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AGENDA

MINUTES

EXPERT PANEL MEETING

SEPTEMBER 8-9, 2025

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: 174th Meeting of the Panel — Monday and Tuesday, September 8th – 9th, 2025
Date: August 15th, 2025

Welcome to the third Panel Meeting of 2025! The agenda and accompanying materials for the 174th Expert Panel Meeting, to be held on September 8th – 9th, 2025, are now available. ***The location is different from the one in June*** – and it is virtual via MS Teams. ***The meeting will start later, on both days at 9:30 AM EST***, for the benefit of our colleagues in the west. Invitations (3) 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:

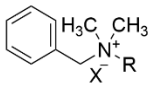
https://www.cir-safety.org/meeting/174th-expert-panel-meeting

The meeting agenda includes the consideration of 13 reports advancing in the review process, including 6 draft final reports, 5 draft tentative reports, and 2 draft reports (both of which are re-opened reviews). Also on the agenda is 1 previous report proposed for rereview; ***for this proposed rereview, the Panel is only being asked if the report should be reopened.*** There are also 3 administrative items, including a proposal to amend the Brown Algae report, finalization of the 2026 Priorities, and finalization of a journal submission regarding hair dye epidemiology. Finally, **both the RAWG and the full Panel will address the report on Fatty Amphocaboxylates**. Day 1 will start with a RAWG session for this ingredient group, followed by the traditional team breakout sessions.

As we continue with our efforts to reduce the quantity of late-breaking information, we are making a cutoff for most 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 4-Chloro-2-Aminophenol, Octoxynols, Basic Blue 7, *Lactobacillus* Ferment ingredients, 4-Nitro-*o*-Phenylenediamine, and *Nelumbo nucifera*-derived ingredients.) ***Submissions received on non-final reports, after the issuance of the Wave 2 supplement on August 28th, will be held back until the next Panel review of those reports.***

Draft Reports - There are 2 draft reports for review. Sufficient data to proceed to a tentative conclusion, or issue an Insufficient Data Announcement (IDA)?

1. Alkoniums – DAR (Priya) – ***Dr. Cohen reports on day 2*** – The original review of Stearalkonium Chloride was published in 1982 with the conclusion that is "safe when incorporated in cosmetic products similar to those presently marketed." The Panel considered a re-review of this report and re-affirmed the 1982 conclusion, as published in 2003. In March 2023, the Panel determined to re-open this safety assessment for the addition of structurally similar ingredients.

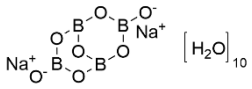


   One of the structurally similar ingredient additions, Benzalkonium Chloride, was also previously reviewed by the Panel in a safety assessment published in 1989 with the conclusion that "Benzalkonium Chloride, at concentrations up to 0.1% free, active ingredient, is safe as a cosmetic ingredient as presently used." The Panel considered a re-review of this ingredient, and re-affirmed the 1989 conclusion, as published in 2008. Accordingly, a Draft Amended Report on these ingredients, as well as 4 previously unreviewed ingredients (Behenalkonium Chloride, Benzalkonium Bromide, Cetearalkonium Bromide, and Lauralkonium Bromide) has been prepared and submitted for review.

   Benzalkonium Chloride and Stearalkonium Chloride were previously reported to be used in 79 (as of 2006) and 151 total formulations (as of 2001), respectively. According to 2023 VCRP data, these ingredients were used in 69 and 88 formulations, respectively. The maximum reported concentration of use for Benzalkonium Chloride has remained consistent, with usage up to 0.5% reported in both 2006 and 2023. The maximum concentration of use for Stearalkonium Chloride has decreased from a reported 7% in 2001 to 3.8%in 2022. RLD (2024) indicate that Stearalkonium Chloride is currently used in 885 formulations, while Benzalkonium Chloride appears in 565 formulations.

   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. Sodium Borate – DAR (Temima) – ***Dr. Belsito reports on day 2*** – The Panel first published a review of the safety of these two ingredients in 1983 and concluded that Sodium Borate and Boric Acid, in concentrations less than or equal to 5%, are safe as cosmetic ingredients when used as currently recommended (as described in that safety assessment); however, cosmetic formulations containing free Sodium Borate or Boric Acid at this concentration should not be used on infant skin or injured skin. The Panel previously considered a re-review of this report in February 2003 and reaffirmed the 1983 conclusion, as published in 2006. At the June 2024 meeting, the Panel determined to re-open this safety assessment due to a change in the reported use categories, to evaluate new data, and to explore the reasoning for why these ingredients have been banned by the European Union.

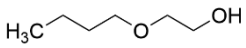


   According to 2023 VCRP survey data, Sodium Borate was reported to be used in 30 formulations and Boric Acid was reported to be used in 8 formulations; in 2002, 280 and 77 uses were reported, respectively. In 2024, RLD reported that these ingredients have a higher frequency of use. Boric Acid and Sodium Borate were reported to be in use in 40 formulations and 144 formulations, respectively. In 2002, the highest reported concentration of use for Boric Acid was 2% in conditioners and 3% for Sodium Borate in paste masks/mud packs; the highest leave-on concentration of use was 2% in other eye make-up preparations. The results of the 2025 concentration of use survey conducted by the Council indicate that all reported concentrations of use are for rinse-off products; the maximum concentration of use has decreased to 0.00016% Boric Acid in shampoos (rinse-off) and bath soaps and body washes, and that the highest concentration of use for Sodium Borate increased slightly to 3.7% is skin cleansing products.

   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 5 draft tentative reports for consideration. Issue a tentative conclusion?

1. Butoxyethanol – TAR (Christina) – ***Dr. Belsito reports on day 2*** – At the June 2025 meeting, the Panel determined that the data were insufficient to support safety of this cosmetic ingredient. The additional data needs are:

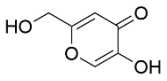


   - Maximum concentration of use in hair dye formulations
   - Maximum concentration of use in non-hair dye formulations

   Since the IDA, CIR has received an updated concentration of use survey from the Council. The survey found no uses for Butoxyethanol. No other data were received.

   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.

2. Kojic Acid – TAR (Christina) – ***Dr. Cohen reports on day 2*** – At the June 2025 meeting, the Panel determined that the data were insufficient to support safety of this cosmetic ingredient, and an IDA was issued identifying the additional data needs:

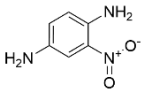


   - A margin of exposure (MOE) calculation for whole body exposure
   - An explanation as to why the European Union (EU) restricted use of Kojic Acid to the face and hands only

   Since the IDA, CIR has received two data submissions, one which came through the Council and the other that was directly received from the submitter, containing MOE calculations for whole body exposure to Kojic Acid and the rationale for the EU restrictions. The MOE values for whole body application were less than 100, indicating a potential for health risks when used at high levels of exposure. The concern of potential risk to human health when Kojic Acid is used at high levels is what prompted the EU to restrict the use of Kojic Acid to the face and hands only.

   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. 2-Nitro-*p*-Phenylenediamine – TAR (Christina) – ***Dr. Belsito reports on day 2*** – A report on the 2 original ingredients was reopened by the Panel in December 2024; however, at the June 2025 meeting, the Panel split 4-Nitro-*o*-Phenylenediamine into a separate report from 2-Nitro-*p*-Phenylenediamine, as the data from these 2 ingredients cannot be read across. Subsequently at that meeting, the Panel determined that the data were insufficient to support safety of 2-Nitro-*p*-Phenylenediamine as a hair dye ingredient. Accordingly, an IDA was issued identifying the following data needs; CIR has received no new data in response to this IDA:



   - Maximum concentration of use in hair dye formulations
   - A 90-d oral repeated dose study with a no-observable-adverse-effect level (NOAEL) that shows a dose-response relationship
   - Phototoxicity/photosensitization data

   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.

4. *Acacia senegal* – TAR (Thushara) – ***Dr. Cohen reports on day 2*** – In March 2025, the Panel rereviewed the safety data of these two ingredients, Acacia Senegal Gum and Acacia Senegal Gum Extract, and issued an IDA. The Panel identified the following data needs:

   - For both ingredients
     - UV absorption, if absorbed, phototoxicity/photosensitization data are needed
     - Ocular irritation data

- For Acacia Senegal Gum Extract
  - Composition/impurities
  - Method of manufacture
  - Irritation and sensitization data

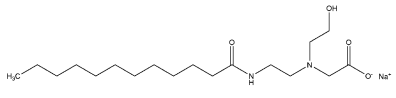
The following data were received in response to the IDA. This information has been included in this iteration of the report.

- Institute for In Vitro Sciences Inc. 2014. Tissue equivalent assay with EpiOcular™ cultures (1% Acacia Senegal gum in a mascara).
- MatTek Corporation. 2020. Ocular Irritation Protocol: Neat method (MTT ET-50).
- Anonymous. 2025. Information on Acacia Senegal Gum (UV absorption and ocular irritation).
- Reliance Clinical Testing Services, Inc. 2023. Four Week Safety-In-Use Test for Eye Area (Mascara with 3% Acacia Senegal Gum Extract).
- Institute for In Vitro Sciences, Inc. 2023. Topical Application Ocular Irritation Screening Assay Using EpiOcularTM Human Cell Construct (Mascara with 3% Acacia Senegal Gum Extract).
- Farcoderm. 2013. In Vitro Product Safety Study: In vitro evaluation of the eye irritation potential of cosmetic products (mascara containing 2.9% Acacia Senegal Gum).
- Farcoderm. 2013. Clinical test aimed at evaluating the tolerability and safety of a cosmetic product used around the eyes (mascara containing 2.9% Acacia Senegal Gum)
- Anonymous. 2025. Summary information: Eye irritation studies of a mascara containing 6% Acacia Senegal Gum.

Updated concentration of use data were also received and incorporated herein. According to a 2022 use survey, the maximum reported concentration of use was 26.7% Acacia Senegal Gum in other oral hygiene products; according to a 2025 survey, which used the new FDA cosmetic product categories under MoCRA, the maximum concentration of use is 4% Acacia Senegal Gum in mascaras and in eyelash and eyebrow preparations. The maximum reported concentration of use in oral products is now 2.9% in dentifrices.

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.

5. Fatty Amphocarboxylates – TR (Priya) – ***Dr. Belsito reports on day 2*** – The Panel reviewed the Revised Draft Report at the June 2024 meeting, and issued an IDA for the following data:



- Dermal absorption data
- DART data on Disodium Cocoamphodiacetate
- Further information regarding the composition and impurities of these ingredients as cosmetics (particularly percentage of actives in ingredients, fatty acid compositions, and degrees of esterification (e.g., how much of Sodium Cocoamphoacetate has 0, 1, or 2 acetate substitutions)
- Sensitization data on Sodium Lauroamphoacetate at maximum use concentration
- Sensitization data on Disodium Lauroamphodiacetate at maximum use concentration
- Any information (e.g., clarification on compositions) to support the use of the read-across sources previously suggested to Panel

In December 2024, the Panel decided to table the report following a request from the REACH Amphoacetates Consortium proposing the tabling of the assessment for the receipt of a prenatal developmental toxicity study performed in rabbits using C8-18 (diacetate form). Since the tabling of the report, the following data have been received (data have been incorporated into the report in highlighted text):

- HRIPT on a shampoo containing 5.25% Sodium Lauroamphoacetate (final test concentration contained 0.16% Sodium Lauroamphoacetate)

- HRIPT on a body soap containing 9.6% Sodium Cocoamphoacetate (final test concentration contained 0.096% Sodium Cocoamphoacetate)
- HRIPT on a facial cleanser containing 2.7% Sodium Lauroamphoacetate (final test concentration contained 0.27% Sodium Lauroamphoacetate)
- 4-wk in use assay on a product containing 2.7% Sodium Lauroamphoacetate
- HRIPT on a product containing 4.56% Disodium Lauroamphodiacetate (final test concentration contained 0.046% Disodium Lauroamphodiacetate)
- HRIPT on a product containing 2.8% Sodium Cocoamphoacetate (final test concentration contained 0.028% Sodium Cocoamphoacetate)
- HRIPT on a product containing 4.39% Sodium Lauroamphoacetate (final test concentration contained 0.044% Sodium Lauroamphoacetate)
- Composition information on Disodium Lauroamphodiacetate
- Concentration of use data updated in 2024
- Concentration of use data based on MoCRA categories

Also received were information that were sent to the Read-Across Working Group (RAWG) for discussion at this meeting. **Incorporation of the majority of this data into the report will depend on the outcome of the RAWG's deliberation**s. These data include the following:

- Prediction report on Amphoacetate C12 Diacetate 1
- Prediction report on Amphoacetate C12 Diacetate 2
- Prediction report on Amphoacetate C12 Monoacetate 1
- Prediction report on Amphoacetate C12 Monoacetate 2
- EU Alkylamphoacetates Consortium – OECD 414 Prenatal Developmental Toxicity Study of Amphoacetates C8-C18 by Oral Gavage in Time-Mated New Zealand White Rabbits
- Lavin Williams,DeSesso, and Richmond – Expert Opinion Regarding Impact of the Rabbit OECD 414 Study of Amphoacetates C8-C18 on Potential Need for Reproductive Toxicity Classification in Accordance with GHS and EU CLP
- Lavin Williams and DeSesso – Review of results from the OECD 414 Study in Rabbits to Assess Whether the Increase in Post-Implantation Loss at the Mid-Dose is Secondary to Maternal Toxicity
- EU Alkylamphoacetates Consortium – OECD 443 Extended One Generation Reproductive Study (including Cohort 1) of Amphoacetates C8-C18 (diacetate form) by Oral Gavage in Rats
- Charles River Laboratories - Analogue Approach for REACH Registration of Alkylamphoacetates version March 2025
- Bigorra, Amela, and Bonastre - Amphoteric Surfactants: Structure-Performance Correlation. Proceedings (Vol 2) of the 5th World Surfactants Conference
- DeSesso and Lavin Williams - Expert Review of Available Repeat-Dose and Developmental and Reproductive Toxicity (DART) Studies for Amphoacetates

Several submissions include expert opinions on the received DART studies. The Panel should assess whether these expert insights warrant inclusion in the report. If so, the Panel should specify which key points from these opinions should be incorporated and identify the appropriate section of the report for their inclusion.

In addition, it should be noted that 2024 RLD have been incorporated into this report. The number of uses for the majority of these ingredients are higher than what was reported in 2023 VCRP data. In addition, although new concentration of use data have been received since the last iteration of this report, the maximum leave-on use concentration has remained 5.4% (reported for Disodium Cocoamphodiacetate and Disodium Lauroamphodiacetate).

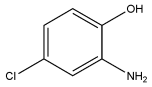
Of the 11 ingredients reviewed in this report, 4 (i.e., Disodium Cocoamphodiacetate, Disodium Cocoamphodipropionate, Sodium Cocoamphoacetate, and Sodium Cocoamphopropionate) have previously been reviewed by the Panel in a report published in 1990; the Panel concluded that these 4 ingredients are safe as used, as described in that report. Furthermore, these ingredients were re-reviewed in 2006, at which time the Panel reaffirmed the original conclusion (as published in 2008).

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 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.

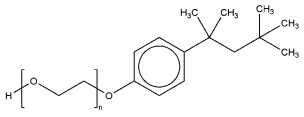
Draft Final Reports - There are 6 Draft Final Reports for consideration. Review these drafts, especially the rationale provided in the Discussion sections, and issue final reports, as appropriate.

1. 4-Chloro-2-Aminophenol – FAR (Christina) – ***Dr. Belsito reports on day 2*** – At the June 2025 meeting, the Panel issued a revised Tentative Amended Report for public comment with the conclusion that 4-Chloro-2-Aminophenol is unsafe for use as a hair dye ingredient. The Panel determined that while absorption data are lacking, it is likely that this aromatic amine will absorb to some extent. Positive genotoxicity results were observed, specifically in Ames tests, and bladder tumors were observed in an oral carcinogenicity study in rats.



   Since the June meeting, CIR has received no new data. No uses have been reported for this ingredient by the FDA RLD, FDA VCRP, or the Council. The Panel should carefully review the Abstract, Discussion, and Conclusion, and issue a Final Amended Report.

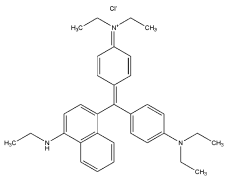
2. Octoxynols – FAR (Priya) – ***Dr. Cohen reports on day 2*** – At the March 2025 meeting, the Panel concluded that the 25 octoxynol ingredients reviewed in this report are safe in the present practices of use and concentration when formulated to be non-irritating, and a Tentative Amended Report was issued. Comments received from the Council on the Tentative Amended Report have been addressed; some of these comments require the Panel's response (as indicated in the included response document).



   It should be noted that these ingredients were previously reviewed in a report published in 2004. In that report, the Panel issued a conclusion stating that 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, and 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 $\leqslant$ 5% in leave on cosmetic products.

   According to updated concentration of use data, Octoxynol-9 may result in mucous membrane exposure as it is reported to be used in disposable wipes at 0.36%. The Panel should carefully review the Abstract, Discussion, and Conclusion, and issue a Final Amended Report.

3. Basic Blue 7 – FR (Christina) – ***Dr. Belsito reports on day 2*** – At the March 2025 meeting, the Panel concluded that the available data are insufficient to make a determination of safety for Basic Blue 7 under the intended conditions of use as a hair dye ingredient. The data required to come to a conclusion of safety for this hair dye ingredient are as follows:



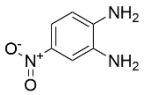
   - Chemical properties data
   - Method of manufacturing
   - Composition/impurities data
   - Concentration of use
   - Dermal absorption data or 28-day dermal toxicity data
     - If absorbed, additional data, including developmental and reproductive toxicity data are needed
   - Genotoxicity data

   Since that meeting, no new data have been received. Comments received on the Tentative Amended Report have been addressed. The Panel should carefully review the Abstract, Discussion, and Conclusion and issue a Final Report.

4. *Lactobacillus* Ferment ingredients – FR (Priya) – ***Dr. Cohen reports on day 2*** – At the June 2025 meeting, the Panel concluded that Lactobacillus Ferment, Lactobacillus Ferment Filtrate, Lactobacillus Ferment Lysate, Lactobacillus Ferment Lysate Filtrate are safe as used in cosmetics.

Since the Tentative Report was issued, CIR has received no new data. Comments and responses for the Draft and Tentative Reports have been addressed. The Panel should carefully review the Abstract, Discussion, and Conclusion, and issue a Final Report.

5. 4-Nitro-*o*-Phenylenediamine – FAR (Christina) – ***Dr. Belsito reports on day 2*** – At the June 2025 meeting, the Panel issued a Tentative Amended Report for public comment with the conclusion that 4-Nitro-*o*-Phenylenediamine is safe for use as an oxidative hair dye ingredient.



However, in both the original report conclusion from 1985 and the affirmation in the first re-review conducted in 2003, the Panel concluded that this ingredient is, "*safe as a hair dye ingredient at the current concentration of use;*" this prior conclusion was broader, including permanent and non-permanent uses (i.e., not limited to use as "an oxidative" hair dye). Accordingly, if the narrower conclusion (i.e., not concluding on non-oxidative uses) stated in the current Tentative Amended Report is to be kept, the Panel should explain the rationale for such in the Discussion section.

Since the June meeting, CIR has received no new data. Comments received from the Council prior to the June meeting on the Draft and Tentative Amended Reports have been addressed. The Panel should carefully review the Abstract, Discussion, and Conclusion, and issue a Final Amended Report.

6. *Nelumbo nucifera* – FR (Thushara) – ***Dr. Cohen reports on day 2*** – At the March 2025 meeting, the Panel issued a Tentative Report concluding that the available data are insufficient to make a determination of safety for all 14 *Nelumbo nucifera*-derived ingredients. The Panel determined that the requirements listed in the IDA remained unmet and reiterated that following data are needed to arrive at a conclusion.

- For all ingredients
  - Composition and impurities
  - Methods of manufacturing
  - 28-d dermal toxicity data
    - if positive, additional data may be needed (e.g., development and reproductive toxicity data).
  - Ultraviolet (UV) absorption data (as well as more detailed information about the previously submitted UV spectra)
    - if absorbed, phototoxicity/photosensitization data are needed (additional protocol details are needed for the previously-submitted studies)
- For the callus-, phytoplacenta-, stamen-, and seed-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 flower- and whole plant-derived ingredients
  - Developmental and reproductive toxicity data
- For all except flower- and leaf-derived ingredients
  - In vitro ocular irritation data

In response to the IDA the following data were received and incorporated into the report:

- Concentration of use by FDA product category: *Nelumbo nucifera*-derived ingredients, Correction
- Clinical safety evaluation study - repeated insult patch test of Nelumbo Nucifera Callus Culture Extract
- Summary Information- HRIPT data for a serum containing 0.001% Nelumbo Nucifera Germ Extract
- Safety data of Nelumbo Nucifera Germ Extract short-time exposure (STE) test (OECD TG 491) (Raw material containing 1% Nelumbo Nucifera Germ Extract)
- Summary information- UV absorption of Nelumbo Nucifera Germ Extracts in water and butylene glycol. Corresponding UV spectra (with absorption maxima and solvents used) for the data submitted on January 2, 2025.

The Council has also suggested clarifying as to why the Panel has not used the reported food use of *Nelumbo nucifera* plant or parts to mitigate potential systemic toxicity concerns, which is consistent with the strategy used in previous CIR reports involving edible plants. The Council requests that the

Discussion include an explanation as to why the reported food use is not sufficient to address systemic toxicity concerns for of the flower-, germ-, leaf-, and root-derived ingredients.

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

Abbreviated Re-review (i.e., re-review proposal) – There is 1 re-review document. Because it has at least been 15 years since the previous review was published, in accordance with CIR Procedures, the Panel is only being asked if the reports should be reopened.

1. Fossil Waxes – RR (Temima) – ***Dr. Cohen reports on day 2*** - The Panel first published a review of the safety of Fossil and Synthetic Waxes in 1984. The Panel concluded these 8 ingredients are safe in cosmetics under the present practices of concentration and use. The Panel previously considered a re-review of this report and re-affirmed the 1984 conclusion, as published in 2005.

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

Read-Across Working-Group (RAWG) meeting item. The RAWG should confer on the following item; this item will then be reviewed by the breakout teams and the Full Panel at this meeting, with RAWG support.

1. Fatty Amphocarboxylates – RAWG (Priya/Jinqiu) – ***RAWG members support the breakout sessions on day 1*** - The RAWG is asked to convene at this meeting on September 8th, immediately following the welcome and prior to the beginning of the Panel Team Breakouts. In addition to the RAWG deliberations on this ingredient group, the breakout teams and full Panel will be considering advancement of this report at this same meeting.

   At the June 2024 meeting, the Panel issued an IDA on fatty amphocarboxylates, requesting the following data:

   - Dermal absorption data
   - Developmental and reproductive toxicity data on Disodium Cocoamphodiacetate
   - Further information regarding the composition and impurities of these ingredients as used in cosmetics (particularly percentage of actives in ingredients, fatty acid compositions, and degrees of esterification (e.g., how much of Sodium Cocoamphoacetate has 0, 1, or 2 acetate substitutions)
   - Sensitization data on Sodium Lauroamphoacetate and Disodium Lauroamphodiacetate at maximum use concentrations
   - Any information (e.g., clarifications on compositions) to support the use of previously suggested read-across sources

   Since the last review of these ingredients, additional documentation related to Fatty Amphocarboxylates was received (data_FattyAmphocarboxylates_092025 in this pdf; please note that these data are also part of the Fatty Amphoacetate report pdf so that you have them readily available when reviewing the document named data10_FattyAmphocarboxylates_092025 in that pdf). These materials include the following:

   - EU Alkylamphoacetates Consortium. 2025. OECD 414 Prenatal Developmental Toxicity Study of Amphoacetates C8-C18 by Oral Gavage in Time-Mated New Zealand White Rabbits.
   - Lavin Williams A, DeSesso JM, and Richmond E. 2024. Expert Opinion Regarding Impact of the Rabbit OECD 414 Study of Amphoacetates C8-C18 on Potential Need for Reproductive Toxicity Classification in Accordance with GHS and EU CLP.
   - Lavin Williams A and DeSesso JM. 2024. Review of results from the OECD 414 Study in Rabbits to Assess Whether the Increase in Post-Implantation Loss at the Mid-Dose is Secondary to Maternal Toxicity.
   - EU Alkylamphoacetates Consortium. 2025. OECD 443 Extended One Generation Reproductive Study (including Cohort 1) of Amphoacetates C8-C18 (diacetate form) by Oral Gavage in Rats.

- Charles River Laboratories. 2025. Analogue Approach for REACH Registration of Alkylamphoacetates version March 2025.
- Bigorra J, Amela C, Bonastre N, et al. 2000. Amphoteric Surfactants: Structure-Performance Correlation. Proceedings (Vol 2) of the 5th World Surfactants Conference.
- DeSesso JM and Lavin Williams A. 2023. Expert Review of Available Repeat-Dose and Developmental and Reproductive Toxicity (DART) Studies for Amphoacetates.

Two new DART studies were provided (on "amphoacetates C8-C18") in response to the Panel's IDA for developmental and reproductive toxicity data on Disodium Cocoamphodiacetate. These include a prenatal developmental toxicity study in rabbits (OECD TG 414) and an extended one-generation reproductive toxicity study in rats (OECD TG 443). The rabbit study identified maternal toxicity at 175 and 350 mg/kg/d, with increases in resorptions and post-implantation loss observed at 175 mg/kg/d. The NOAEL for both maternal and developmental toxicity was determined to be 75 mg/kg/d. Expert reviewers from Exponent concluded that the increased early resorptions were likely secondary to maternal toxicity and did not warrant self-classification for adverse effects on development in accordance with GHS and EU CLP. The rats study further supported the absence of reproductive toxicity: no adverse effects on reproductive performance, fertility, or developmental endpoints–including offspring viability, growth, sexual maturation, organ weights, and histopathology–were observed at doses up to the highest level tested. An NOAEL of 1000 mg/kg/d was established for developmental and reproductive toxicity. The updated Charles River document (March 2025), titled Analogue Approach for REACH Registration of Alkylamphoacetates reflects these new findings. The RAWG should determine if inclusion of these 2 studies is appropriate based off of the test substance used (amphoacetates C8-C18). Experts from Exponent's broader review of available repeat-dose and DART studies for amphoacetates found no evidence of adverse effects on fertility, reproductive organs, or fetal development at non-maternally toxic dose of the four commercial amphoacetates surfactant products tested (Dehyton® DC (INCI name, Disodium Cocoamphodiacetate); Miranol Ultra C32 (INCI name, Sodium Cocoamphoacetate); PC-2020-926 (no INCI name); and Sodium Lauroamphoacetate), with exposures up to 1000 mg/kg bw/d.

Additionally, the submission included a technical paper titled *Amphoteric Surfactants: Structure–Performance Correlation*, which was provided in partial response to the IDA for further information on ingredient composition and impurities. This paper presents a structural-performance analysis of amphoacetate surfactants using NMR-based techniques, identifying monoacetate, diacetate, and quaternized species formed under varying synthetic and hydrolysis conditions. It indicates that the chemical structure and functional properties of these surfactants are influenced by multiple factors, including the type of amine (e.g., AEEA), the alkylating agent, and most critically, the source of fatty acid (e.g., coconut oil, hydrogenated coconut oil, lauric acid). These variables affect the distribution of molecular species and, consequently, alter key performance attributes such as surface activity and foaming. The paper also describes the formation of substituted imidazolines and their subsequent ring-opening reactions (amidation and carboxymethylation), which depend on reaction parameters like pH, time, and molar ratios.

The RAWG has reviewed data regarding read-across for this ingredient group at previous meetings. For the Panel's recollection, links to these meetings have been provided below:

- June 2023 Wave 2 (https://www.cir-safety.org/sites/default/files/w2_FA_1.pdf)
- June 2024 Wave 2 (https://www.cir-safety.org/sites/default/files/Data%20Supplement_Wave%202_062024.pdf), starting on p 4

The RAWG is requested to review the new submissions, and to reassess the appropriateness of the proposed read-across strategies in light of the additional source materials and external expert evaluations. The members of the RAWG are requested to support the breakout teams during their sessions.

Administrative Items - there are 3 administrative items.

Brown Algae – Petition to Reconsider - The Panel is asked to reconsider the conclusion in light of newly submitted data.

1. Cladosiphon Novae-Caledoniae Extract – Admin – (Priya) – ***Dr. Belsito reports on day 2*** – In September 2019, the Panel issued a final report on 82 brown algae-derived ingredients, with the conclusion that

68 of these ingredients were safe in the present practices of use and concentration. The Panel also concluded that the available data were insufficient to support a conclusion of safety for the remaining 14 ingredients. Since then, relevant data were received on Cladosiphon Novae-Caledoniae Extract (a brown algae-derived ingredient that was previously found insufficient).

Accordingly, the Panel is being asked if this report should be re-opened for the addition of this new data and for a potential change to the conclusion. **In other words, considering this submission, are the data now sufficient to conclude on the safety of Cladosiphon Novae-Caledoniae Extract as used in cosmetics?** If so, CIR staff will issue a revised report with such a conclusion.

Resource Document – The Panel is asked to provide edits prior to submission to the journal.

2. Hair Dye Epi – Admin (Jinqiu) – ***Dr. Cohen reports on day 2*** – At the June meeting, the Panel reviewed a revised draft of the Hair Dye Epidemiology Resource Document and acknowledged the significant improvements, including the incorporation of newly published studies and enhanced clarity. The Panel reiterated the importance of continued monitoring of emerging epidemiological data and reaffirmed the need for well-designed studies with adequate statistical power to robustly evaluate potential differences by race and tumor subtype. To increase its scientific impact and public accessibility, the Panel recommended submitting the document to a peer-reviewed journal with high impact factors, e.g., *Critical Reviews in Toxicology*, following appropriate formatting, editorial revisions, and individual review by each Panel member. Accordingly, the Panel is requested to review this reformatted draft and determine whether it is ready for submission to *Critical Reviews in Toxicology*.

2026 Draft Final Priorities List

3. Priorities – Admin (Bart) – ***Dr. Belsito reports on day 2*** - There are 16 reports docketed, covering 36 ingredients, on the 2026 Draft Final Priorities List. Three previously proposed ingredient reports (from the 2026 Draft Priorities in March), have been deleted for either inclusion in other reports or lack of relevant cosmetic use; ***three new ingredient reports are therefore now proposed herein***. Additionally, the Hair Color Technical Committee nominated Basic Orange 31 for inclusion as the annual hair ingredient. Reports previously prioritized and on the CIR docket, as well as an extensive number of re-reviews of previous assessments, will supplement the total number of reports/ingredients to be assessed in 2026, and beyond. The Panel should take note of the new additions to the list, changes to groupings, and finalize next year's priorities.

Full Panel Meeting

The Panel will consider the 6 reports to potentially issue 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 the hair dye epi paper, and a majority vote should be reached in each case for the algae petition and the priorities.

Please remember, the meeting starts at 9:30 AM EST on day 1 and day 2.

Looking forward to seeing you all ***virtually***!

Agenda
174th Meeting of the Expert Panel for Cosmetic Ingredient Safety
September 8-9, 2025

Virtual via Microsoft Teams

Monday, September 8, 2025

9:30 AM EST	**WELCOME TO THE 174th EXPERT PANEL TEAM MEETINGS**	**Drs. Bergfeld/Heldreth**
9:45 AM	**READ-ACROSS WORKING GROUP (RAWG)**	**Dr. Rettie**
10:45AM – 12 PM	**TEAM MEETINGS**	**Drs. Belsito/Cohen**
12 PM – 1 PM	**Lunch break**	
1 PM - 5 PM	**TEAM MEETINGS (con't)**	**Drs. Belsito/Cohen**

Dr. Belsito's Team*

FR (CB)	Basic Blue 7
FAR (CB)	4-Chloro-2-Aminophenol
FAR (CB)	4-Nitro-*o*-Phenylenediamine
TAR (CB)	2-Nitro-*p*-Phenylenediamine
TAR (CB)	Butoxyethanol
TAR (CB)	Kojic Acid
DAR (TN)	Sodium Borate
RR (TN)	Fossil Waxes
FR (TD)	*Nelumbo nucifera*
TAR (TD)	*Acacia senegal*
Admin (MF|BH)	Priorities
Admin (JZ)	Hair Dye Epi
TR (PF)	Fatty Amphocarboxylates
FAR (PF)	Octoxynols
FR (PF)	*Lactobacillus* Ferment
DAR (PF)	Alkonium Chlorides
Admin (PF)	Brown Algae

Dr. Cohen's Team

TR (PF)	Fatty Amphocarboxylates
FAR (PF)	Octoxynols
FR (PF)	*Lactobacillus* Ferment
DAR (PF)	Alkonium Chlorides
Admin (PF)	Brown Algae
Admin (BH|MF)	Priorities
Admin (JZ)	Hair Dye Epi
FR (TD)	*Nelumbo nucifera*
TAR (TD)	*Acacia senegal*
DAR (TN)	Sodium Borate
RR (TN)	Fossil Waxes
FR (CB)	Basic Blue 7
FAR (CB)	4-Chloro-2-Aminophenol
FAR (CB)	4-Nitro-*o*-Phenylenediamine
TAR (CB)	2-Nitro-*p*-Phenylenediamine
TAR (CB)	Butoxyethanol
TAR (CB)	Kojic Acid

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

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

BH: Bart Heldreth || MF: Monice Fiume || CB: Christina Burnett || PF: Priya Ferguson || TD: Thushara Diyabalanage || TN: Temima Nguyen || JZ: Jinqiu Zhu

*Team moves to the breakout room. For the virtual component of this meeting, that is a separate MS Teams meeting room.

Cosmetic Ingredient Review

Tuesday, September 9, 2025			
9:30 AM EST	**WELCOME TO THE 174th FULL EXPERT PANEL MEETING**		**Dr. Bergfeld**
9:40 AM	Admin **MINUTES OF THE JUNE 2025 EXPERT PANEL MEETING**		**Dr. Bergfeld**
9:45 AM	**DIRECTOR'S REPORT**		**Dr. Heldreth**
10:00 AM	**FINAL REPORTS, REPORTS ADVANCING TO THE NEXT LEVEL, OTHER ITEMS**		
	Final Reports		
	FAR (CB)	4-Chloro-2-Aminophenol – ***Dr. Belsito reports***	
	FAR (PF)	Octoxynols – ***Dr. Cohen reports***	
	FR (CB)	Basic Blue 7 – ***Dr. Belsito reports***	
	FR (PF)	*Lactobacillus* Ferment ingredients – ***Dr. Cohen reports***	
	FAR (CB)	4-Nitro-*o*-Phenylenediamine – ***Dr. Belsito reports***	
	FR (TD)	*Nelumbo nucifera-derived ingredients* **– *Dr. Cohen reports***	
	Reports Advancing		
	TAR (CB)	Butoxyethanol – ***Dr. Belsito reports***	
	TAR (CB)	Kojic Acid – ***Dr. Cohen reports***	
	TAR (CB)	2-Nitro-*p*-Phenylenediamine – ***Dr. Belsito reports***	
	TAR (TD)	*Acacia senegal*-derived ingredients – ***Dr. Cohen reports***	
	TR (PF)	Fatty Amphocarboxylates – ***Dr. Belsito reports***	
	DAR (PF)	Alkonium Chlorides and Bromides – ***Dr. Cohen reports***	
	DAR (TN)	Sodium Borate – ***Dr. Belsito reports***	
	Other Items		
	RR (TN)	Fossil Waxes – ***Dr. Cohen reports***	
	Admin (PF)	Brown Algae – ***Dr. Belsito reports***	
	Admin (JZ)	Hair Dye Epi Resource Paper – ***Dr. Cohen reports***	
	Admin (BH)	2026 Final Priorities – ***Dr. Belsito reports***	

ADJOURN – – *The next will be held virtually on Thursday and Friday, December 4-5, 2025. Please check the CIR website for details as the meeting approaches, and to register to attend.*

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

BH: Bart Heldreth || MF: Monice Fiume || CB: Christina Burnett || PF: Priya Ferguson || TD: Thushara Diyabalanage || TN: Temima Nguyen || JZ: Jinqiu Zhu

ONE HUNDRED SEVENTY-THIRD MEETING

OF THE

EXPERT PANEL FOR COSMETIC INGREDIENT SAFETY

June 9-10, 2025

Westin Georgetown
2350 M Street NW
Washington DC, 20037

Expert Panel Members

Wilma F. Bergfeld, M.D., Chairperson

Donald V. Belsito, M.D., Teamleader

David E. Cohen, M.D., Teamleader

Samuel M. Cohen, M.D., Ph.D.

Curtis D. Klaassen, Ph.D.

Allan E. Rettie, Ph.D., RAWG leader

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 Ferguson, MS - Senior Scientific Analyst

Temima Nguyen, MS - Scientific Analyst

Thushara Diyabalanage, PhD - Scientific Analyst

Information Services
Kevin Stone Fries, MLS - Information Services Manager

Other In-Person Attendees

Name	Organization
Jay Ansell	EAS Consulting
Jennifer Ator	ToxServices
Don Bjerke	Procter & Gamble
Joe Dages	Steptoe LLP
Jacob Dayan	Dr. Nava Dayan Ltd
Nava Dayan	Dr. Nava Dayan Ltd
Carol Eisenmann	Personal Care Products Council
Linda Giles	Transcription Etc.
Jeff Nicoloi	J Nicoloi Law
Kim Norman	Personal Care Products Council
Elizabeth Petro	FDA
Allison Schafer	Procter & Gamble
Maged Sharaf	EAS Consulting
Nick Skoulis	Steptoe LLP

Other Virtual Meeting Attendees

Name	Organization
Ayodele Ajayi	June Jacobs Labs
Xylia Ajose	FDA
Nan An	FDA
Monica Autiero	ToxMinds
Jacob Howard-Robinson	Synergy Labs
Miao Li	FDA
Christin Liu	
Sanghamitra Mishra	ToxMinds
Sarvin Moghaddam	FDA
Lauren Nardella	HBW Insight
Nina Pendergraph	Intertek
Thomas Petry	ToxMinds
Carol Pratt	Lee & Hayes
Yasuko Shibata	
Brenda Shinyashiki	Edgewell Personal Care
Dustin Strickland	Synergy Labs
Liz Toledo	Rodan + Fields
Patra Volarath	FDA
Zemin Wang	FDA
Andrew Warren	Estée Lauder
Teresa Washington	FDA
Austin Whisnant	Synergy Labs

CHAIRPERSON'S OPENING REMARKS

Dr. Bergfeld welcomed the attendees to the 173rd meeting of the Expert Panel for Cosmetic Ingredient Safety. Dr. Bergfeld thanked the speakers that gave presentations on the first day of the meeting: Dr. Elizabth Petro from the FDA, Dr. Jennifer Ator from ToxServices, and Ms. Sanghamitra Mishra and Dr. Thomas Petry from ToxMinds.

The Panel reviewed 11 ingredient reports at this meeting, including 4 finals, 2 tentative reports, 5 draft reports, and 5 re-review summaries. The Panel also reviewed a strategy memo on the Phthalates, and the hair dye epidemiology resource paper, as well as Wave 2 data and comments from the CIR Science and Support Committee and Women's Voice for the Earth.

Dr. Bergfeld thanked the CIR staff, the Council, the CIR Science and Support Committee, and Women's Voice for the Earth for all of their efforts in preparing for this meeting.

APPROVAL OF MINUTES

The minutes of the March 13-14, 2024 (172nd) 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 Dr. Don Bjerke, for whom this was the last meeting, after years of dutiful service to the Panel as the Chair of the CIR Science and Support Committee.

This meeting was the first for new CIR Staff member, Temima Nguyen, who joined CIR just a few weeks prior as a Scientific Analyst. Temima has a Bachelor of Science in Pharmaceutical Sciences from the University of Toledo and a Master of Science in Cosmetic Science from the University of Cincinnati. Prior to CIR, she worked as a cosmetic chemist (hair colors) and a regulatory specialist for food, dietary supplements, and cosmetic labeling. We greatly look forward to working with her.

FINAL SAFETY ASSESSMENTS

Tetrabromophenol Blue

The Panel issued a Final Report 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 an oxidative and direct 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 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.

Propylene Carbonate

The Panel reviewed the available data and issued a Final Amended Report with the conclusion that Propylene Carbonate is safe in cosmetics in the present practices of use and concentration described in the safety assessment, when formulated to be non-irritating. According to 2023 FDA VCRP data, Propylene Carbonate is reported to be used in 882 total formulations. RLD data collected in 2024 indicate that Propylene Carbonate is used in 13,340 total formulations. This ingredient is used at up to 17.9% in leave-on products (according to a 2022 concentration of use survey conducted by the Council).

Paeonia suffruticosa-derived ingredients

The Panel reviewed the available data and issued a Final Report concluding that Paeonia Suffruticosa Seed Oil, Paeonia Suffruticosa Root Extract, and Paeonia Suffruticosa (Tree Peony) Root Bark Extract are safe in cosmetics in the present practices of use and concentration described in the safety assessment. The Panel also concluded that the available data are insufficient to make a determination of safety for Paeonia Suffruticosa Bark Extract and Paeonia Suffruticosa Extract. Considering newly received information, the Panel determined that the ingredients named Paeonia Suffruticosa (Tree Peony) Root Bark Extract and Paeonia Suffruticosa Root Bark Extract are equivalent. Additionally, this information supported the common reference of these ingredients to "root bark cortex" or "moutan cortex."

TENTATIVE SAFETY ASSESSMENTS

4-Chloro-2-Aminophenol

The Panel issued a revised Tentative Amended Report for public comment with the conclusion that 4-Chloro-2-Aminophenol is unsafe for use as a hair dye ingredient. The Panel determined that, while the absorption data is lacking, it is likely that this aromatic amine will absorb to some extent. Positive genotoxicity results were observed, specifically in Ames tests, and bladder tumors were observed in an oral carcinogenicity study in rats.

4-Nitro-*o*-Phenylenediamine

The Panel issued a Tentative Amended Report for public comment with the conclusion that 4-Nitro-*o*-Phenylenediamine is safe for use as an oxidative hair dye ingredient in the present practices of use and concentration described in the safety assessment.

4-Nitro-*o*-Phenylendiamine is reported to function as an 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 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.

***Lactobacillus* Ferment Ingredients**

The Panel reviewed the report on Lactobacillus Ferment, Lactobacillus Ferment Lysate, Lactobacillus Ferment Lysate Filtrate, and Lactobacillus Ferment Filtrate, and issued a Tentative Report for public comment with the conclusion that these ingredients are safe in cosmetics in the present practices of use and concentration described in the safety assessment. The Panel noted that these ingredients may have a skin lightening effect; however, the Panel noted that skin lightening is considered a drug effect and should not occur during the use of cosmetic products. In addition, concern for this effect was further mitigated due to the Panel's knowledge of the mechanism of action (i.e., inhibition of tyrosinase activity) and their clinical experience. However, formulators should only use these ingredients in products in a manner that does not cause depigmentation.

According to 2023 VCRP and 2024 RLD data, Lactobacillus Ferment is reported to have the highest number of uses among the four ingredients reviewed in this report (it is used in 266 and 2106 formulations, respectively). Results of a 2025 concentration of use survey conducted by Council indicate that Lactobacillus Ferment also has the highest concentration of use in leave-on formulations; it is reported to be used at up to 5.6% in face and neck products and in "other" skin care products.

2-Bromo-2-Nitropropane-1,3-Diol

The Panel reviewed the available data and issued a Tentative Amended Report concluding that 2-Bromo-2-Nitropropane-1,3-Diol is safe in cosmetics in the present practices of use and concentration described in the safety assessment. The Panel noted that this ingredient may both act as a formaldehyde-releaser and participate in the formation of N-nitrosamines. Based on the low maximum concentration of use of 2-Bromo-2-Nitropropane-1,3-Diol in cosmetics, along with the low amount of formaldehyde that could be potentially be released from this ingredient, concerns about this ingredient as a formaldehyde releaser were mitigated; specifically, the Panel determined that the potential amount of formaldehyde resulting from the cosmetic use of this ingredient would be below the level they considered safe in their previous safety assessment of formaldehyde as a cosmetic ingredient. The Panel cautions that this ingredient should not be used in cosmetic products in which N-nitroso compounds can be formed.

RLD submitted in 2024 showed that 2-Bromo-2-Nitropropane-1,3-Diol is used in 167 cosmetic formulations. The highest use category was hair preparations (non-coloring; 64 total uses). According to the results of Council surveys that were submitted, the maximum reported concentration of use is 0.05% (as reported in 2023 for leave-on skin cleansing hand wipes and eye makeup removers, and as reported in 2025 for disposable wipes); in 2003, the maximum reported concentration of use was 0.1%.

Cocoyl Hydrolyzed Collagens

The Panel reviewed the available data and issued a Tentative Amended Report concluding that Potassium Cocoyl Hydrolyzed Collagen, TEA-Cocoyl Hydrolyzed Collagen, Cocoyl Hydrolyzed Collagen, and Sodium Cocoyl Hydrolyzed Collagen are safe in cosmetics in the present practices of use and concentration described in the safety assessment. Insufficiencies noted in a prior IDA were considered met by responsive data submissions. The Panel noted that current concentration of use data were not reported for Cocoyl Hydrolyzed Collagen, the ingredient in this report which has the highest reported frequency of use; accordingly, receipt of maximum concentration of use data on this ingredient would help inform this safety assessment. The Panel also noted that the paucity of systemic toxicity data available for these ingredients was mitigated by the low potential for dermal absorption.

The Panel was concerned with the risks inherent in using animal-derived ingredients, namely the transmission of infectious agents and biologically-derived impurities (e.g., nucleic acids, proteins, endotoxins). The Panel stressed that these ingredients must be free of detectible pathogenic viruses, infectious agents and/or biologically-derived impurities. Additionally, the Panel cautioned that TEA-Cocoyl Hydrolyzed Collagen should not be used in cosmetic products in which N-nitroso compounds can be formed**.**

INSUFFICIENT DATA ANNOUNCEMENTS (IDA)

2-Nitro-*p*-Phenylenediamine

The Panel issued an IDA for 2-Nitro-*p*-Phenylenediamine. The following information is required to determine the safety of this ingredient:

- Maximum concentration of use in hair dye formulations
- A 90-d oral repeated dose study with a NOAEL that shows a dose-response relationship
- Phototoxicity/photosensitization data

Pyrogallol

The Panel issued a second IDA for Pyrogallol. The additional data needed to determine safety for this ingredient are:

- Maximum concentration of use
- Genotoxicity studies, with metabolic activation, that test for damage to DNA adducts
- Dermal irritation and sensitization data at maximum concentration of use for non-hair dye uses
- Clarification on the type of use around the eyes
- Ocular irritation data at maximum concentration of use for products used around the eyes

Dimer Dilinoleates

The Panel issued an IDA for the following 7 dimer dilinoleate ingredients:

Bis-Behenyl/Isostearyl/Phytosteryl Dimer Dilinoleyl Dimer Dilinoleate
Bis-Behenyl/Phytosteryl Dimer Dilinoleate
Dimer Dilinoleyl Dimer Dilinoleate
Octyldodecyl/PPG-3 Myristyl Ether Dimer Dilinoleate
Phytosteryl/Isostearyl/Cetyl/Stearyl/Behenyl Dimer Dilinoleate
Phytosteryl Isostearyl Dimer Dilinoleate
Stearyl/PPG-3 Myristyl Ether Dimer Dilinoleate

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

- Structures for all ingredients
- Method of manufacturing for all ingredients
- Impurities/composition data for all ingredients
- Repeated oral-dose toxicity data for Dimer Dilinoleyl Dimer Dilinoleate at maximum concentrations of use
- DART data
- Ocular irritation data
- Dermal irritation and sensitization data at maximum concentration of use for Octyldodecyl/PPG-3 Myristyl Ether Dimer Dilinoleate and Stearyl/PPG-3 Myristyl Ether Dimer Dilinoleate

Oxyquinoline and Oxyquinoline Sulfate

The Panel reviewed the Draft Amended Report on Oxyquinoline and Oxyquinoline Sulfate and issued an IDA. The data needs include the following:

- Impurities data on Oxyquinoline
- Phototoxicity data on Oxyquinoline
- Maximum concentration of use data on Oxyquinoline
- Dermal absorption data on Oxyquinoline
- DART data, including an NOAEL on Oxyquinoline (suitable for margin of exposure calculation)
- Clarification on the type of use around the eyes

The Panel also requested clarification regarding the basis of the decision on these ingredients, as imposed by the EU. According to the EU, Oxyquinoline and Oxyquinoline Sulfate may be used as a stabilizer for hydrogen peroxide in rinse-off hair products at a maximum concentration of 0.3% (as base). Also according to the EU, these ingredients may be used as a stabilizer for hydrogen peroxide in leave-on hair products at a maximum concentration of 0.03% (As base).

Furthermore, the Panel requested clarification on the reported use of these ingredients in eyelash and eyebrow dyes. According to 2024 RLD data, Oxyquinoline Sulfate is reported to be used in 2 eyelash and eyebrow preparation (primers, conditioners, serums, fortifiers). Given that these ingredients are used as stabilizers in hydrogen peroxide, the Panel was concerned that these 2 eyelash and eyebrow preparations were miscategorized, and may instead be eyelash and eyebrow dyes.

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 5 re-review summaries, for which they had previously chosen not to reopen the reports. The Panel reaffirmed the conclusion reached in 4 of these safety assessments, and issued a new conclusion for 1 (following an amendment to the Procedures that allows for the conclusion recategorization of a report comprising ingredients not in current use). A re-review summary for each of these safety assessments was approved by the Panel at this meeting.

1. Glyceryl Isostearates and Glyceryl Stearate/Acetate - 2 ingredients, original conclusion reaffirmed
2. Glyceryl Collagenate, Glyceryl Sesquioleate, Glyceryl/Sorbitol Oleate/Hydroxystearate, Glyceryl Stearate/Maleate, and Glyceryl Thiopropionate – 5 ingredients, conclusion transmuted to use not supported
3. Beeswax, Copernica Cerifera (Carnauba) Wax, Euphorbia Cerifera (Candelilla) Wax, and Rhus Succedanea Fruit Wax - 4 ingredients, original conclusion reaffirmed
4. Diisopropanolamine, Triisopropanolamine, Isopropanolamines, and Mixed Isopropanolamines – 4 ingredients, original conclusion reaffirmed
5. L-Ascorbic Acid, Calcium Ascorbate, Magnesium Ascorbate, Magnesium Ascorbyl Phosphate, Sodium Ascorbate, and Sodium Ascorbyl Phosphate – 6 ingredients, original conclusion reaffirmed

OTHER ITEMS & DOCUMENTS

Presentations (slides available on the meeting page)

FDA's Views on Cosmetics vs. Drugs – Dr. Elizabeth Petro, Branch Chief for Cosmetics Regulatory Activities Branch at the US FDA
Dr. Petro reviewed how the FDA considers cosmetic use versus drug use in consumer products.

Application of Current Read-Across Methodologies to the Safety Assessment of a Cosmetic Ingredient – Dr. Jennifer Ator, ToxServices
Dr. Ator reviewed frameworks on read-across and a read-across approach used for isopropyl cloprostenate in cosmetic eyelash serums.

New Data Supporting the Use of Read-Across in the Safety Assessment of DDDE as a Cosmetic Ingredient – Ms. Sanghamitra Mishra and Dr. Thomas Petry, ToxMinds
Ms. Mishra and Dr. Petry reviewed new data for read-across to use in the safety assessment of ethyl tafluprostamide (DDDE).

Strategy Memo - Phthalates

Dibutyl Phthalate was placed on the 2024 Priorities List following nomination by the FDA for cause due to restrictions imposed on uses of plasticizers in food contact applications. The Panel first published the Final Report of the Safety Assessment of Dibutyl Phthalate, Dimethyl Phthalate, and Diethyl Phthalate in 1985, and concluded that these ingredients are safe for topical application in the present practices of use and concentration in cosmetics. Upon re-review in 2002, the Panel reaffirmed the original conclusion, as published in 2005. In December 2012, the Panel deliberated on studies separately concerning endocrine disruption and diabetes, and Dibutyl Phthalate, Diethyl Phthalate, Dimethyl Phthalate, and Butyl Benzyl Phthalate; however, the Panel chose not to re-open the safety assessment of these ingredients and published their discussion as a re-review summary in 2017.

In a strategy memo, the Panel was asked,

- Does the Panel, or any other stakeholder, have a particular expert in these areas they would like to invite to give a presentation on these DART and endocrine studies?
    - The Panel responded in the affirmative and provided potential experts to invite.
- Does the Panel support the idea of having Dimethyl Phthalate in a separate re-review proposal document or would the Panel prefer that this ingredient stay in the safety assessment with Dibutyl Phthalate and Diethyl Phthalate?
    - The Panel determined to keep these ingredients together in one report.

Hair Dye Epidemiology Resource Document

The Panel reviewed the revised draft of the Hair Dye Epidemiology Resource Document and commended the improvements, including the incorporation of newly published studies and enhanced clarity. The Panel reaffirmed the importance of ongoing surveillance of emerging epidemiological data and discussed the necessity of well-designed studies with adequate statistical power to robustly evaluate potential differences by race and tumor subtype. In addition, the Panel discussed inconsistencies observed across subpopulations and noted the lack of reproducibility in follow-up studies. The Panel emphasized that, as a living resource, the document's conclusions will be periodically reassessed in light of new scientific evidence. To broaden the document's impact and increase public accessibility, the Panel recommended submitting it to a peer-reviewed journal, following appropriate formatting, editorial revisions, and individual review by each Panel member.

RAWG: 2026 Draft Priorities – clustering/groupings & Prostaglandins – read-across discussion

The Read-Across Working Group (RAWG) convened to discuss both the clustering/grouping of ingredients on the 2026 Draft Priorities and the utilization of read-across in evaluating the safety of 2 prostaglandin ingredients. The members of the RAWG reviewed the available information about the designated ingredients therein. The RAWG will prepare and submit draft recommendations for consideration by the entire Expert Panel to be considered at a future meeting.