR (PR)	*Portulaca oleracea*
DR (PR)	Hydroxyacetophenone
FR (PC)	Acrylamide/Acrylate Copolymers
TR (PC)	Glucosamine
TR (PC)	Glycolactones
SM (PC)	Yeast-derived ingredients
Admin (BH/MF)	Priorities
TAR (CB)	Zeolites
TR (CB)	Diatomaceous Earth
DAR (CB)	Clays
TR (CB)	Barley
TR (RT)	Glyceryl Acrylates
DR (RT)	*Rosa centifolia*
DR (RT)	Starch Phosphates
RRsum (RT)	Methacrylate Ester Monomers

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

(BH) Bart Heldreth || (MF): Monice Fiume || (CB): Christina Burnett || (PC): Priya Cherian || (PR): Preethi Raj || (RT): Regina Tucker || (JZ): Jinqiu Zhu

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

Tuesday, March 8th			
8:30 AM	**WELCOME TO THE 160th FULL EXPERT PANEL MEETING**		**Dr. Bergfeld**
8:40 AM	Admin	**MINUTES OF THE DECEMBER 2021 EXPERT PANEL**	**Dr. Bergfeld**
9:00 AM	**DIRECTOR'S RPORT**		**Dr. Heldreth**
9:10 AM	**FINAL REPORTS, REPORTS ADVANCING TO THE NEXT LEVEL, OTHER ITEMS**		

Final Reports

FR (PC)	Acrylamide/Acrylate Copolymers – *Dr. Belsito reports*
FAR (PR)	Methicones – *Dr. Cohen reports*
FR (PR)	*Rosa damascena* – *Dr. Belsito reports*
FR (PR)	Ubiquinone – *Dr. Cohen reports*

Reports Advancing

TR (PR)	*Portulaca oleracea* – *Dr. Belsito reports*
DR (PR)	Hydroxyacetophenone – *Dr. Cohen reports*
TR (PC)	Glucosamine – *Dr. Belsito reports*
TR (PC)	Glycolactones – *Dr. Cohen reports*
TR (CB)	Diatomaceous Earth - *Dr. Belsito reports*
TAR (CB)	Zeolites – *Dr. Cohen reports*
DAR (CB)	Clays – *Dr. Belsito reports*
TR (RT)	Glyceryl Acrylates – *Dr. Cohen reports*
TR (CB)	Barley – *Dr. Belsito reports*
DR (RT)	*Rosa centifolia* – *Dr. Cohen reports*
DR (RT)	Starch Phosphates – *Dr. Belsito reports*

Other Items

SM (PC)	Yeast-derived ingredients – *Dr. Cohen reports*
Admin (BH)	Priorities – *Dr. Belsito reports*
RRsum (RT)	Methacrylate Ester Monomers – *Dr. Cohen reports*

ADJOURN - *Next meeting Thursday and Friday, **June 16-17, 2022**, 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

(BH) Bart Heldreth || (MF): Monice Fiume || (CB): Christina Burnett || (PC): Priya Cherian || (PR): Preethi Raj || (RT): Regina Tucker || (JZ): Jinqiu Zhu

ONE HUNDRED FIFTY- NINTH MEETING

OF THE

EXPERT PANEL FOR COSMETIC INGREDIENT SAFETY

December 6-7, 2021

Microsoft Teams Virtual Meeting

Expert Panel Members

Wilma F. Bergfeld, M.D., Chairperson

Donald V. Belsito, M.D., Teamleader

David E. Cohen, M.D., Teamleader

Curtis D. Klaassen, Ph.D.

Daniel C. Liebler, Ph.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

Prashiela Manga, Ph.D.

Adopted (Date)

Wilma F. Bergfeld, M.D.

CIR Staff

Administration
Bart Heldreth, PhD - Executive Director

Monice Fiume, MBA - Senior Director

Carla Jackson - Administrative Coordinator

Subject Matter Expertise
Jinqiu Zhu, PhD, DABT, ERT - Toxicologist

Analysis
Christina L. Burnett, MSES - Senior Scientific Analyst

Wilbur Johnson, Jr., MS - Senior Scientific Analyst

Preethi S. Raj, MS - Senior Scientific Analyst

Priya Cherian –Scientific Analyst

Information Services
Kevin Stone Fries, MLS - Information Services Manager

Other Meeting Attendees

Name	Organization
Asma Abbas	Beesline International SAL
Irina Agro	Ashland
Nosheen Ahmad	Mary Kay, Inc.
Jay Ansell	Personal Care Products Council
Nadine Bewry	Sanofi
Jeffrey C. Brown	BASF
Roshil Budhram	Masts
Erica Denham	Transcriptionist
Tracy Dunn	Church & Dwight Co.
Carol Eisenmann	Personal Care Products Council
Mark Ellis	International Diatomite Producers Association
Howard Epstein	EMD Surface Solutions
Sara Farahmand	Edgewell Personal Care
James Flanagan	Coty, Inc.
Karine Ghalayini	Beesline International SAL
Katie Gibbs	Cardno ChemRisk
Lina Giles	Transcriptionist
Marita Grothus	IKW
Chris Greissing	Industrial Mineral Association-NA
Tracy Guerrero	American Chemistry Council
Claudia Jackson	Carma Laboratories, Inc.
Sandra James-Yi	Nu Skin Enterprises
Alexandro Juarez	MANE
Brett Jurd	W.R. Grace
Jon Lalko	Estee Lauder
Martha Elena Leal	Mary Kay, Inc.
Linda Loretz	Personal Care Products Council
Zydnia Madera	E.T. Browne Drug Company, Inc.
Rola Masrieh	Beesline International SAL
Michael Maynard	Beiersdorf
Ariel McWhorter	Procter and Gamble
Wilmelys Mendez	International Flavors & Fragrances, Inc.
Demetrius Michos	W.R. Grace
Kris Miles	Nouryon
Lauren Nardella	The Rose Sheet
Edmund O'Brien	L'Oreal USA S/D, Inc.
Stefanie O'Neal	Kao Corp.
Jillian Parker	Cardno ChemRisk
Karen Rauen-Jean	SGS
Sonia Sandoval	Cosmetic Group USA, Inc.
Alexandra Gorman Scranton	Women's Voices for the Earth
Julianne Sortino-Smith	Arxada
Regina Tucker	CIR
Larissa Walker	MatTek Corp.
Lisa Wiseman	Kolmar Laboratories, Inc.
Michael Wyatt	U.S. FDA
Hong Xie	U.S. FDA
Lisa Yin	Infinitus (China) Company Ltd.
Janet Zang	U.S. FDA
Merle Zimmermann	AHPA
Gloria Zuclich	Keystone Industries
Lara	Not identified
Brian	Not identified

MINUTES FROM THE 159th EXPERT PANEL FOR COSMETIC INGREDIENT SAFETY MEETING

CHAIRPERSON'S OPENING REMARKS

Dr. Bergfeld welcomed the attendees to the December 6-7, 2021 meeting of the Expert Panel for Cosmetic Ingredient Safety (159th Panel meeting). She then announced the retirement of CIR Senior Analyst and Writer, Wilbur Johnson. On behalf of the Panel, Dr. Bergfeld wished Mr. Johnson the very best in his future endeavors.

Furthermore, Dr. Bergfeld stated that 17 ingredient reports, including 7 final reports, are scheduled for review at today's meeting. Additional data had been received in wave 2 and wave 3 submissions. Dr. Bergfeld noted that comments were received from Women's Voices for the Earth on several ingredients. Additionally, Women's Voice of the Earth and other interested parties also provided comments on the inhalation resource document. Dr. Bergfeld stated that this document is a living document that evolves and will need to be adapted in each report in reflection to the available data and understanding of inhalation science.

A robust discussion on botanical ingredients was expected. Dr. Bergfeld noted that the current boilerplates needed review and improvement. Dr. Bergfeld also noted the language recognizing the European Union and ECHA, the European Chemicals Agency, may need to be modified.

Dr. Bergfeld thanked the CIR staff and everyone associated with the CIR program for all of the hard work and effort involved in the preparation of safety assessments for review. Dr. Bergfeld also thanked the chemists on the Panel for their help with organization of the ingredient lists.

APPROVAL OF MINUTES

The minutes of the September 13-14, 2021 (158th) Expert Panel meeting were approved. Editorial comments were provided by Drs. Belsito and Liebler.

DIRECTOR'S REPORT

Dr. Heldreth expressed gratitude for the Panel's and other stakeholders' continued support of the CIR program. He noted that, sadly, this is the last meeting for long-time Senior Scientific Analyst, Wilbur Johnson Jr. Wilbur is one of the most resolute and polite people. That does not mean he always agrees with you. However, that may be one of the best things about Wilbur; he communicates his position very well.

Wilbur obtained a Bachelor of Science in Biology from Morehouse College, and a Masters of Science in Biology from Florida State University. His only job, outside of working for the Library of Congress (Congressional Research Service, Science Policy Research Division), has been at CIR. In his 37 years of stellar service to CIR, he has seen the progression of technology at CIR, from handing off hand-written research papers to administrative typists and the use of microfiche, to using desktop computers, and now to virtual meetings.

Wilbur will be very happy to be able to spend more time with his wife Sigrid (who retired from being a science teacher last year, after 30 years) and his adult children Jared and Ariana. Dr. Heldreth noted that Wilbur is irreplaceable and that he cannot say enough about how much CIR will miss him.

Nevertheless, the work of CIR and the Panel must march on. To that end, beginning with the new year, Priya Cherian will be promoted to Senior Scientific Analyst, which she so definitely deserves. In addition to Priya's excellent work at CIR, she is working on her Masters of Science in Clinical Toxicology. Also, a new Scientific Analyst, Regina Tucker, will start in the new year. Regina is also working on her Masters of Science, but in Skin Biology.

Final Safety Assessments

Silicates

The Panel issued a Final Amended Report with the conclusion that the following 24 silicate ingredients are safe in cosmetics in the present practices of use and concentration described in the safety assessment when formulated to be non-irritating, with the exception that the available data are insufficient to make a determination of safety for the use of naturally sourced (i.e., mined) silicate ingredients in products that may be incidentally inhaled.

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

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

The Panel expressed concern that the potential exists for dermal irritation with the use of products formulated using silicate ingredients. Therefore, the Panel specified that products containing these ingredients must be formulated to be non-irritating. Silicates used in cosmetics may be either naturally-sourced or

synthetically-derived. The Panel is of the understanding that only naturally-sourced silicates can contain crystalline silica, a known cause of significant lung diseases, including cancer. The available data are insufficient for determining safety of formulations containing naturally-sourced silicate used under consumer conditions wherein there is the potential for incidental inhalation, in the absence of composition/impurities data or negative repeat-dose inhalation toxicity data.

Basic Yellow 57

The Panel issued a Final Report with the conclusion that Basic Yellow 57 is safe for use as a hair dye ingredient in the present practices of use and concentration described in the safety assessment. Basic Yellow 57 is reported to function as a direct, non-oxidative hair dye in hair coloring products.

The Panel recognizes that hair dyes containing this ingredient, as coal tar hair dye products, are exempt from certain adulteration and color additive provisions of the Federal Food, Drug, and Cosmetic Act, when the label bears a caution statement and patch test instructions for determining whether the product causes skin irritation. The Panel expects that following this procedure will identify prospective individuals who would have an irritation/sensitization reaction and allow them to avoid significant exposures. The Panel considered concerns that such self-testing might induce sensitization, but agreed that there is not a sufficient basis for changing this advice to consumers at this time.

The Panel noted that the available toxicokinetic studies show that Basic Yellow 57 absorbs slowly through the skin, is not genotoxic, has low concentrations of use, and is not sensitizing in animal studies. The Panel considered these findings, coupled with the short exposure time as a rinse-off product, and determined that the data are sufficient to conclude that Basic Yellow 57 is safe in the present practices of use and concentration in hair dye formulations.

Diacetone Alcohol

The Panel issued a Final Report with the conclusion that Diacetone Alcohol is safe in cosmetics in the present practices of use and concentration described in the safety assessment. The safety of this ingredient is supported by the available systemic toxicity and dermal irritation/sensitization data. Safety is further supported by low concentrations of use.

According to 2021 VCRP data, Diacetone Alcohol is reported to be used in 107 nail formulations (uses were not reported in any other product category in the VCRP). However, the results of a concentration of use survey conducted by the Council in 2019 indicate that Diacetone Alcohol is used in several different product categories. The highest leave-on use concentration resulting in dermal contact is reported to be 0.25% in “other” eye makeup preparations, and the highest rinse-off concentration is reported to be 9.2% in rinse-off shaving products.

***Saccharum officinarum* (Sugarcane)**

The Panel issued a Final Report with the conclusion that following 4 ingredients are safe in cosmetics in the present practices of use and concentrations described in the safety assessment. The safety of these ingredients was supported by available oral toxicity, genotoxicity, carcinogenicity, and irritation/sensitization data, as well as low concentrations of use.

Saccharum Officinarum (Sugarcane) Bagasse Powder*
Saccharum Officinarum (Sugarcane) Juice Extract
Saccharum Officinarum (Sugarcane) Extract
Saccharum Officinarum (Sugarcane) Wax

**Not reported to be in current use. If this ingredient were 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 2021 VCRP data, the ingredient with the most reported uses, Saccharum Officinarum (Sugarcane) Extract, is reported to be used in 211 formulations (121 of which are leave-on formulations). The results of concentration of a use survey conducted by

Equisetum arvense

The Panel issued a Final Report with a conclusion stating that the following 5 *Equisetum arvense*-derived ingredients are safe in cosmetics in the present practices of use and concentration described in the safety assessment.

Equisetum Arvense Extract Equisetum Arvense Juice*
Equisetum Arvense Leaf Powder*
Equisetum Arvense Leaf Extract
Equisetum Arvense Powder

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

The Panel noted that non-specific ulcerative dermatitis was observed in an oral dosing study in which Sprague-Dawley rats were fed a 4% *Equisetum arvense* powder in a cholesterol diet for 14 d. However, they also noted no obvious clinical signs in another study in which F344 rats were fed *Equisetum arvense* (hot water extract of powder) at concentrations up to 3% in a basal diet for 13 wk. Based on negative HRIPT data on products containing 0.000049% (209 subjects) and 0.6% (100 subjects) Equisetum Arvense Extract, and a negative in-use safety evaluation (31 subjects) on nail products containing 0.000049% Equisetum Arvense Extract, the Panel agreed that the skin irritation and sensitization potential of this ingredient at the maximum reported use concentration of 0.4% in cosmetics is mitigated. Slight ocular irritation was observed in a study in which Equisetum Arvense Extract (hydroglycolic extract containing ~2% dry extract) was instilled into the eyes of rabbits. However, the Panel noted that this test concentration is greater than the maximum reported use concentration of 0.4% for *Equisetum arvense*-derived ingredients in cosmetics. Furthermore, the Panel stated that, in the absence of a no-observable adverse effect level (NOAEL) for ocular irritation and use concentration data on products applied near the eye, manufacturers should assure that these products are non-irritating.

Tentative Safety Assessments

Methicones

The Panel issued a Revised Tentative Amended Report, with a split conclusion, for these 30 ingredients. Specifically, the Panel concluded that these ingredients are safe in cosmetics in the present practices of use and concentration as described in the safety assessment when formulated to be non-irritating, with the exception that the data are insufficient to support the safety of products containing these ingredients when applied via airbrush technology.

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

**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.*

At the September 2021 meeting, the Panel was presented with the possibility that other spray products (such as deodorant and hair sprays) may be in the respirable range, and could therefore be incidentally inhaled. At the December 2021 meeting, the Panel felt that these concerns regarding incidental inhalation are mitigated, after considering data on particle size distributions for these products, duration of exposure, updates to the Respiratory Resource document, a lack of toxicity in a short-term inhalation study, and an overall favorable toxicological profile for this ingredient group. However, the Panel noted that, in addition to particle size distribution, other information is still needed to make a determination of safety for the use of these ingredients in products delivered via airbrush technology, including: dose, chemistry, duration of exposure, particle volume and density, and details regarding the mode/device used for application of the cosmetic. Thus, the Panel deemed the available data insufficient to make a determination of safety for this product category.

***Salvia officinalis* (Sage)**

The Panel issued a Tentative Report for public comment with the split conclusion that the following 6 (of 12) *Salvia officinalis* (sage)-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:

Salvia Officinalis (Sage) Leaf
Salvia Officinalis (Sage) Leaf Extract
Salvia Officinalis (Sage) Leaf Oil
Salvia Officinalis (Sage) Leaf Powder
Salvia Officinalis (Sage) Leaf Water
Salvia Officinalis (Sage) Oil

The Panel discussed that most of these ingredients are derived from the leaf, and subsequently have GRAS status, mitigating systemic toxicity concerns. The Panel acknowledged that constituents with the highest potential for sensitization are found in the leaf and oil ingredients, and accordingly, identified the need for manufacturers and cosmetic formulators to avoid reaching levels of plant constituents that may cause sensitization or adverse aggregate exposures.

However, the Panel also concluded that the available data are insufficient to make a determination that the following 6 Salvia officinalis (sage)-derived ingredients are safe under the intended conditions of use in cosmetic formulations:

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

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

- 28-day dermal toxicity data for the Salvia Officinalis (Sage) Flower/Leaf/Stem Extract, Salvia Officinalis (Sage) Root Extract, or for the whole plant
    - Depending on the results of the study, additional toxicity data may be needed

Radish Root

The Panel issued a Tentative Report for public comment with a conclusion that these 7 radish root-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:

Lactobacillus/Radish Root Ferment Extract Filtrate*
Lactobacillus/Radish Root Ferment Filtrate
Leuconostoc/Radish Root Ferment Filtrate
Leuconostoc/Radish Root Ferment Lysate Filtrate*
Raphanus Sativus (Radish) Root Extract
Raphanus Sativus (Radish) Root Juice*
Raphanus Sativus (Radish) Root Powder*

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

The Panel considered that the root portion of the *Raphanus sativus* plant is consumed as food, and that foods fermented with lactic acid and the *Leuconostoc* bacterial strains have GRAS status, mitigating any systemic or dermal toxicity concerns. The Panel discussed data suggesting the potential for a root juice and a methanolic root extract of *Raphanus sativus* to cause skin-lightening, and concluded that the use concentrations of these ingredients in cosmetics are too low, and not purified or potent enough to produce a skin-lightening effect; the Panel also acknowledged that skin lightening is considered to be a drug effect, and should not occur during the use of cosmetic products. Additionally, the Panel acknowledged the need for manufacturers and cosmetic formulators to avoid reaching levels of plant constituents that may cause sensitization or adverse aggregate exposures.

Acryloyloxyethyl Phosphorylcholine

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

Acrylic Acid/Phosphorylcholine Glycol Acrylate Crosspolymer
C4-18 Alkyl Methacrylate/Methacryloyloxyethyl Phosphorylcholine Copolymer*
Hydroxyethylcellulose/Phosphorylcholine Glycol Acrylate Copolymer*
Phosphorylcholine Glycol Methacrylate/PEG-10 Dimethacrylate Crosspolymer*
Polyphosphorylcholine Glycol Acrylate
Polyquaternium-10/Phosphorylcholine Glycol Acrylate Copolymer*
Polyquaternium-51
Polyquaternium-61

**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 considered the available data to be adequate for determining safety. It was noted that the data provided indicate that Phosphorylcholine Glycol Acrylate, Polyquaternium-51, and Polyquaternium-61 are high molecular weight polymers. In the absence of molecular weight data on the remaining 5 acryloyloxyethyl phosphorylcholine polymers in this safety assessment, the expectation is that their molecular weights are comparable. The only skin penetration data in this report (which indicate a lack of penetration) are on poly(2-methacryloyloxyethyl phosphorylcholine-co-n-butyl methacrylate), which is considered by the Panel to be a sufficient read-across source chemical for Polyquaternium-51. Furthermore, the Panel agrees that these skin penetration data essentially eliminate the need for systemic toxicity data (i.e., subchronic/chronic toxicity, carcinogenicity, and reproductive/developmental toxicity data) on the acryloyloxyethyl phosphorylcholine polymers. It was also noted that the absence of structural alerts for genotoxicity in these polymers obviates the need for genotoxicity data.

The chemical characterization data provided include information on the residual monomer content of Polyquaternium-51 (100 ppm max, for butyl methacrylate), and the Panel noted the sensitization potential of butyl methacrylate. However, because the method of manufacture of amphiphilic block copolymers based on poly(2-acryloyloxyethyl phosphorylcholine) involves purification (dialysis and rinsing) of the final product, the Panel agreed that residual monomer content is not a major concern. Additionally, the volatility of acrylate and methacrylate monomers was considered, and supports the lack of concern over monomer content. In addition to the issue of monomer-induced sensitization potential, the issue of skin sensitization potential of acryloyloxyethyl phosphorylcholine polymers was also addressed. The Panel noted that the absence of skin penetration mitigates concern over the skin irritation/sensitization potential of these polymers. Furthermore, the absence of skin sensitization potential was confirmed in a human repeated insult patch test on a serum containing 0.12% Polyquaternium-51, a guinea pig maximization test on Polyquaternium-51 at challenge concentrations up to 100%, and a guinea pig adjuvant and patch test on Polyquaternium-61 at a challenge concentration of 25%.

Acrylamide/Acrylate Copolymers

The Panel issued a Tentative Report for public comment with the conclusion that the following 16 acrylamide/acrylate copolymer ingredients are safe in cosmetics in the present practices of use and concentration described in the safety assessment.

Acrylamide/Ammonium Acrylate Copolymer
Acrylamide/Sodium Acrylate Copolymer
Acrylates/Acrylamide Copolymer
Acrylates/t-Butylacrylamide Copolymer
Acrylates/Methacrylamide Copolymer
Acrylates/Octylacrylamide Copolymer
AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl Acrylamide Copolymer
AMP-Acrylates/C1-18 Alkyl Acrylate/C1-8 Alkyl
Acrylamide/Hydroxyethylacrylate Copolymer
t-Butylacrylamide/Dimethylacrylamide/PEG-14 Diacrylate Crosspolymer
Butyl Acrylate/Isopropylacrylamide/PEG-18 Dimethacrylate Crosspolymer

Corn Starch/Acrylamide/Sodium Acrylate Copolymer
Dimethyl Acrylamide/Hydroxyethyl Acrylate/Methoxyethyl Acrylate Copolymer
Dimethylacrylamide/Lauryl Methacrylate Copolymer
Potassium Acrylates/Acrylamide Copolymer
Sodium Acrylate/Hydroxyethyl Acrylamide Copolymer
Starch/Acrylates/Acrylamide Copolymer

Formulators utilizing these ingredients should ensure that the concentration of acrylamide monomer in cosmetic formulations does not exceed 5 ppm. The Panel determined that the available manufacturing, composition and impurities, systemic toxicity, and dermal irritation and sensitization data are sufficient to support the safety of these ingredients. Safety is further supported by the large molecular weights of these ingredients, which precludes dermal absorption. The Panel noted the use of these ingredients in aerosolized and pump spray hair products, and determined that the potential for inhalation toxicity following exposure to these products was unlikely due to low concentrations of use, a lack of systemic toxicity, and large, irrespirable molecule sizes.

Insufficient Data Announcement

Barley

The Panel issued an Insufficient Data Announcement (IDA) for these 16 barley-derived ingredients.

Hordeum Distichon (Barley) Extract
Hordeum Distichon (Barley) Seed Flour
Hordeum Vulgare Extract
Hordeum Vulgare Flower/Leaf/Stem Juice
Hordeum Vulgare Juice
Hordeum Vulgare Leaf Extract
Hordeum Vulgare Leaf Juice
Hordeum Vulgare Leaf Powder
Hordeum Vulgare Leaf/Stem Powder
Hordeum Vulgare Powder
Hordeum Vulgare Root Extract
Hordeum Vulgare Seed Extract
Hordeum Vulgare Seed Flour
Hordeum Vulgare Seed Water
Hordeum Vulgare Sprout Extract
Hordeum Vulgare Stem Water

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

- Clarification of the plant parts used to make the whole plant extracts Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract
- Method of manufacturing for Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract
- Composition and impurities data for Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract
- 28-day dermal toxicity data on the whole plant extract Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract
    - If positive, additional data, such as developmental and reproductive toxicity and genotoxicity data, may be needed
    - Alternatively, acceptable evidence of safe use as food for ingredients derived from the flower, leaf, stem, and root
- Dermal irritation and sensitization data for Hordeum Leaf Extract or other leaf ingredients

Zeolites

The Panel issued an IDA for these 6 zeolite ingredients.

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

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

- Maximum use concentration for both mined and synthetic zeolites
- Method of manufacturing and/or source data for Ammonium Silver Zeolite, Gold Zeolite, Silver Copper Zeolite, Titanium Zeolite, and Zinc Zeolite
- Chemical characterization, including specific framework(s), and composition and impurities data for mined Zeolite, Ammonium Silver Zeolite, Gold Zeolite, Silver Copper Zeolite, Titanium Zeolite, and Zinc Zeolite
    - Depending on composition, additional toxicity data may be needed
- The range of particle sizes that is used in spray and powder formulations
- Human dermal irritation and sensitization data at maximum use concentrations

Fatty Ethers (e.g., Dicaprylyl Ether)

The Panel issued an IDA for these 8 fatty ethers.

Cetyl Dimethylbutyl Ether
Dicaprylyl Ether
Dicetyl Ether
Didecyl Ether
Diisononyl Ether
Dilauryl Ether
Dimyristyl Ether
Distearyl Ether

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

- Method of manufacture data (specific to cosmetic ingredient production) for Dicaprylyl Ether and Distearyl Ether

Fatty Ester End-Capped Alkoxylates

The Panel issued an IDA for these 14 fatty ester end-capped alkoxylates.

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

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

- Use concentrations for PEG/PPG-8/3 Diisostearate
- Method and manufacturing for all ingredients except PEG/PPG-8/3 Diisostearate
- Composition and impurities data for all ingredients except PEG/PPG-8/3 Diisostearate

Portulaca oleracea

The Panel issued an IDA for these 4 Portulaca oleracea-derived ingredients:

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

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

- 28-day dermal toxicity data at the maximum reported concentration of use for Portulaca Oleracea Extract, preferably in an hydroalcoholic solvent
    - If positive additional toxicity data, such as developmental and reproductive toxicity and genotoxicity data, may be needed
- Clarification on which part(s) of the plant are consumed as a food, and which plant part(s) are used in cosmetics

Glucosamine

The Panel issued an IDA for Acetyl Glucosamine, Glucosamine, Glucosamine HCl, and Glucosamine Sulfate. In order to conclude on safety for these ingredients, the Panel has requested:

- Impurities data on Acetyl Glucosamine
- Dermal irritation and sensitization data on all ingredients at maximum use concentration

The Panel noted the reproductive effects observed in animals following oral ingestion and intraperitoneal injections of Glucosamine, and determined that these effects would not be relevant to cosmetic exposure as these methods of exposure would result in a much higher systemic concentration of Glucosamine compared to dermal cosmetic application. The Panel also noted a lack of inhalation data, but determined that these data are unnecessary as inhalation toxicity following cosmetic exposure to these ingredients would be unlikely due to low concentrations of use and a lack of systemic toxicity. In addition, data included in this report indicate that Acetyl Glucosamine may have a skin lightening effect. The Panel noted that skin lightening is considered to be a drug effect, and should not occur during the use of cosmetic products. Cosmetic formulators should only use this ingredient in products in a manner that does not cause depigmentation.

***Zingiber officinale* (Ginger)**

The Panel issued an IDA for the following 9 Zingiber officinale (ginger)-derived ingredients:

Zingiber Officinale (Ginger) Extract
Zingiber Officinale (Ginger) Leaf Cell Extract
Zingiber Officinale (Ginger) Rhizome Extract
Zingiber Officinale (Ginger) Root
Zingiber Officinale (Ginger) Root Extract
Zingiber Officinale (Ginger) Root Juice
Zingiber Officinale (Ginger) Root Oil
Zingiber Officinale (Ginger) Root Powder
Zingiber Officinale (Ginger) Water

In order to conclude on safety for these ingredients, the Panel requested the following:

- Method of manufacturing, composition, and impurities data on Zingiber Officinale (Ginger) Leaf Cell Extract.
    - If the composition of Zingiber Officinale (Ginger) Leaf Cell Extract notably differs from the composition of the remaining ginger ingredients, systemic toxicity data (28-day dermal toxicity, genotoxicity, developmental/reproductive toxicity, and carcinogenicity data) and dermal irritation/sensitization data would be required
- Dermal irritation and sensitization data on Zingiber Officinale (Ginger) Extract at maximum concentrations of use

The Panel noted that information regarding the specific plant parts (e.g., leaves, rhizome) used in the preparation of the whole plant extract (Zingiber Officinale (Ginger) Extract) would help to inform the safety assessment.

Additional Panel Deliberations

Methacrylate Ester Monomers

The Panel determined that the published final report on methacrylate ester monomers should not be reopened and that the original conclusion on these ingredients remains valid. It was agreed that an updated search of the published literature did not reveal toxicity data that warrant re-evaluation of the safety of these ingredients in cosmetic products.

Inhalation Document

The Panel reviewed a revised Inhalation Resource Document, and agreed it should replace the current version at the CIR website (https://www.cir-safety.org/cirfindings); the previous version was approved by the Panel at the September 2019 meeting. (This document will replace the 2019 version after a few editorial changes are made.) The Panel agreed that the CIR Resource Document – Respiratory Exposure to Cosmetic Ingredients would be a living document, that would evolve and incorporate emerging data for evaluating inhalation safety of ingredients.

At the September 2021 meeting, the Panel discussed the particle size distribution of diverse aerosol sprays, in consideration of prolonged duration of nanomaterial exposures in sprayable applications. Per the Panel's request, this resource document has been updated to incorporate new data on characterization of deposited dose of inhalable aerosols released from nano-enabled cosmetics, and consequently, to address the health challenges associated with usage of relevant sprayers.

At this current meeting, the Panel further discussed the potential inhalation risks resulting from the aerosolization of common nano-enabled cosmetics. The Panel re-emphasized that while particle/droplet size is an important parameter, the physicochemical properties of ingredients in a spray formulation, the systemic and local (e.g., lung and skin) toxicity, as well as the realistic exposure factors under in-use conditions (e.g., exposure estimates incorporating spray product use levels and ingredient concentrations, exposure duration and frequency, and adjusted for particle/droplet deposition in human lung airways) also play significant roles in evaluating inhalation safety of ingredients in spray formulations. When spray parameters are insufficient to support a robust inhalation exposure assessment, the Panel would request additional information from Industry and further evaluate the sufficiency of other exposure and toxicity data on a case-by-case basis. The Panel agreed to incorporate sample calculations via a tiered approach to assess inhalation safety of cosmetic products, which were submitted by the CIR Science and Support Committee (CIR SSC) in the memo dated October 30, 2018. In addition, the Panel requested further clarification on current federal regulations regarding the categorization and safety management of consumer products applied with airbrush technologies.

MCI/MI Re-Open Request - Reply

A letter was received from Women's Voices for the Earth (WVE), requesting that the Panel re-open the safety assessment report on the combination use of Methylchloroisothiazolinone/Methylisothiazolinone (MCI/MI). However, this request is denied. The following is the Panel's rationale for not re-opening this report.

First and foremost, it is important to note that there are numerous other sources for sensitization, particularly to these ingredients, like paints and household cleansers and detergents (which are not the purview of this Panel) that are not labeled, and that the WVE is not taking these other sources for sensitization into consideration. Cosmetics are labeled, and consumers allergic to these ingredients can avoid exposure by avoiding products labeled as such. Cosmetic formulators can protect all other consumers from sensitization induction (i.e., becoming allergic) by formulating based on the Panel's most recent conclusions on MCI/MI, and MI by itself. Additionally, while the data submitted by WVE (original data came from North American Contact Dermatitis Group) indicate increasing sensitization incidence in the United States in recent years, it should be noted the incident rates of positive patch test were reported in diseased populations instead of general population, which were subjected to relatively high level of exposure, i.e., 2000 ppm for MI and 200 ppm for MCI/MI.

The Panel agreed that in the last few years, the available data made it apparent that their previous conclusion made in 2005 warranted re-review. Firstly, since that time, it had become apparent that these ingredients are more potent than previously understood. Perhaps more importantly, however, the Panel began to appreciate that induction of sensitization can be very dependent not only on final formulation concentration, but on how that formulation is used (such as on shaved underarms versus palms versus other body sites). Thus, the Quantitative Risk Assessment (QRA) was developed in 2008 and further refined into the QRA 2.0. The Panel chose to follow this plan of assessing risk (and utilizing newer methods for sensitization screening), instead of eliminating another preservative from the ever-shrinking universe of preservatives.

If cosmetics are not preserved, consumers may be put at risk of returning to the dark days when mascaras were causing blindness because of microorganism contamination. Furthermore, when potent preservatives (such as MCI/MI) are removed from the market, less potent ones (such as Phenoxyethanol) must be used instead. Unfortunately, that means these less potent preservatives must be used at much higher concentrations to be effective. At those higher concentrations, those preservatives are much more likely to induce sensitization (and thus, ultimately be banned if a risk-based approach is not taken). Preservatives such as MCI/MI can be safely formulated in finished cosmetic products, by adhering to the Panel's most recent conclusions.

Methacrylate Ester Monomers

The Expert Panel for Cosmetic Ingredient Safety (Panel) first published the Final Report on the Safety Assessment of Methacrylate Ester Monomers Used in Nail Enhancement Products in 2005.[1] The Panel concluded that the 22 methacrylate ester monomers listed below are safe as used in nail enhancement products when skin contact is avoided. The conclusion also states that products containing these ingredients should be accompanied with directions to avoid skin contact, because of the sensitizing potential of methacrylates.

Bis(Glyceryl Dimethacrylate) Pyromellitate (formerly Pyromellitic Glycidyl Dimethacrylate)
Butylcarbamoethyl Methacrylate (formerly Urethane Methacrylate)
Butyl Methacrylate
t-Butyl Methacrylate
Cyclohexylmethacrylate (formerly Cyclohexyl Methacrylate)
Ethoxyethyl Methacrylate
2-Ethoxy Ethoxy Ethyl Methacrylate
Glycol Dimethacrylate (formerly Ethylene Glycol Dimethacrylate)
Hexyl Methacrylate
HEMA (2-Hydroxyethyl Methacrylate)
HEMA Acetoacetate (formerly Hydroxyethylmethacrylate Acetoacetate)
Di-HEMA Trimethylhexyl Dicarbamate
Hydroxypropyl Meth acrylate
Isobornyl Methacrylate
Isobutyl Methacrylate
Isopropylidenediphenyl Bisoxyhydroxypropyl Methacrylate (formerly Isopropylidenediphenyl Bisglycidyl Methacrylate)
Lauryl Methacrylate
Methoxydiglycol Methacrylate
PEG-4 Dimethacrylate
Tetrahydrofurfuryl Methacrylate
Triethylene Glycol Dimethacrylate
Trimethylolpropane Trimethacrylate

It should be noted that 2 of the ingredients reviewed in the published final report, 2-Ethoxy Ethoxy Ethyl Methacrylate and Hexyl Methacrylate, are no longer listed in the *International Cosmetic Ingredient Dictionary and Handbook*.[2] Because it has been at least 15 years since the final report was published, in accordance with CIR Procedures, the Panel should determine whether the safety assessment should be reopened. At the December 2021 meeting, the Panel considered updated information regarding product types and ingredient use frequencies as reported in the US Food and Drug Administration (FDA) Voluntary Cosmetic Registration Program (VCRP) database,[3] and the maximum use concentrations provided by the Personal Care Products Council (Council).[4] The cumulative frequency and concentration of use data are presented in Table 1 and described briefly below.

Data submitted to the FDA in 2001 did not include any uses for 21 of the methacrylate ester monomers that were reviewed; only Tetrahydrofurfuryl Methacrylate had a reported use in one nail extender product. However, concentration of use data received from the cosmetics industry in 2001 indicated that all ingredients had reported uses, with maximum use concentrations of methacrylate ester monomers up to 85% (reported for Methoxydiglycol Methacrylate and Ethoxyethyl Methacrylate) in nail enhancement products. The results of a concentration of use survey conducted by the Council in 2020, and 2021 FDA VCRP data were provided. Collectively, these data indicate use of 8 methacrylate ester monomers in products that are applied to the nail. The most frequently used methacrylate ester monomer is HEMA, which has 149 uses and a reported maximum use concentration of 79% (in other manicuring products). Di-HEMA Trimethylhexyl Dicarbamate has a reported maximum use concentration 91.8% (in nail extenders). Of the ingredients that are being reviewed, this is the highest reported maximum use concentration

Importantly, the Panel also reviewed safety data identified as published since 2001.[3-193] The Panel agreed that an updated search of the published literature did not reveal toxicity data that warrant re-evaluation of the safety of these ingredients in cosmetic products. After reviewing data on ingredient use frequencies and concentrations and safety data, the Panel determined to not reopen this safety assessment on methacrylate ester monomers and reaffirmed the original conclusion.

Current and historical frequency and concentration of use according to duration and exposure

	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	Bis(Glyceryl Dimethacrylate) Pyromellitate (previously, Pyromellitic Glycidyl Dimethacrylate)				**Butylcarbamoethyl Methacrylate (previously, Urethane Methacrylate)**			
	2021[3]	**2001[1]**	**2020[4]**	**2001[1]**	**2021[3]**	**2001[1]**	**2020[4]**	**2001[1]**
Totals*	**19**	**NR**	**NR**	**5**	**NR**	**NR**	**NR**	**3**
Duration of Use								
Leave-On	*19*	*NR*	*NR*	*5*	*NR*	*NR*	*NR*	*3*
Rinse-Off	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Powder	NR	NR	NR	NR	NR	NR	NR	NR
Dermal Contact	NR	NR	NR	NR	NR	NR	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	19	NR	NR	5	NR	NR	NR	3
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	*NR*	NR	NR	NR	NR	NR
	Butyl Methacrylate				**t-Butyl Methacrylate**			
	2021[3]	**2001[1]**	**2020[4]**	**2001[1]**	**2021[3]**	**2001[1]**	**2020[4]**	**2001[1]**
Totals*	**NR**	**NR**	**NR**	**7**	**NR**	**NR**	**NR**	**7**
Duration of Use								
Leave-On	*NR*	*NR*	*NR*	*7*	*NR*	*NR*	*NR*	*7*
Rinse-Off	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Powder	NR	NR	NR	NR	NR	NR	NR	NR
Dermal Contact	NR	NR	NR	NR	NR	NR	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	7	NR	NR	NR	7
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR
	Cyclohexylmethacrylate (previously, Cyclohexyl Methacrylate)				**Di-HEMA Trimethylhexyl Dicarbamate**			
	2021[3]	**2001[1]**	**2020[4]**	**2001[1]**	**2021[3]**	**2001[1]**	**2020[4]**	**2001[1]**
Totals*	**NR**	**NR**	NR	**2**	**76**	**NR**	**35.8-91.8**	**3**
Duration of Use								
Leave-On	*NR*	*NR*	*NR*	*2*	*76*	*NR*	*35.8-91.8*	*3*
Rinse-Off	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*50.2*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Powder	NR	NR	NR	NR	NR	NR	NR	NR
Dermal Contact	NR	NR	NR	NR	NR	NR	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	2	76	NR	35.8-91.8	3
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

Current and historical frequency and concentration of use according to duration and exposure

	# of Uses		Max Conc of Use (%)		# of Uses		Max Conc of Use (%)	
	2-Ethoxy Ethoxy Ethyl Methacrylate				**Ethoxyethyl Methacrylate**			
	2021[3]	**2001[1]**	**2020[4]**	**2001[1]**	**2021[3]**	**2001[1]**	**2020[4]**	**2001[1]**
Totals*	**NA**	**NR**	**NA**	**75**	**NR**	**NR**	**NR**	**85**
Leave-On	*NA*	*NR*	*NA*	*85*	*NR*	*NR*	*NR*	*85*
Rinse-Off	*NA*	*NR*	*NA*	*NR*	*NR*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*NA*	*NR*	*NA*	*NR*	*NR*	*NR*	*NR*	*NR*
Eye Area	NA	NR	NA	NR	NR	NR	NR	NR
Incidental Ingestion	NA	NR	NA	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NA	NR	NA	NR	NR	NR	NR	NR
Incidental Inhalation-Powder	NA	NR	NA	NR	NR	NR	NR	NR
Dermal Contact	NA	NR	NA	NR	NR	NR	NR	NR
Deodorant (underarm)	NA	NR	NA	NR	NR	NR	NR	NR
Hair - Non-Coloring	NA	NR	NA	NR	NR	NR	NR	NR
Hair-Coloring	NA	NR	NA	NR	NR	NR	NR	NR
Nail	NA	NR	NA	85	NR	NR	NR	85
Mucous Membrane	NA	NR	NA	NR	NR	NR	NR	NR
Baby Products	NA	NR	NA	NR	NR	NR	NR	NR
	Glycol Dimethacrylate (previously, Ethylene Glycol Dimethacrylate)				**HEMA**			
	2021[3]	**2001[1]**	**2020[4]**	**2001[1]**	**2021[3]**	**2001[1]**	**2020[4]**	**2001[1]**
Totals*	**17**	**NR**	**1.2**	**5**	**149**	**NR**	**0.11-79**	**30**
Duration of Use								
Leave-On	*17*	*NR*	*1.2*	*5*	*149*	*NR*	*0.11-79*	*30*
Rinse-Off	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	NR	NR	NR	NR	1	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Powder	NR	NR	NR	NR	NR	NR	NR	NR
Dermal Contact	NR	NR	NR	NR	1	NR	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	17	NR	1.2	5	148	NR	0.11-79	30
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR
	HEMA Acetoacetate (previously, Hydroxyethylmethacrylate Acetoacetate)				**Hexyl Methacrylate**			
	2021[3]	**2001[1]**	**2020[4]**	**2001[1]**	**2021[3]**	**2001[1]**	**2020[4]**	**2001[1]**
Totals*	**NR**	**NR**	**NR**	**10**	**NR**	**NR**	**NR**	**5**
Duration of Use								
Leave-On	*NR*	*NR*	*NR*	*10*	*NR*	*NR*	*NR*	*NR*
Rinse-Off	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Powder	NR	NR	NR	NR	NR	NR	NR	NR
Dermal Contact	NR	NR	NR	NR	NR	NR	NR	5
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	10	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

Current and historical frequency and concentration of use according to duration and exposure

	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	Hydroxypropyl Methacrylate				**Isobornyl Methacrylate**			
	2021[3]	**2001[1]**	**2020[4]**	**2001[1]**	**2021[3]**	**2001[1]**	**2020[4]**	**2001[1]**
Totals*	**40**	**NR**	**0.8-23**	**25**	**NR**	**NR**	**8.3-20.2**	**5**
Duration of Use								
Leave-On	*40*	*NR*	*0.8-23*	*25*	*NR*	*NR*	*8.3-20.2*	*5*
Rinse-Off	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Powder	NR	NR	NR	NR	NR	NR	NR	NR
Dermal Contact	NR	NR	NR	NR	NR	NR	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	40	NR	0.8-23	25	30	NR	8.3-20.2	5
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	Isobutyl Methacrylate				**Isopropylidenediphenyl Bisoxyhydroxypropyl Methacrylate (previously, Isopropylidenediphenyl Bisglycidyl Methacrylate**			
	2021[3]	**2001[1]**	**2020[4]**	**2001[1]**	**2021[3]**	**2001[1]**	**2020[4]**	**2001[1]**
Totals*	**NR**	**NR**	**0.0005**	**10**	**1**	**NR**	**4.3-9.5**	**5**
Duration of Use								
Leave-On	*NR*	*NR*	*0.0005*	*10*	*1*	*NR*	*4.3-9.5*	*5*
Rinse-Off	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Powder	NR	NR	NR	NR	NR	NR	NR	NR
Dermal Contact	NR	NR	NR	NR	NR	NR	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	19	NR	0.0005	10	1	NR	4.3-9.5	5
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	*NR*	NR	NR	NR	NR	NR

	Lauryl Methacrylate				**Methoxydiglycol Methacrylate**			
	2021[3]	**2001[1]**	**2020[4]**	**2001[1]**	**2021[3]**	**2001[1]**	**2020[4]**	**2001[1]**
Totals*	**1**	**NR**	**NR**	**5**	**NR**	**NR**	**24.8-65**	**85**
Duration of Use								
Leave-On	*1*	*NR*	*NR*	*5*	*NR*	*NR*	*24.8-65*	*85*
Rinse-Off	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Powder	NR	NR	NR	NR	NR	NR	NR	NR
Dermal Contact	NR	NR	NR	NR	NR	NR	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	1	NR	NR	5	NR	NR	24.8-65	85
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

Current and historical frequency and concentration of use according to duration and exposure

	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	PEG-4 Dimethacrylate				**Tetrahydrofurfuryl Methacrylate**			
	2021[3]	**2001[1]**	**2020[4]**	**2001[1]**	**2021[3]**	**2001[1]**	**2020[4]**	**2001[1]**
Totals*	**NR**	**NR**	**6.6-10**	**15**	**NR**	**1**	**20.6-38.2**	**7**
Duration of Use								
Leave-On	*NR*	*NR*	*6.6-10*	*15*	*NR*	*1*	*20.6-38.2*	*7*
Rinse-Off	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Powder	NR	NR	NR	NR	NR	NR	NR	NR
Dermal Contact	NR	NR	NR	NR	NR	NR	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	6.6-10	15	NR	1	20.6-38.2	7
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	Triethylene Glycol Dimethacrylate				**Trimethylolpropane Trimethacrylate**			
	2021[3]	**2001[1]**	**2020[4]**	**2001[1]**	**2021[3]**	**2001[1]**	**2020[4]**	**2001[1]**
Totals*	**NR**	**NR**	**8.7-20**	**7**	**1**	**NR**	**25.3**	**5**
Duration of Use								
Leave-On	*NR*	*NR*	*8.7-20*	*7*	*1*	*NR*	*25.3*	*5*
Rinse-Off	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Powder	NR	NR	NR	NR	NR	NR	NR	NR
Dermal Contact	NR	NR	NR	NR	NR	NR	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	8.7-20	7	1	NR	25.3	5
Mucous Membrane	NR	NR	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

*Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.
**at the time of the 2003 safety assessment, concentration of use data were not reported by the FDA; however, industry provided a maximum concentration of use
[a] It is possible these products are sprays, but it is not specified whether the reported uses are sprays.
[b] It is possible these products are powders, but it is not specified whether the reported uses are powders.
[c] Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories
NR – not reported
NA – this ingredient is no longer in use; therefore 2021 data are not applicable

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