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EXPERT PANEL MEETING

March 13-14, 2025

Cosmetic Ingredient Review

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MEMORANDUM

To: The Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Bart Heldreth, Ph.D., Executive Director, Cosmetic Ingredient Review
Subject: 172nd Meeting of the Panel — Thursday and Friday, March 13th – 14th, 2025
Date: February 14, 2025

Welcome to the first Panel Meeting of 2025! The agenda and accompanying materials for the 172nd Expert Panel Meeting, to be held on March 13th – 14th, 2025, are now available. ***The location is different (this is our 1st time meeting here)*** – and it is in-person at the Marriott Georgetown, 1221 22nd St., NW, Washington, DC 20037. ***The meeting will start on both days, promptly, at 8:30 AM EST***. The meeting is open to the public; no prior registration is required. While participation in this meeting will be exclusively in-person, audience members may view the meeting live, via MS Teams (note: there will be no option to participate in the discussions virtually). Invitations (3) to join the virtual component of the meeting may be received by request in advance of the meeting at the meeting page:

https://www.cir-safety.org/meeting/172nd-expert-panel-meeting

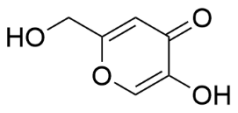
The meeting agenda includes the consideration of 11 reports advancing in the review process, including 3 draft final reports, 3 draft tentative reports, and 5 draft reports (4 of which are re-opened reviews). Also on the agenda are 2 previous reports proposed for rereview; ***for these proposed rereviews, the Panel is primarily being asked if the reports should be reopened.*** There are also 3 administrative items, including a new iteration of the Inhalation Resource Document, a new iteration of the Margin of Exposure (MOE) Resource Document, and the 2026 Draft Priorities.

As we continue with our efforts to reduce the quantity of late-breaking information, we are making a cutoff for nearly all information sent to the Panel. The exception to this cutoff is any pertinent information relevant to a Draft Final Report. (For this meeting, the reports that fall into this category are 2,4-Diaminophenoxyethanol HCl, *p*-Phenylenediamine, and Copper Gluconate.) ***Submissions received on non-final reports, after the issuance of the Wave 2 supplement on March 3rd, will be held back until the next Panel review of those reports.***

Finally, the CIR staff join with the the Panel in welcoming the newest member to the table, Samuel Cohen, M.D., Ph.D., Havlik-Wall Professor of Oncology in the University of Nebraska Medical Center, Department of Pathology and Microbiology. Dr. Samuel Cohen will join the Dr. David Cohen team at this meeting. Welcome!

Draft Reports - There are 5 draft reports for review. Sufficient data to proceed to a tentative conclusion, or issue an Insufficient Data Announcement (IDA)?

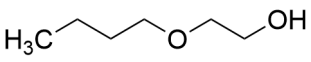
1. Kojic Acid – DAR (Christina) – ***Dr. Belsito reports on day 2*** – The original review of Kojic Acid was published in 2010 with the conclusion that "Kojic Acid is safe for use in cosmetic products up to a concentration of 1%." In June 2022, the Panel determined that this safety assessment should be re-opened for re-evaluation due to reported restrictions by the European Commission on the use of Kojic Acid and because of reported increases in uses in skin care products.



   According to 2024 RLD data, Kojic Acid is reported to be used in 1,114 formulations, most of which are skin care preparations. The 2023 VCRP data reported use in 123 formulations, most of which were leave-on products. In the 2010 original report, Kojic Acid was reported in 16 formulations, most of which were leave-on products. The results of the concentration of use survey conducted by the Council in 2024 indicate Kojic Acid is used at up to 1% in leave-on skin care preparations. In 2008, the maximum concentration of use for Kojic Acid was reported to be 2% in leave-on skin preparations.

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

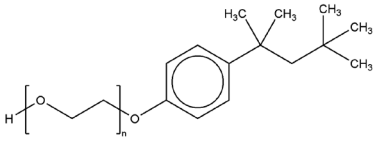
2. Butoxyethanol – DAR (Christina) – ***Dr. Cohen reports on day 2*** – The original review of Butoxyethanol was published in 1996 with the conclusion that "Butoxyethanol is safe in hair and nail products at concentrations up to 10.0%." The Panel reassessed the safety of Butoxyethanol in cosmetics because of questionable evidence of carcinogenicity (in mice and rats) in a 2-year NTP inhalation carcinogenicity study on Butoxyethanol that was published in 2000. The Panel determined that the results were not relevant to humans, and reaffirmed the original conclusion in a rereview that was published in 2005. In June 2024, the Panel determined that this safety assessment should be re-opened for re-evaluation due to reported restrictions by the European Commission on the use of Butoxyethanol.



   According to RLD that CIR received in 2024, Butoxyethanol is used in 81 formulations, with 79 uses reported in hair dyes and colors. A single use each was reported in perfumes and makeup fixatives. VCRP survey data received in 2023 reported Butoxyethanol was used in 3 hair dyes and colors. When comparing the VCRP data received in 2023 to that received in 2001, the frequencies of use for Butoxyethanol have greatly decreased since the re-review was performed; in 2001, Butoxyethanol was reported to have 110 uses, with the majority in hair coloring formulations. No uses were reported in response to the concentration of use survey conducted by the Council in 2020. In 2001, the maximum concentration of use range for Butoxyethanol was 3% in leave-on products (i.e., eye shadow, blushers, and nail polish and enamel formulations) and 50% in rinse-off products (i.e., nail polish and removers). Concentrations of use were not reported for hair coloring preparations in 2001.

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

3. Octoxynols – DAR (Priya) – ***Dr. Belsito reports on day 2*** – The Panel first published a Final Report on these 25 ingredients in 2004, with the conclusion that based on the animal and clinical data included in the report, Octoxynol-9, -10, -11, -12, -13, -16, -20, -25, -30, -33, -40, and -70, Octoxynol-9 Carboxylic Acid, Octoxynol-20 Carboxylic Acid, Potassium Octoxynol-12 Phosphate, and Sodium Octoxynol-9 Sulfate are safe as used in rinse-off and leave-on cosmetic products. The Panel also concluded that Octoxynol-1, -3, -5, -6, -7, and -8, Sodium Octoxynol-2 Ethane Sulfonate, Sodium Octoxynol-2 Sulfate, and Sodium Octoxynol-6 Sulfate are safe as used in rinse-off cosmetic products and safe at concentrations of ≤ 5% in leave on cosmetic products. At its June 2023 meeting, the Panel decided to reopen this safety assessment to explore the mucous membrane irritation potential of these ingredients, and due to the newly reported use of Octoxynol-9 at 0.1% in other baby products (according to 2022 concentration of use data). In December 2023, the Panel reviewed the Draft Amended Report and determined to table the assessment until the receipt of RLD on these ingredients.



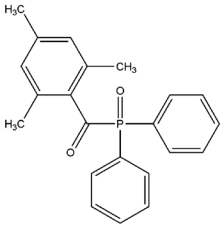
RLD collected in 2024 indicate that Octoxynol-9 is used in formulations that may result in mucous membrane exposure (e.g., bath soaps and body washes and disposable wipes). These data do not indicate that these ingredients are used in baby products. Also according to the RLD, Octoxynol-9 is the ingredient with the highest number of uses (it is used in a total of 38 formulations). According to 2023 FDA VCRP data, Octoxynol-11 was reported to be the ingredient with the highest number of uses (8 formulations). The highest reported concentration of use resulting in leave-on dermal exposure, according to 2022 concentration of use data, is 1.5% Octoxynol-12, in face and neck preparations.

Much of the published literature has been identified under the name "Triton X-100." According to different sources, this name corresponds to several different octoxynol ingredients reviewed in the report (e.g., Octoxynol-1, Octoxynol-9). However, during the time of the original review of this report, it was thought that Triton X-100 referred only to Octoxynol-9, and therefore, for that report, data on Triton X-100 was included under Octoxynol-9. Accordingly, as the Panel reviews the data from the previous iteration of this report (as indicated by italicized text), they should note that data listed as "Octoxynol-9" may be referring to other octoxynols. In addition, much of the new data found since the last iteration of the report are on Triton X-100. As instructed by the Panel at the last review, these data have been included; however, because it is now known that this ingredient may refer to more than one octoxynol, these data have been incorporated into the report under a subheading of "an octoxynol (number of ethoxy repeat units unknown)." Several studies were found using Triton X-100 as a model irritant/cytotoxic agent in dermal, ocular, and mucous membrane assays.

The Panel published reviews on the safety of nonoxynols in 1983, 1999, and in 2015. In the original safety assessment of octoxynols, the Panel relied on the chemical similarity of nonoxynols (which are 1 carbon longer) to support the safety of octoxynols. Therefore, when data on octoxynols are absent, supporting data on nonoxynols has been included, as was done in the previous safety assessment of octoxynols; data from the 2015 Final Amended Report on nonoxynols have also been included for potential read-across sources, as appropriate.

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

4. Trimethylbenzoyl Diphenylphosphine Oxide – DR (Priya) – ***Dr. Belsito reports on day 2*** – This is the first time the Panel is reviewing a safety assessment of Trimethylbenzoyl Diphenylphosphine Oxide as used in cosmetics. The Scientific Literature Review (SLR) was issued by CIR on November 21, 2024. Since the issuing of the SLR, a use study was received evaluating the irritation potential of gel nail application using products containing Trimethylbenzoyl Diphenylphosphine Oxide (base, color, and topcoats containing 0.25, 3.65, and 1.5%, respectively). These data have been added to the report.



RLD (2024) indicate that Trimethylbenzoyl Diphenylphosphine Oxide is used in 1849 total formulations, (including manicuring preparations, makeup preparations, fragrance preparations, eye makeup preparations, and children's makeup preparations (not eye)). According to 2023 VCRP data, Trimethylbenzoyl Diphenylphosphine Oxide was used in 127 total formulations, all of which were manicuring preparations. The results of the concentration of use survey conducted by the Council in 2023 state that the maximum reported concentration of use of this ingredient is 4% in nail polishes and enamels. RLD indicate that Trimethylbenzoyl Diphenylphosphine Oxide is used in products that may be incidentally ingested (lipstick and lip glosses), used near the eyes (eyelash and eyebrow adhesives, glues, and sealants), or used by children (children's foundations); concentrations were not provided for any of these uses. In addition, this ingredient is reported to be used in formulations that may be inhaled (perfumes; concentration not provided).

According to the European Union, Trimethylbenzoyl Diphenylphosphine Oxide has restricted use in cosmetics. Regulations state that this ingredient may be safely used in artificial nail systems at a maximum concentration of 5%. In addition, products containing this ingredient should be for professional use only, skin contact should be avoided, and product directions should be carefully read.

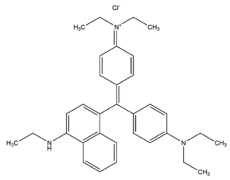
If no further data are needed, the Panel should formulate an updated Discussion and issue a Tentative Report. However, if additional data are required, the Panel should be prepared to identify those needs and issue an IDA.

5. <u>*Acacia senegal*</u> – DAR (Thushara) – ***Dr. Belsito reports on day 2*** – 
The Panel previously reviewed the safety of Acacia Senegal Gum and Acacia Senegal Gum Extract as part of a larger group of ingredients derived from the *Acacia* plant. In 1998, the Panel initially issued a Final Report with an insufficient data conclusion for the entire group of *Acacia* ingredients reviewed at that time, including Acacia Senegal Gum and Acacia Senegal Gum Extract; this report was never published. Subsequently, data were submitted, but the Panel's needs were met for only Acacia Senegal Gum and Acacia Senegal Gum Extract, and an Amended Final Report was published in 2005. At that time, the Panel concluded that Acacia Senegal Gum and Acacia Senegal Gum Extract are safe as used in cosmetic products. In September 2023, the Panel re-opened the safety assessment for these 2 ingredients. (Those ingredients for which the conclusion was insufficient data are not re-reviewed unless data are submitted and a request to reconsider received.) In its decision to reopen the assessment, the Panel considered increases in frequency and concentration of use and new product category usage in baby products. The Panel also wanted to reassess the potential risks of IgE mediated sensitivity caused by these ingredients.

   According to 2023 VCRP frequency of use data and the result of a 2022 Council maximum reported concentration of use survey, Acacia Senegal Gum was reported to be used in 287 formulations and at up to 26.7% in other oral hygiene products, respectively. In the previous report, there were no reported uses that could result in incidental ingestion. In 2001, it was reported to be used in 1 formulation; concentration of use data were reported for several categories, with a maximum use of 9% reported for mascara formulations. RLD received in 2024 indicate that Acacia Senegal Gum is used in 1833 formulations. The largest product group using this ingredient is mascara, where there are 555 uses reported.

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

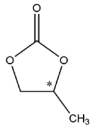
Draft Tentative Reports - There are 3 draft tentative reports for consideration. Issue a tentative conclusion?

1. <u>Basic Blue 7</u> – TR (Christina) – ***Dr. Cohen reports on day 2*** – 
At the September 2024 meeting, the Panel issued an IDA for Basic Blue 7. The following information was requested to determine the safety of this ingredient:

   - Chemical properties data
   - Method of manufacturing
   - Composition/impurities data
   - Concentration of use
   - Dermal absorption data or 28-day dermal toxicity data
     - If absorbed, additional data, including developmental and reproductive toxicity data are needed
   - Genotoxicity data
   - Dermal irritation and sensitization data

   Since the September meeting, no new data have been received or identified in an updated literature search. The report has been updated with RLD that were received in 2024. According to those RLD, Basic Blue 7 is used in 11 formulations, which included non-coloring (1 use) and coloring hair preparations (10 uses). VCRP survey data received in 2023 reported Basic Blue 7 to be used in 1 nail polish and enamel product. No uses of this ingredient were reported in response to the concentration of use survey submitted by the Personal Care Products Council in 2023. The Panel should carefully consider and discuss the data (or lack thereof), and issue a Tentative Report with a safe, safe with qualifications, insufficient data, unsafe, or split conclusion, and identify any additional items for inclusion in the Discussion.

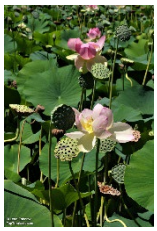
2. Propylene Carbonate – TAR (Priya) – ***Dr. Cohen reports on day 2*** – At the September 2024 meeting, the Panel determined that the data were insufficient to support safety of this ingredient and issued an IDA. The insufficiencies include:



- Concentrations of use in baby products
- Ultraviolet absorption data (if absorption is evident, phototoxicity/photosensitization data requested)

Since the IDA was issued, CIR has received no new data. However, RLD received in 2024 have been incorporated into the report. According to these data, Propylene Carbonate is used in a total of 13,340 formulations. In addition, comments on the Draft Amended Report were received from the Council and responses to these comments have been provided herein. A draft Abstract and Discussion have been included in this report version. 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, and identify any additional items for inclusion in the Discussion.

3. *Nelumbo nucifera* – TR (Thushara) – ***Dr. Cohen reports on day 2*** – At the December 2024 meeting, the Panel determined that the data were insufficient to support safety of these 14 *Nelumbo nucifera*-derived ingredients and issued an IDA. The insufficiencies include:



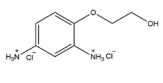
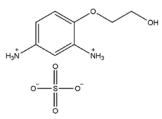
- For all ingredients
  - Composition and impurities
  - Methods of manufacturing
  - 28-day dermal toxicity assays
    - if positive, additional data (e.g., developmental and reproductive toxicity data) may be needed
  - In vivo genotoxicity data
  - UV absorption spectra
- For the callus, phytoplacenta and stamen-derived ingredients
  - Dermal irritation and sensitization data at maximum concentration of use
- For all except the flower and germ-derived ingredients
  - In vitro genotoxicity data
- Flower and whole plant-derived ingredients
  - Developmental and reproductive toxicity data
- For all except flower-derived ingredients
  - In vitro ocular irritation data

Comments and the following information received in response to the IDA is included with this submission and has been incorporated into the report: concentration of use by FDA product category for Nelumbo Nucifera Phytoplacenta Extract; UV absorption of Nelumbo Nucifera Germ Extract in water and butylene glycol; studies completed on a trade name mixture containing a maximum of 1.2% Nelumbo Nucifera Leaf Extract; studies completed on a foundation containing 0.2% Nelumbo Nucifera Flower Water; studies completed on a foundation containing 0.2% Nelumbo Nucifera Root Water; repeated insult patch test of a foundation containing 0.00001% Nelumbo Nucifera Flower Extract; and repeated insult patch test of an emulsion containing 0.0001% Nelumbo Nucifera Germ Extract.

The Panel should carefully consider and discuss the data (or lack thereof) and be prepared to issue a Tentative Report with a safe, safe with qualifications, insufficient data, unsafe, or split conclusion, and identify any additional items for inclusion in the Discussion.

Draft Final Reports - There are 3 Draft Final Reports for consideration. Review these drafts, especially the rationale provided in the Discussion sections, and issue final reports, as appropriate.

1. 2,4-Diaminophenoxyethanol HCl – FAR (Christina) – ***Dr. Belsito reports on day 2*** – At the September 2024 meeting, the Panel issued a Tentative Amended Report for public comment with the conclusion that 2,4-Diaminophenoxyethanol HCl and 2,4-Diaminophenoxyethanol Sulfate are safe for use as hair dye ingredients in the present practices of use and concentration described in the safety assessment.

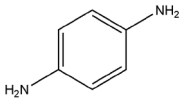



   Since the September meeting, no new data have been received or identified in an updated literature search. Comments provided by the Council on the draft Tentative Report received prior to the September 2024 Panel meeting and on the Tentative Amended Report released for public comment after the meeting have been addressed.

   The report has been updated with RLD received in 2024. According to the RLD, 2,4-Diaminophenoxyethanol HCl is used in 4,459 formulations, which include uses in eye makeup preparations, non-coloring hair preparations, hair coloring preparations (with the majority of the uses (4,438) reported in hair dyes and colors), and skin care preparations. 2,4-Diaminophenoxyethanol Sulfate is used in 149 formulations, which include uses in eye makeup preparations and hair coloring preparations (with the majority of uses (137) reported in hair dyes and colors). It should be noted that under hair coloring preparations, leave-on uses have been reported (1 in a hair rinse and 16 in "other" hair coloring preparations for 2,4-Diaminophenoxyethanol HCl; 1 in "other" hair coloring preparations for 2,4-Diaminophenoxyethanol Sulfate). Furthermore, use in eyelash and eyebrow dyes has been reported for both ingredients.

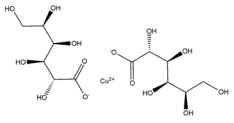
   The Panel should carefully review the Abstract, Discussion, and Conclusion, and issue a Final Amended Report.

2. *p*-Phenylenediamine – FAR (Christina) – ***Dr. Cohen reports on day 2*** – At the December 2024 meeting, the Panel determined that the conclusion needed to be revised in order to emphasize that these hair dyes ingredients should not be used around the eye (prompted by the reporting of such use in the RLD), and the Panel issued a second Revised Tentative Amended Report. The Panel concluded that *p*-Phenylenediamine, *p*-Phenylenediamine HCl, and *p*-Phenylenediamine Sulfate are safe for use as hair dye ingredients in the present practices of use and concentration described in this safety assessment; furthermore, these ingredients are unsafe for use in dermal coloring applications (e.g., temporary black henna tattoos) and for use in eyelash and eyebrow dyes.



   Since the December meeting, no unpublished data have been received for this report and no new data have been identified in an updated literature search. Comments provided by the Council on the Revised Tentative Amended Report have been addressed. The Panel should carefully review the Abstract, Discussion, and Conclusion, and issue a Final Amended Report.

2. Copper Gluconate – FR (Christina) – ***Dr. Belsito reports on day 2*** – At the September 2024 meeting, the Panel issued a Tentative Report for public comment with the conclusion that Copper Gluconate is safe for use as a cosmetic ingredient in the present practices of use and concentration described in the safety assessment.

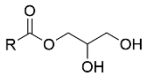


   Since the September meeting, no new data have been received or identified in an updated literature search. Comments provided by the Council on the draft Tentative Report received prior to the September 2024 Panel meeting have been addressed. The report has been updated with RLD that were received in 2024. According to the RLD, Copper Gluconate is used in 666 formulations, with the majority of the uses reported in skin care preparations (492 uses, with the highest concentration of use reported (from Council surveys) at 0.1% in rinse-off cleansing products and 0.008% in leave-on night products). This new use data along with the informational text on Wilson's disease and Menkes disease have been incorporated.

   The Panel should carefully review the Abstract, Discussion, and Conclusion and issue a Final Report.

Abbreviated Rereviews (i.e., rereview proposals) – There are 2 rereview documents. Because it has at least been 15 years since the previous reviews were published, in accordance with CIR Procedures, the Panel is being asked if the reports should be reopened.

1. Glyceryl Monoesters – RR (Monice) – ***Dr. Cohen reports on day 2*** - The Panel first published a review of the safety of Glyceryl Collagenate, Glyceryl Isostearates, Glyceryl Sesquioleate, Glyceryl/Sorbitol Oleate/Hydroxystearate, Glyceryl Stearate/Acetate, Glyceryl Stearate/Maleate, and Glyceryl Thiopropionate in 2000 in a report that originally reviewed 43 ingredients. The Panel concluded that the 7 glyceryl monoesters in this re-review are safe as cosmetic ingredients in the present practices of use and concentration. Since the original report was published, several of the other ingredients in the original report have been included in other safety assessments and are thus not recounted herein.



   In January 2025, an extensive search of the world's literature was performed for studies dated 1999 forward. No relevant published studies were found. However, the use data have been updated. According to RLD received by CIR in 2024, Glyceryl Isostearates has 2 uses in makeup preparations and Glyceryl Stearate/Acetate has 4 uses across eye makeup preparations, makeup preparations, and skin care preparations. No uses were reported for these ingredients in the 2023 VCRP.

   In the original 2004 safety assessment, concentrations of use were reported only for Glyceryl Stearate/Acetate; it was reported to be used at up to 7% in hair tonics and dressings. No uses were reported in the original report or at present for the remaining 5 ingredients in this re-review. No new concentration of use data have been received for any of the ingredients in this report.

   If upon review of the new data, the Panel determines that a re-review is warranted, a full Draft Amended Report will be presented at an upcoming meeting.

2. Waxes – RR (Priya) – ***Dr. Belsito reports on day 2*** – The Panel first published a review of the safety of Candelilla Wax, Carnauba Wax, Japan Wax, and Beeswax in 1984. The Panel concluded that these ingredients are safe in cosmetics under the present practices of concentration and use, as stated in that assessment. The Panel previously considered a rereview of this report and re-affirmed the 1984 conclusion, as published in 2005. It should be noted that after the publishing of the 1984 report and prior to the publishing of the 2005 rereview, Candelilla Wax, Carnauba Wax, and Japan Wax were re-named Euphorbia Cerifera (Candelilla) Wax, Copernica Cerifera (Carnauba) Wax, and Rhus Succedanea Fruit Wax, respectively.

   In January 2025, an extensive search of the world's literature was performed for studies dated 2000 forward. The ingredients included for consideration for re-review, the original report journal citation, the original conclusion, a comparison of original and new use data, and the search strategy are provided.

   According to 2002 VCRP Beeswax, Copernicia Cerifera (Carnauba Wax), Euphorbia Cerifera (Candelilla) Wax, and Rhus Succedanea Fruit Wax were used in 1,074, 1,194, 701, and 528 formulations, respectively. Recent (2023) VCRP data indicated that these ingredients are used in 1,758, 808, 703, and 16 formulations, respectively. The ingredient with the highest concentration of use in 2003 was Beeswax (it was used at up to 56% in lipsticks and lip glosses); while the ingredient with the highest concentration of use according to a Council survey in 2022 was Rhus Succedanea Fruit Wax (it is used at up to 37.9% in eyebrow pencils). RLD data collected in 2024 indicate frequencies of use greater than 5,000 formulations for Beeswax, Copernicia Cerifera (Carnauba) Wax, and Euphorbia Cerifera (Candelilla) Wax. These data also indicate the use of these ingredients in children's eye and non-eye makeup preparations, hair sprays, airbrush products (foundations, leg and body paints, makeup bases), oral products, and tattoo preparations.

   If upon review of the new studies and updated use data the Panel determines that a re-review is warranted, a full Draft Amended Report will be presented at an upcoming meeting. If the Panel instead determines that this report should not be reopened, they may choose to issue a rereview summary or expanded rereview summary, affirming their original conclusion.

Administrative Item - there are 3 administrative items.

Resource Documents – The Panel is being asked if these are ready for posting.

1. Inhalation – Admin (Jinqiu) – ***Dr. Cohen on day 2*** – The Panel last published an update of this document to the CIR website at the December 2021 meeting. Subsequent revisions were made at the December 2023 and 2024 meetings, incorporating additional particle size distribution data for certain propellant-based spray, including dry shampoo and propellant deodorant, along with relevant exposure calculations. Modifications were also made to the inhalation boilerplate (BP) language to better reflect the Panel's perspective on the associated health risks.

   At the December 2024 meeting, the Panel evaluated the appropriateness of applying the updated BP language across various categories of cosmetic spray products, with focus on the precise characterization of respiratory fractions of particles/droplets emitted by propellant-based sprays. The discussion also addressed specific aspects of cosmetic spray safety evaluations, such as assessing nanoparticle exposure in non-airbrush spray products, the challenges of using occupational exposure limits, the regional lung deposition of aerosols and particles, and the associated toxic effects in both the upper and deep respiratory tracts.

   The Panel should review the revised Document to evaluate the suitability of the inhalation BP language and update it as necessary to reflect their understanding of exposure to airborne particles/droplets from the use of cosmetic sprays. The Panel should finalize this version and replace the December 2021 version of it currently posted on the website.

2. MOE – Admin (Jinqiu) – ***Dr. Belsito reports on day 2*** - At the December 2024 meeting, the Panel discussed the varying terminology used in the systemic quantitative risk assessment (QRA) and the application of measured and realistic data versus conservative exposure parameters. The Panel requested revisions to the document to address the received comments, clarify the preferred terminology, and provide a clearer explanation of how the MOE approach should be performed in their safety evaluation process, such as the application of uncertainty factors for study duration extrapolation, avoiding over conservatism, and utilizing practice and habits data that better reflect the US consumer population.

   Comments provided by the Council on the Revised Document have been carefully addressed. The Panel is requested to review this draft resource paper and determine whether it accurately reflects their understanding and perspective on the concept and application of MOE within a QRA framework for evaluating the potential risks posed by exposure to cosmetic ingredients, and if it should be posted on the CIR website. If there are concerns that are not adequately addressed, the Panel should determine the necessary revisions and the extent to which further modifications are required.

Priorities

3. Draft 2026 Priorities – Admin (Bart) – ***Dr. Cohen reports on day 2*** –The draft priority list commonly comprises nominated-for-cause ingredients and ingredients with the highest frequency of use (FOU), out of those that have yet to be reviewed by the Panel. CIR has yet to receive any nominated-for-cause ingredient proposals; such proposals may yet be made, as late as the September 8-9, 2025 meeting of the Panel, wherein this priorities will be finalized. FOU data are provided via FDA's RLD; for this priority setting process, RLD were received from the FDA in July 2024 (in response to a Freedom of Information Act request).

   There are 15 reports proposed, covering 43 ingredients, on the 2026 Draft Priorities List. Once a proposal of a hair dye for assessment has been received from the PCPC Hair Color Technical Committee (HCTC), 16 new reports in total will be proposed for the 2026 docket. Reports previously prioritized and on the CIR docket at the end of 2025, as well as an extensive number of re-reviews of previous assessments, will supplement the total number of reports to be assessed in 2026.

   While this list includes only the lead ingredients, groupings of ingredients drafted by CIR Staff can be found on the following pages. ***Following the conclusion of the March meeting and prior to the June meeting***, the Read Across Working Group (RAWG) is asked to consider the Draft Priority List and determine if any changes should be made to the groupings. If the RAWG determines that changes to the groupings should be made, time will be docketed on the June meeting agenda to discuss with the full Panel.

Full Panel Meeting

The Panel will consider the 3 reports to potentially be issued as Final Reports, followed by the remaining reports advancing in the process (i.e., the Tentative Reports and Draft Reports). In addition, a consensus should be reached for each of the resource documents and the draft priorities.

Please remember, the meeting starts at 8:30 AM EST on day 1 and day 2.

Looking forward to seeing you all ***in-person***!

Agenda
172nd Meeting of the Expert Panel for Cosmetic Ingredient Safety
March 13-14, 2025

Thursday, March 13, 2025

8:30 AM EST	**WELCOME TO THE 172nd EXPERT PANEL TEAM MEETINGS**	**Drs. Bergfeld/Heldreth**
8:45 AM - 12 PM	**TEAM MEETINGS**	**Drs. Belsito/Cohen**
12 PM – 1 PM	**Lunch break**	
1:00 PM - 5 PM	**TEAM MEETINGS (continued)**	**Drs. Belsito/Cohen**

	Dr. Belsito's Team*		**Dr. Cohen's Team**
FAR (CB)	*p*-Phenylenediamine	DAR (PC)	Octoxynols
FAR (CB)	2,4-Diaminophenoxyethanol HCl	TAR (PC)	Propylene Carbonate
FR (CB)	Copper Gluconate	DR (PC)	Trimethylbenzoyl Diphenylphosphine Oxide
TR (CB)	Basic Blue 7	RR (PC)	Waxes
DAR (CB)	Kojic Acid	TR (TD)	*Nelumbo nucifera*-derived ingredients
DAR (CB)	Butoxyethanol	DAR (TD)	*Acacia senegal*-derived ingredients
RR (MF|BH)	Glyceryl Monoesters	Admin (JZ)	MOE Resource Paper
Admin (MF|BH)	2026 Draft Priorities	Admin (JZ)	Inhalation Resource Paper
DAR (PC)	Octoxynols	RR (BH|MF)	Glyceryl Monoesters
TAR (PC)	Propylene Carbonate	Admin (BH|MF)	2026 Draft Priorities
DR (PC)	Trimethylbenzoyl Diphenylphosphine Oxide	FAR (CB)	*p*-Phenylenediamine
RR (PC)	Waxes	FAR (CB)	2,4-Diaminophenoxyethanol HCl
TR (TD)	*Nelumbo nucifera*-derived ingredients	FR (CB)	Copper Gluconate
DAR (TD)	*Acacia senegal*-derived ingredients	TR (CB)	Basic Blue 7
Admin (JZ)	MOE Resource Paper	DAR (CB)	Kojic Acid
Admin (JZ)	Inhalation Resource Paper	DAR (CB)	Butoxyethanol

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 || Rev: Revised || SM: Strategy Memo || Admin: Administrative item

BH: Bart Heldreth || MF: Monice Fiume || CB: Christina Burnett || PC: Priya Cherian || TD: Thushara Diyabalanage || JZ: Jinqiu Zhu

*Team moves to the breakout room.

Friday, March 14, 2025			
8:30 AM EST	**WELCOME TO THE 172nd FULL EXPERT PANEL MEETING**		**Dr. Bergfeld**
8:40 AM	Admin **MINUTES OF THE DECEMBER 2024 EXPERT PANEL MEETING**		**Dr. Bergfeld**
8:45 AM	**DIRECTOR'S REPORT**		**Dr. Heldreth**
9:00 AM	**FINAL REPORTS, REPORTS ADVANCING TO THE NEXT LEVEL, OTHER ITEMS**		
	Final Reports		
	FAR (CB)	2,4-Diaminophenoxyethanol HCl – ***Dr. Belsito reports***	
	FAR (CB)	*p*-Phenylenediamine – ***Dr. Cohen reports***	
	FR (CB)	Copper Gluconate – ***Dr. Belsito reports***	
	Reports Advancing		
	TR (CB)	Basic Blue 7 – ***Dr. Cohen reports***	
	DAR (CB)	Kojic Acid – ***Dr. Belsito reports***	
	DAR (CB)	Butoxyethanol – ***Dr. Cohen reports***	
	DAR (PC)	Octoxynols – ***Dr. Belsito reports***	
	TAR (PC)	Propylene Carbonate – ***Dr. Cohen reports***	
	DR (PC)	Trimethylbenzoyl Diphenylphosphine Oxide – ***Dr. Belsito reports***	
	TR (TD)	*Nelumbo nucifera*-derived ingredients – ***Dr. Cohen reports***	
	DAR (TD)	*Acacia senegal*-derived ingredients – ***Dr. Belsito reports***	
	Other Items		
	RR (MF)	Glyceryl Monoesters – ***Dr. Cohen reports***	
	RR (PC)	Waxes – ***Dr. Belsito reports***	
	Admin (JZ)	Inhalation Resource Paper – ***Dr. Cohen reports***	
	Admin (JZ)	MOE Resource Paper – ***Dr. Belsito reports***	
	Admin (BH)	2026 Draft Priorities – ***Dr. Cohen reports***	

ADJOURN – *The next will be held in-person on Monday and Tuesday,* ***June 9-10, 2025,*** *at the Westin Georgetown, 2350 M Street, NW, Washington, DC. 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, or unsafe, or if 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 || Rev: Revised || SM: Strategy Memo || Admin: Administrative item

BH: Bart Heldreth || MF: Monice Fiume || CB: Christina Burnett || PC: Priya Cherian || TD: Thushara Diyabalanage || JZ: Jinqiu Zhu

ONE HUNDRED SEVENTY-FIRST MEETING

OF THE

EXPERT PANEL FOR COSMETIC INGREDIENT SAFETY

December 2-3, 2024

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.

Allan E. Rettie, Ph.D.

David Ross, Ph.D.

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

Susan Tilton, Ph.D.

Liaison Representatives

Consumer

Courtney Griffin, J.D.

Industry

Alex Kowcz, M.B.A.

Government

Prashiela Manga, Ph.D.

Jannavi Srinivasan, Ph.D.

Janet Zang, Ph.D.

Hong Xie, 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, DCST - Toxicologist

Analysis
Christina L. Burnett, MSES - Senior Scientific Analyst

Priya Cherian, MS - Senior Scientific Analyst

Thushara Diyabalanage, PhD–Senior Scientific Analyst

Information Services
Kevin Stone Fries, MLS - Information Services Manager

Other Vitrual Meeting Attendees

Name	Organization
Ayodele Ajayi	June Jacobs Labs
Nan An	FDA
Jennifer Ator	ToxServices
John Bailey	JEB Consulting
Don Bjerke	Procter & Gamble
Jennifer Cazabon	Arxada
Anne Corriou	Givaudan
Carol Eisenmann	Personal Care Products Council
Linda Giles	Transcription Etc.
Rebecca Justiniano	OPI
Dr. Linda Katz	FDA
Lauren Kavanagh	Innospec
Miao Li	FDA
Lauren Nardella	HBW Insight
Kimberly Norman	Personal Care Products Council
Allison Schafer	Procter & Gamble
Barbara Schmitt	Evonik
Alexandra Scranton	Women's Voices for the Earth
Prajakta Shimpi	L'Oreal
Kathy Stanton	Personal Care Products Council
Erica Todd	Mibelle Group
Angelique van Geresteijn	Keune Haircosmetics
Patra Volarath	FDA
Zemin Wang	FDA
Teresa Washington	FDA
Leah Yip	Unilever

CHAIRPERSON'S OPENING REMARKS

Dr. Bergfeld welcomed the attendees to the 171st meeting of the Expert Panel for Cosmetic Ingredient Safety. At this meeting, Dr. Bergfeld noted that the Panel reviewed 8 ingredient reports, including 2 finals, 2 tentative reports, and 4 draft reports. The Panel also reviewed 2 re-reviews, 2 re-review summaries, a strategy memo on fatty amphocarboxylates, the inhalation resource paper, and the margin of exposure resource paper. Dr. Bergfeld acknowledged the comments made by Women's Voices for the Earth on the *p*-Phenylenediamine report.

Dr. Bergfeld thanked the CIR staff for their continuing work in presenting high-quality documents to the Panel and the Personal Care Products Council and CIR Science and Support Committee for their helpful input.

APPROVAL OF MINUTES

The minutes of the September 30 and October 1, 2024 (170th) Expert Panel meeting were approved.

DIRECTOR'S REPORT

Dr. Heldreth thanked the members of and liaisons to the Panel for their tireless efforts to protect consumers. He also thanked colleagues at the Office of Cosmetics and Colors (OCAC) for their assistance in understanding the US FDA Registration and Listing Data (RLD), which CIR received in response to a FOIA request this summer. While CIR had grown accustomed to the format of the VCRP data received in the past, colleagues at the OCAC have since been very helpful with adjusting to the differences in the format of the RLD. In additional news from OCAC, Dr. Linda Katz announced her upcoming retirement from the FDA. Dr. Katz has been the Director of the Office for over 20 years, as well as the FDA liaison to this Panel for the same course of years. CIR and the Panel recognized and thanked Dr. Katz for her monumental contributions to public safety over the last few decades.

Additionally, Dr. Heldreth announced the retirement of Dr. Tom Slaga. Dr. Slaga, a noted cancer expert, Panel member, and friend, formally retired from this Panel. He is an absolute giant in the field of cancer research, leaving some large shoes to fill. Dr. Slaga served this Panel for many years, and we will dearly miss working with him. Largely due in part to his retirement, the CIR Steering Committee convened in November of this year. The Committee was spoiled for choice with 6 excellent candidates to be elected to just one position on the Panel. After much deliberation, the Committee elected Dr. Sam Cohen, MD, PhD, Havlik-Wall Professor of Oncology in the University of Nebraska Medical Center, Department of Pathology and Microbiology to this Panel. His tenure with the Panel will commence with the March 2025 meeting.

The Committee also approved the addition of 2 new rereview report pathways for the Panel's use. When the Panel is presented with a rereview proposal wherein the use of an ingredient has been discontinued, they may proceed to immediately issue a "use not supported" conclusion. As well, when the Panel is presented with a rereview proposal wherein no change of conclusion is desired but expanded summarization and publication of the new data therein would be in the best interest of the public, they may immediately issue an "expanded rereview summary" inclusive of expanded data recitations.

Also of note in 2024, Dr. Heldreth highlighted the issuance of 4 CIR issues of the International Journal of Toxicology (IJT). All 4 of CIR's 2024 IJT issues are now published, directly accessible in standard format at IJT (https://journals.sagepub.com/loi/IJT), and free, report-by-report, from both the CIR portal (https://cir-reports.cir-safety.org/) and PubChem (https://pubchem.ncbi.nlm.nih.gov/source/Cosmetic%20Ingredient%20 Review%20(CIR)). Additionally, copies of these issues in IJT's Nxtbook format, are available here:

Feb 2024- https://www.nxtbook.com/sage/sage/ijt_cir_202402/

Apr 2024- https://www.nxtbook.com/sage/sage/ijt_cir_202404/

Aug 2024- https://www.nxtbook.com/sage/sage/ijt_cir_202408/

Oct 2024- https://www.nxtbook.com/sage/sage/ijt_cir_202410/

Furthermore, CIR is extremely delighted about the establishment this year of a cooperation agreement with the International Collaboration of Cosmetics Safety and presentations on cosmetic ingredient risk & safety assessment in both China and South Korea, by CIR Toxicologist Dr. Jinqiu Zhu.

FINAL SAFETY ASSESSMENTS

Inositol

The Panel reviewed the available data and issued a Final Report with the conclusion that Inositol is safe in cosmetics in the present practices of use and concentration as described in the safety assessment. According to 2023 FDA VCRP survey and 2022 concentration of use data, this ingredient is used in 212 formulations and at up to 2%. However, according to concentration of use data updated in 2024, Inositol is used at up to 4% in face and neck preparations. The Panel noted this increased concentration of use, and determined that the available data are still in support of the safe use of this ingredient. The safety of Inositol is supported by its widespread use, GRAS status, endogenous nature, low concentrations of use, and lack of positive alerts in various toxicological studies.

TENTATIVE SAFETY ASSESSMENTS

***p*-Phenylenediamine, *p*-Phenylenediamine HCl, and *p*-Phenylenediamine Sulfate**

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

p-Phenylenediamine *p*-Phenylenediamine HCl *p*-Phenylenediamine Sulfate

However, the Panel also concluded that these ingredients are unsafe for use in dermal coloring applications (e.g., temporary black henna tattoos) and for use in eyelash and eyebrow dyes.

p-Phenylenediamine is a known dermal sensitizer. It is highly inappropriate for this ingredient to be used in products outside of hair dyes as evidenced by multiple case reports of severe adverse skin reactions to dark henna temporary tattoos. Reactions include severe allergic contact dermatitis, permanent hyper-and hypopigmentation, and keloid formation. *p*-Phenylenediamine is an unapproved color additive in cosmetic products, and thereby, such use is not permitted under the US Federal Food, Drug and Cosmetic Act (FD&C Act), which mandates that color additives must be approved by the FDA for their intended use before they are used. *p*-Phenylenediamine is exempt from certain adulteration and color additive provisions of the FD&C Act only when it is used as a coal tar hair dye.

In addition, the Panel noted that use of *p*-Phenylenediamine has been reported in eye makeup preparations, non-coloring hair preparations, and skin care preparations. Accordingly, because *p*-Phenylenediamine is not an approved color additive in cosmetics products, use in eye makeup products, non-coloring hair preparations, and skin care preparations is not permitted. Furthermore, the Panel noted that hair dyes, such as those containing *p*-Phenylenediamine, should not be applied to the eyebrows and eyelashes in that such use can result in lost or permanently damaged vision.

4-Chloro-2-Aminophenol

The Panel issued a Tentative Amended Report for public comment with the conclusion that the available data are insufficient to make a determination that 4-Chloro-2-Aminophenol is safe under the intended conditions of use in hair dye formulations. The Panel determined that the data needs from the Insufficient Data Announcement (IDA) issued following the June 2024 Panel meeting remain unmet. In order to come to a conclusion of safety for this hair dye, the following data are needed:

- Maximum concentration of use data
- Composition/impurities data
- Toxicokinetics data, especially dermal absorption data
  - If absorbed, additional data, including developmental and reproductive toxicity data, may be needed
- Micronucleus genotoxicity assay data

Tetrabromophenol Blue

The Panel issued a Tentative Report for public comment with the conclusion that Tetrabromophenol Blue is safe for use as a hair dye ingredient in the present practices of use and concentration described in the safety assessment.

Tetrabromophenol Blue is reported to function as a hair colorant and is used in oxidative and direct hair dye 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 FD&C 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.

***Paeonia suffruticosa* – Derived Ingredients**

The Panel issued a Tentative Report for public comment with a conclusion of safe in cosmetics in the present practices of use and concentration as described in the safety assessment for Paeonia Suffruticosa Seed Oil. The safety of this ingredient is supported by its chemical composition and very low concentration of use. However, the Panel also issued an insufficient data conclusion regarding the 4 remaining *Paeonia suffruticosa*-derived ingredients.

Paeonia Suffruticosa Bark Extract
Paeonia Suffruticosa Extract
Paeonia Suffruticosa (Tree Peony) Root Bark Extract
Paeonia Suffruticosa Root Extract

For these 4 ingredients, the Panel determined that data needs from the IDA issued following the June 2024 Panel meeting remain unmet. In order to come to a conclusion of safety for these ingredients, the following data are needed:

- For Paeonia Suffruticosa Root Bark Extract
  - Clarification on the definition, method of manufacture, and composition, as applicable to cosmetic use
  - Clarification as to whether Paeonia Suffruticosa Root Extract included the root bark of the plant

- For Paeonia Suffruticosa Bark Extract, Paeonia Suffruticosa Extract, and Paeonia Suffruticosa Root Extract

  - Maximum concentrations of use
  - Ocular irritation data (in vitro) at the maximum reported concentrations of use for uses near the eye

- For all 4 insufficient ingredients:
  - 28-Day dermal toxicity assays on all ingredients
    - if positive, data on systemic toxicity endpoints (e.g., developmental and reproductive toxicity) may be needed
  - Genotoxicity data

- For Paeonia Suffruticosa Bark Extract, Paeonia Suffruticosa Extract, and Paeonia Suffruticosa (Tree Peony) Root Bark Extract:
  - Dermal irritation and sensitization data

INSUFFICIENT DATA ANNOUNCEMENTS

Pyrogallol

The Panel issued an IDA for Pyrogallol. The following information is required to determine the safety of this hair dye:

- Maximum concentration of use
- Dermal irritation and sensitization data at maximum concentration of use for non-hair dye uses
- Ocular irritation data at maximum concentration of use for products used around the eyes

Cocoyl Hydrolyzed Collagens

The Panel issued an IDA for Potassium Cocoyl Hydrolyzed Collagen and TEA-Cocoyl Hydrolyzed Collagen. The additional data needed to determine the safety of these ingredient are:

- Maximum concentration of use
- Dermal irritation and sensitization data at a maximum concentration of use that does not induce sensitization
- UV absorption spectra; if absorbed, phototoxicity and/or photosensitization data are needed

In addition to Potassium Cocoyl Hydrolyzed Collagen and TEA-Cocoyl Hydrolyzed Collagen, the Panel has considered the addition of Cocoyl Hydrolyzed Collagen and Sodium Cocoyl Hydrolyzed Collagen. While CIR will conduct a full search of the publicly available literature for these 2 additional ingredients, all relevant unpublished data, including the data needs above, are requested for these ingredients.

***Nelumbo nucifera* – Derived Ingredients**

The Panel issued an IDA after reviewing the safety information related to 14 *Nelumbo nucifera*-derived ingredients. The additional data needed to determine the safety of these ingredients are:

- For all ingredients
  - Composition and impurities
  - Method of manufacturing
  - 28-Day dermal toxicity assays on all ingredients
    - if positive, additional data (e.g., developmental and reproductive toxicity data) may be needed
  - In vivo genotoxicity data
  - UV absorption spectra
- For the callus, phytoplacenta, and stamen derived ingredients
  - Dermal irritation and sensitization data at maximum concentration of use
- For all except the flower and germ derived ingredients
  - In vitro genotoxicity data
- For the flower and whole plant derived ingredients
  - Developmental and reproductive toxicity data
- For all except the flower derived ingredients
  - In vitro ocular

RE-REVIEWS

In accordance with its Procedures, the Panel evaluates the conclusions of previously-issued safety assessments approximately every 15 years. At this meeting, the Panel considered 2 previous assessments for rereview. The Panel determined that the following reports should be reopened; Draft Amended Reports will be presented to the Panel for these rereviews at a future meeting.

- 2-Nitro-p-Phenylenediamine & 4-Nitro-o-Phenylenediamine – 2 ingredients
- Oxyquinoline & Oxyquinoline Sulfate – 2 ingredients

The Panel reaffirmed the conclusions reached in these 2 safety assessments (i.e., chose not to re-open the original reports) at a prior meeting. A rereview summary for each of these safety assessments was prepared and presented to the Panel at this meeting. The Panel approved both of these documents.

- Castor Oil - 8 ingredients
- PEG Stearates – 30 ingredients

Inhalation Resource Document

The Panel reviewed the revised Inhalation Resource Document and the respiratory boilerplate (BP) language therein. The Panel discussed the suitability of applying the BP to address various categories of cosmetic spray products, with particular focus on the precise characterization of respiratory fractions of particles/droplets generated during uses of different spray products. Additionally, the Panel considered some special aspects of cosmetic spray safety evaluation, including the assessment of nanoparticle exposure in non-airbrush spray products, the limitations of applying the Occupational Safety and Health Administration (OSHA) permissible exposure limits (PEL), the regional lung deposition of aerosols and particles and the associated toxic effects in both the upper and deep respiratory tract, as well as the feasibility of obtaining the necessary data through RLD for assessing the safety of ingredients used in airbrush devices. After the suggested changes and relevant concerns are addressed, the document and the BP will be presented to the Panel for further review at a future meeting.

MOE Resource Document

The Panel reviewed a draft margin of exposure (MOE) resource document and discussed the varying terminology used in the systemic quantitative risk assessment (QRA). They further deliberated the application of using known values, rather than parameters that are conservative. The Panel requested revisions to the document to address the received comments, clarify the preferred terminology, and differently apply uncertainty factors to improve the estimation of systemic exposure doses. Upon addressing these concerns, the document will be resubmitted to the Panel for further review at a future meeting.

Strategy Memo – Fatty Amphocarboxylates

The Panel responded to a strategy memo regarding received data (quantitative structure-activity relationship (QSAR) skin sensitization predictions on C12 diacetate 1, C12 diacetate 2, C12 monoacetate 1, and C12 monoacetate 2) and a statement from the Amphoacetates Consortium suggesting the tabling of this report for forthcoming DART data. Following deliberations with industry, the Panel are expecting additional data on the chemical structures, composition, and impurities on these ingredients to aid with the review of this group, and to determine whether the use of this read-across approach is appropriate. In addition, the Panel agreed to table the Fatty Amphocarboxylates report to allow for the receipt of a prenatal developmental toxicity study in rabbits performed using C8-18 (diacetate form). All data are requested to be submitted as soon as possible. The next iteration of this report will be presented to the Panel at either their June or September meetings in 2025, depending in part on the timing of relevant data submissions.

Commitment & Credibility since 1976

Memorandum

Date: February 14th, 2025

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

To: All Stakeholders

Re: 2026 Draft Priority List

The CIR Procedures require preparation of the 2026 Draft Priority List for public comment by June 1, 2025. However, it is advantageous for the 2026 Draft Priority List to be issued for public comment earlier (March 2025) in the process to allow more time for the acquisition of data. The draft priority list commonly comprises nominated-for-cause ingredients and ingredients with the highest frequency of use (FOU), out of those that have yet to be reviewed by the Panel. CIR has yet to receive any nominated-for-cause ingredient proposals; such proposals may yet be made, as late as the September 8-9, 2025 meeting of the Panel, wherein this priorities will be finalized. FOU data are provided via FDA's Registration and Listing Data (RLD); for this priority setting process, RLD were received from the FDA in July 2024 (in response to a Freedom of Information Act request).

There are 15 reports proposed, covering 43 ingredients, on the 2026 Draft Priorities List. Once a proposal of a hair dye for assessment has been received from the PCPC Hair Color Technical Committee (HCTC), 16 new reports in total will be proposed for the 2026 docket. Reports previously prioritized and on the CIR docket at the end of 2025, as well as an extensive number of re-reviews of previous assessments, will supplement the total number of reports to be assessed in 2026.

Alpha-Isomethyl Ionone is the 1st ingredient on the list with nearly 12,000 formulations reported in the RLD. While this ingredient is used as a fragrance and has a published, RIFM-completed safety assessment for that use, Alpha-Isomethyl Ionone is also reported to function as a skin conditioning agent – miscellaneous. Accordingly, is the safety assessment for fragrance uses also sufficient for other cosmetic uses/exposures of this ingredient? According to the RLD, only 3,764 of the formulations reported for this ingredient are linked to fragrance preparation categories (05), including: (a) Colognes and toilet waters, (b) Perfumes, (c) Powders (dusting and talcum) (excluding aftershave talc), and (d) Other fragrance preparations. Which function, and at what concentration, this ingredient is used for in the other 8,165 products is non-obvious.

While this list includes only the lead ingredients, groupings of ingredients drafted by CIR Staff can be found on the following pages. Following the conclusion of the March meeting and prior to the June meeting, the Read Across Working Group (RAWG) is asked to consider the Draft Priority List and determine if any changes should be made to the groupings. If the RAWG determines that changes to the groupings should be made, time will be docketed on the June meeting agenda to discuss with the full Panel.

Interested parties are encouraged to submit pertinent data to the CIR, as soon as possible, for use in the development of the Scientific Literature Reviews (SLR) for these ingredients. Although the specific data needs vary for each safety assessment, the following are typical data that the Panel reviews for each safety assessment.

- Chemistry, impurities, and method of manufacture
- Toxicokinetics data, specifically dermal absorption and/or penetration
- Repeated-dose toxicity data
- Inhalation toxicity data, if the ingredient is used in a product that can be incidentally inhaled
- Reproductive/developmental toxicity data
- Genotoxicity data; if positive, carcinogenicity data may be needed
- Dermal irritation and sensitization data at maximum concentration of use

For the review of botanical ingredients, the additional data needed include: species, plant part, extraction method, solvent, and data on component chemical characterization. It is important that these data are specific for the ingredient(s) as used in cosmetics.

2026 Draft Priorities List

Ingredient	Frequency of Use (FOU) Data Year: 2024
For cause	
To be determined hair dye ingredient by HCTC	-
Per FOU	
Alpha-Isomethyl Ionone	**11,929**
Hydroxycyclohexyl Phenyl Ketone	**2515**
3-*O*-Ethyl Ascorbic Acid	**1947**
Hydrolyzed Quinoa	**1786**
Ethyl Cyanoacrylate	**1659**
Ethyl Trimethylbenzoyl Phenylphosphinate	**1627**
Thioglycerin	**1549**
Tetramethyl Acetyloctahydronaphthalenes	**1505**
Ceteth-10 Phosphate	**1484**
Hydroxypropyltrimmonium Hyaluronate	**1379**
Vaccinium Myrtillus Fruit Extract	**1367**
Diethylhexyl Syringylidenemalonate	**1362**
Etocrylene	**1277**
Dimethyl Isosorbide	**1266**
Polyglyceryl-3 Methylglucose Distearate	**1227**

2026 Draft Priorities Groupings for New Reports

Proposed 2026 Report – per cause

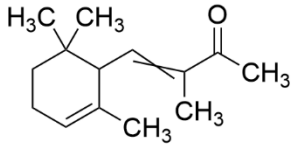
To be determined *– per PCPC Hair Color Technical Committee (HCTC)* **FOU = __**

Reported **Function**: Hair Colorant
Notes: *Since FOU might not be a very accurate surrogate for exposure, with regard to hair dyes, the PCPC HCTC proposes one hair dye ingredient annually for CIR review. The HCTC typically submits a proposed hair dye ingredient between the 1st and 2nd meetings of the year.*
Grouping proposal: None

Proposed 2026 Reports – per FOU

Alpha-Isomethyl Ionone **FOU = 11,929**

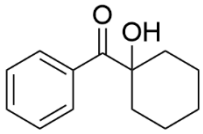
Definition: Alpha-Isomethyl Ionone is the organic compound that conforms to the structure:



Reported **Functions**: Fragrance Ingredients; Skin-Conditioning Agents - Miscellaneous
Notes: *(CAS No. 127-51-5 (alpha-)) While this ingredient is used as a fragrance and has a published, RIFM-completed safety assessment for that use, Alpha-Isomethyl Ionone is also reported to function as a skin conditioning agent – miscellaneous. Accordingly, is the safety assessment for fragrance uses also sufficient for other cosmetic uses/exposures? According to the RLD, only 3,764 of the formulations reported for this ingredient are linked to fragrance preparation categories (05), including: (a) Colognes and toilet waters, (b) Perfumes, (c) Powders (dusting and talcum) (excluding aftershave talc), and (d) Other fragrance preparations. Which function, and at what concentration, this ingredient is used for in the other 8,165 products is non-obvious.*
Grouping proposal: None

Hydroxycyclohexyl Phenyl Ketone **FOU = 2,515**

Definition: Hydroxycyclohexyl Phenyl Ketone is the organic compound that conforms to the structure:

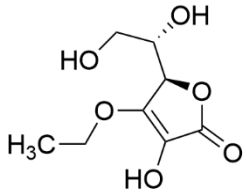


Reported **Function**: Artificial Nail Builders
Notes: *(CAS No. 947-19-3)*
Grouping proposal: None

3-*O*-Ethyl Ascorbic Acid

FOU = 1,947

Definition: 3-*O*-Ethyl Ascorbic Acid is the organic compound that conforms to the structure:



Reported **Function**: Skin-Conditioning Agents - Miscellaneous

Notes: *(CAS No. 86404-04-8)*

CIR draft grouping: (4 ingredients proposed with a total FOU = 2,053)	***FOU***
3-O-Ethyl Ascorbic Acid	*1947*
2-O-Ethyl Ascorbic Acid	*75*
Diethyl Ascorbic Acid	*27*
3-O-Cetyl Ascorbic Acid	*4*

Hydrolyzed Quinoa

FOU = 1,786

Definition: Hydrolyzed Quinoa is the hydrolysate of the quinoa seed, *Chenopodium quinoa*, derived by acid, enzyme or other method of hydrolysis.

Reported **Function**: Skin-Conditioning Agents - Miscellaneous

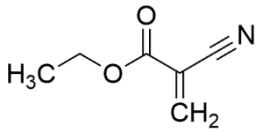
Notes: *These ingredients are each derived from Chenopodium quinoa. The Panel has previously assessed the safety of Chenopodium Quinoa Seed Oil in the Safety Assessment of Plant-Derived Fatty Acid Oils, published in IJT in 2017, concluding that those oils are safe as used.*

CIR draft grouping: (5 ingredients proposed with a total FOU = 2,875)	***FOU***
Hydrolyzed Quinoa	*1786*
Chenopodium Quinoa Seed Extract	*802*
Chenopodium Quinoa Seed	*249*
Chenopodium Quinoa Seed Oil Ethyl Esters	*32*
Hydrolyzed Chenopodium Quinoa Seed (synonym?)	*6*

Ethyl Cyanoacrylate

FOU = 1,659

Definition Ethyl Cyanoacrylate is the ester that conforms to the structure:



***Reported* Function**: **None reported**

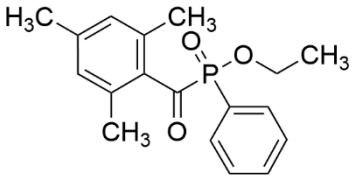
Notes: *(CAS No. 7085-85-0) These 3 ingredients share the same cyanoacrylate core structure and differ only by the alkyl or alkoxy sidechain. This ingredient does not have a reported function but is likely a film former or binder like the other 2 ingredients grouped below.*

CIR draft grouping: (3 ingredients proposed with a total FOU = 1686)	***FOU***
Ethyl Cyanoacrylate	*1659*
Ethoxyethyl Cyanoacrylate	*16*
Methoxyethyl Cyanoacrylate	*11*

Ethyl Trimethylbenzoyl Phenylphosphinate

FOU = 1,627

Definition: Ethyl Trimethylbenzoyl Phenylphosphinate is the organic compound that conforms to the structure:



***Reported* Function**: Light Stabilizers

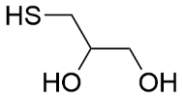
Notes: *(CAS No. 84434-11-7) These 2 ingredients are both light stabilizers and share in common a trimethylbenzoyl phenylphosphine structural core.*

CIR draft grouping: (2 ingredients proposed with a total FOU = 2038)	***FOU***
Ethyl Trimethylbenzoyl Phenylphosphinate	*1627*
Bis-Trimethylbenzoyl Phenylphosphine Oxide	*411*

Thioglycerin

FOU = 1,549

Definition: Thioglycerin is the polyhydric alcohol that conforms to the structure:



Reported **Functions**: Depilating Agents; Hair-Waving/Straightening Agents; Reducing Agents

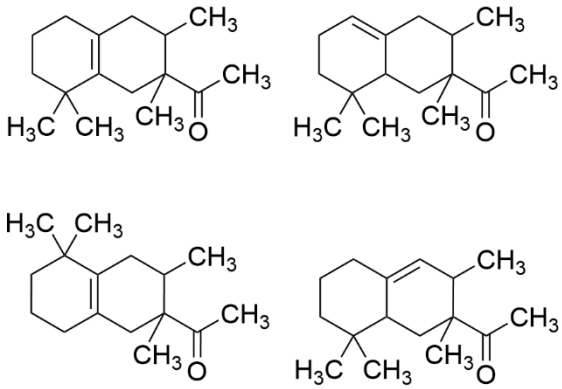
Notes: *(CAS Nos. 38098-46-3; 96-27-5)*

CIR draft grouping: none

Tetramethyl Acetyloctahydronaphthalenes

FOU = 1,505

Definition: Tetramethyl Acetyloctahydronaphthalenes is a mixture of isomers that conforms to the following structures:



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

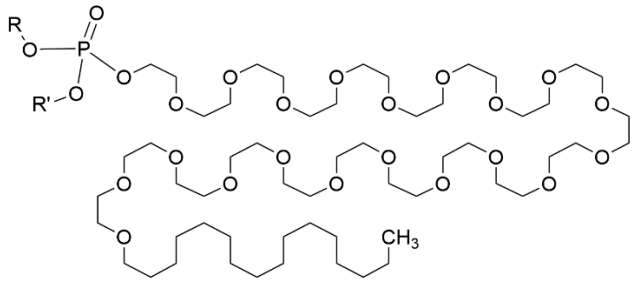
Notes: *(CAS Nos. 54464-57-2; 68155-67-9; 54464-59-4; 68155-66-8) Like Alpha-Isomethyl Ionone above, while this ingredient is used as a fragrance and has a published, RIFM-completed safety assessment for that use, Tetramethyl Acetyloctahydronaphthalenes is also reported to function as a skin conditioning agent – miscellaneous. Accordingly, is the safety assessment for fragrance uses also sufficient for other cosmetic uses/exposures? The function and concentration of this ingredient in many of these 1,505 products is non-obvious.*

CIR draft grouping: none

Ceteth-10 Phosphate

FOU = 1,484

Definition: Ceteth-10 Phosphate is a complex mixture of esters of phosphoric acid and Ceteth-10. Ceteth-10 is the polyethylene glycol ether of cetyl alcohol.



wherein R and R' independently are hydrogen, a salt cation, or another equivalent of ceteth-10.

***Reported* Function**: Surfactants - Cleansing Agents

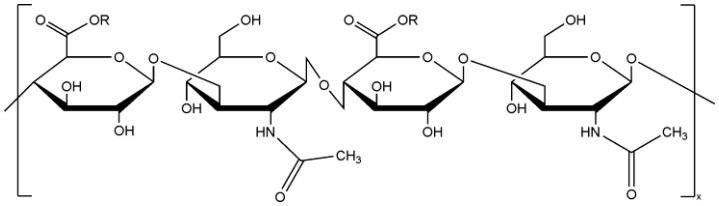
Notes: *(CAS No. unknown) The Panel has previously assessed the safety of a component of this ingredient, ceteth-10, in the Safety Assessment of Alkyl PEG Ethers as Used in Cosmetics, concluding that those Alkyl PEG ethers (including ceteth-10 and similar components for all of the ingredients grouped below) are safe as used when formulated to be nonirritating.*

CIR draft grouping: (9 ingredients proposed with a total FOU = 2,929)	***FOU***
Ceteth-10 Phosphate	*1484*
Oleth-5 Phosphate	*1298*
Di-C12-15 Alketh-2 Phosphate	*3*
Di-C12-15 Alketh-4 Phosphate	*76*
Di-C12-15 Alketh-6 Phosphate	*3*
C12-13 Alketh-2 Phosphate	*2*
C12-15 Alketh-10 Phosphate	*1*
Ceteth-20 Phosphate	*55*
Ceteth-8 Phosphate	*7*

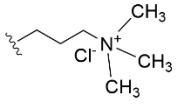
Hydroxypropyltrimonium Hyaluronate

FOU = 1,379

Definition: Hydroxypropyltrimonium Hyaluronate is the quaternary ammonium compound that conforms generally to the structure:



wherein R is hydrogen or hydroxypropyltrimonium:



***Reported* Functions**: Film Formers; Humectants

Notes: (*CAS No. unknown*)

Grouping proposal: None

Vaccinium Myrtillus Fruit Extract

FOU = 1,367

Definition: Vaccinium Myrtillus Fruit Extract is the extract of the fruit of *Vaccinium myrtillus* (Bilberry, European blueberry).

***Reported* Function**: Skin-Conditioning Agents - Miscellaneous

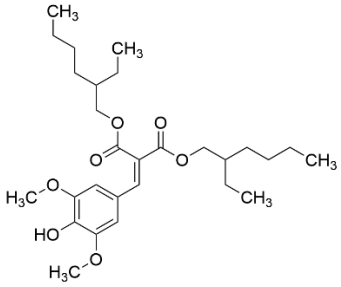
Notes: *(CAS No. 84082-34-8 (generic)) All 10 of these ingredients are derived from the European blueberry plant.*

CIR draft grouping: (10 ingredients proposed with a total FOU = 1,930)	***FOU***
Vaccinium Myrtillus Fruit Extract	*1367*
Vaccinium Myrtillus Fruit/Leaf Extract	*324*
Vaccinium Myrtillus Leaf Extract	*92*
Vaccinium Myrtillus Fruiting Tops (not in INCI; probably means whole fruit)	*57*
Vaccinium Myrtillus Leaf (not in INCI)	*24*
Vaccinium Myrtillus Whole (not in INCI)	*23*
Vaccinium Myrtillus Fruit Juice	*27*
Vaccinium Myrtillus Fruit (not in INCI)	*11*
Vaccinium Myrtillus Bud Extract	*3*
Vaccinium Myrtillus Fruit Water	*2*

Diethylhexyl Syringylidenemalonate

FOU = 1,362

Definition: Diethylhexyl Syringylidenemalonate is the organic compound that conforms to the structure:



***Reported* Functions**: Antioxidants; Light Stabilizers; Skin-Conditioning Agents – Miscellaneous

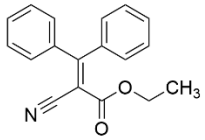
Notes: *(CAS No. 444811-29-4)*

Grouping proposal: None

Etocrylene

FOU = 1,227

Definition: Etocrylene is the organic ester that conforms to the structure:



***Reported* Function**: Light Stabilizers

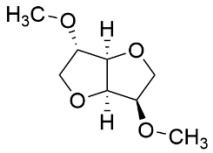
Notes: *(CAS No. 5232-99-5) These 2 ingredients are light stabilizers. Octocrylene is also a sunscreen agent and active ingredient in OTC drug products. Structurally, these 2 chemicals are each alkyl (ethyl or 2-ethylhexyl) esters of 2-cyano-3,3-diphenyl-2-propenoic acid.*

CIR draft grouping: (2 ingredients proposed with a total FOU = 2,784)	***FOU***
Etocrylene	*1227*
Octocrylene	*1557*

Dimethyl Isosorbide

FOU = 1,266

Definition: Dimethyl Isosorbide is a dimethyl ether of an anhydride of an isomer of sorbitol that conforms to the structure:



***Reported* Functions**: Solvents; Viscosity Decreasing Agents

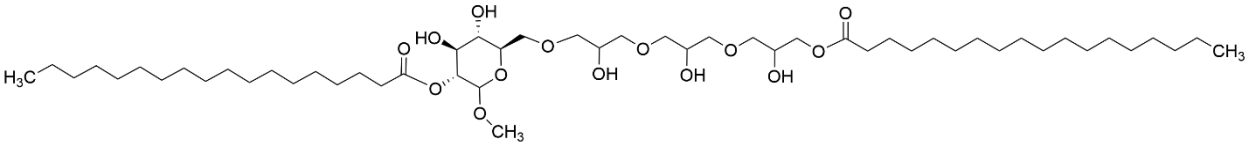
Notes: *(CAS No. 5306-85-4) The Panel has previously assessed the safety of a component of this ingredient, sorbitol, in the Safety Assessment of Mannitol, Sorbitol, and Xylitol as Used in Cosmetics, concluding that these sugar alcohol ingredients are safe in cosmetics in the present practices of use and concentration described in the safety assessment.*

Grouping proposal: None

Polyglyceryl-3 Methylglucose Distearate

FOU = 1,227

Definition: Polyglyceryl-3 Methylglucose Distearate is the diester of stearic acid and the condensation product of methylglucose and Polyglycerin-3.



***Reported* Functions**: Skin-Conditioning Agents – Emollient; Surfactants - Emulsifying Agents

Notes: *(CAS No. unknown)*

Grouping proposal: None