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EXPERT PANEL MEETING

June 9-10, 2025

Cosmetic Ingredient Review

Commitment & Credibility since 1976

MEMORANDUM

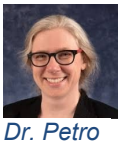
To: The Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Bart Heldreth, Ph.D., Executive Director, Cosmetic Ingredient Review
Subject: 173rd Meeting of the Panel — Monday and Tuesday, June 9th – 10th, 2025
Date: May 16th, 2025

Welcome to the second Panel Meeting of 2025! The agenda and accompanying materials for the 173rd Expert Panel Meeting, to be held on June 9th – 10th, 2025, are now available. ***The location is different from the one in March*** – and it is in-person at the Westin Georgetown, 2350 M Street, 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/173rd-expert-panel-meeting

The meeting agenda includes the consideration of 11 reports advancing in the review process, including 4 draft final reports, 2 draft tentative reports, and 5 draft reports (3 of which are re-opened reviews). Also on the agenda for the 1st day, is a meeting of the Read-Across Working-Group (RAWG); the RAWG is asked to convene and consider the use of read-across strategies and data gaps, with regard to the Prostaglandins report, and to also consider the groupings of ingredients in the Draft 2026 Priorities. The RAWG will convene and deliberate on these matters on June 9th, prior to the Panel Team Breakouts. ***At this meeting, these 2 matters, Prostaglandins and Priorities, are proposed for RAWG analysis only, and are not on the agenda for further discussion during the Team meetings on Day 1 or the Full Panel session on the 2nd day (June 10th).***

There are also 5 rereview summaries and 2 administrative items. Christina has prepared a Phthalates strategy memo and Jinqiu has prepared a new iteration of the Hair Dye Epidemiology Resource Document, for Panel consideration.

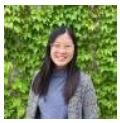

Dr. Petro

Following introductions, first on our agenda for June 9th, however, are 2 presentations. The first talk will be presented by Dr. Elizabeth Petro, Chief, Compliance Regulatory Activities Branch, FDA. Dr. Petro's presentation topic will cover FDA's consideration of what is a drug vs. what is a cosmetic, and related factors. The second talk will be presented by Dr. Jennifer Ator, Principal Toxicologist, ToxServices LLC. Dr. Ator's presentation topic will cover recent studies on the prostaglandin, Isopropyl Cloprostenate. Each presentation will be allotted 1 hour, including time for questions from the members of the Expert Panel. ***Immediately following the presentations, the RAWG will convene, likely concluding just in time for lunch.*** Accordingly, Team Meetings of the Expert Panel are likely to begin following lunch.


Dr. Ator

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 4-Chloro-2-Aminophenol, Tetrabromophenol Blue, *Paeonia suffruticosa*, and Propylene Carbonate.)

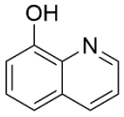
Submissions received on non-final reports, after the issuance of the Wave 2 supplement on May 30th, will be held back until the next Panel review of those reports.


Temima

Finally, please join the Expert Panel and the CIR staff in welcoming the newest member of CIR, Temima Nguyen! Temima joined CIR this year as a Scientific Analyst. She assists with the preparation and presentation of research analyses for submission to the Expert Panel. 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. Welcome, Temima!

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

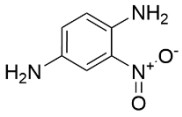
1. Oxyquinoline – DAR (Priya) – ***Dr. Cohen reports on day 2*** – The original review of Oxyquinoline and Oxyquinoline Sulfate was published in 1992 with the conclusion that there were insufficient data to conclude on the safety of these ingredients. In 2001, additional data were submitted and in 2006, the Panel published a Final Amended Report on these ingredients; according to the Discussion, the Panel concluded that Oxyquinoline and Oxyquinoline Sulfate are safe as used as stabilizers for hydrogen peroxide in rinse-off cosmetic products according to the uses and concentrations as stated in that report. However, in the published 2006 report, the Conclusion incorrectly states that Oxyquinoline and Oxyquinoline Sulfate are safe as used as stabilizers for hydrogen peroxide in ***leave-on*** cosmetic products. This was a typographical error, as it should instead say that these ingredients are safe as used as stabilizers for hydrogen peroxide in ***rinse-off*** products (and the data are actually insufficient for leave-on formulations). In December 2024, the Panel determined to re-open this safety assessment to evaluate new data and to correct the conclusion from the 2006 report.



   In 2002, Oxyquinoline and Oxyquinoline Sulfate were reported to be used in 4 and 7 formulations (both at up to 0.1%), respectively. According to FDA Registration and Listing Data (RLD; 2024), Oxyquinoline is used in 11 formulations and Oxyquinoline Sulfate is used in 575 formulations. In 2023, FDA VCRP data indicated that Oxyquinoline and Oxyquinoline Sulfate were used in 1 formulation and 19 formulations, respectively. No concentrations of use were reported for Oxyquinoline according to a 2023 survey performed by Council; however, according to this survey, the concentration of use for Oxyquinoline Sulfate has slightly increased since 2002 (it is now reported to be used at up to 0.15%).

   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. 2-Nitro-*p*-Phenylenediamine – DAR (Christina) – ***Dr. Cohen reports on day 2*** – The Panel first assessed the safety of 2-Nitro-*p*-Phenylenediamine and 4-Nitro-*o*-Phenylenediamine in 1985. Therein, the Panel concluded that for those persons not sensitized, these ingredients are safe as hair dye ingredients at the current concentration of use (this was before the Panel started to utilize the caveat, "when formulated to be non-sensitizing"). The Panel previously considered a re-review of this report and reaffirmed the 1985 conclusion, as published in 2006.



   At the December 2024 meeting, the Panel re-opened the safety assessment for these ingredients to re-evaluate the data on 2-Nitro-*p*-Phenylenediamine, especially since it has been categorized by the European Commission on Annex II, the list of substances prohibited in cosmetic products (with no published SCCS/SCCP opinion available, this categorization is presumably due to no reported use in the EU). While these nitrophenylenediamine ingredients are positional isomers, structure activity relationships between chemicals with different substitution patterns around an aromatic ring are equivocal at best; thereby, the use of read across from one ingredient to the other, in this report, would be challenging.

   Since the December 2024 meeting, the only new data received have been those in an updated concentration of use survey performed by the Council. According to FDA RLD that CIR received in 2024, 2-Nitro-*p*-Phenylenediamine is reported to be used in 3 hair coloring preparations. 2-Nitro-*p*-

Phenylenediamine was reported to have 3 uses in 2023 VCRP data, with 1 use each in an "other" non-coloring hair preparation, a coloring hair rinse, and a coloring hair shampoo. In 2002, notably higher uses were reported in the VCRP; 2-Nitro-*p*-Phenylenediamine was reported to be used in 113 cosmetic formulations, with all uses reported in hair dyes and colors. No concentrations of use were reported in the Council's 2025 survey, whereas the Council's 2003 survey reported a maximum concentration of use range of 0.1 - 1% 2-Nitro-*p*-Phenylenediamine in hair dyes and colors.

For 4-Nitro-*o*-Phenylenediamine, the RLD reported 143 uses in hair dye preparations. In 2023, VCRP data reported 3 uses in hair dyes and colors; in 2002, 22 uses in hair dyes and colors were reported. The maximum concentration of use range reported in 2003 was 0.1 - 0.2% in hair dyes and colors. In 2025, the maximum concentration of use for 4-Nitro-*o*-Phenylenediamine was reported to be slightly decreased, at 0.05 - 0.075% in hair dyes and colors.

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.

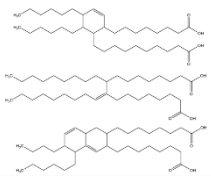
3. *Lactobacillus* Ferment – DR (Priya) – ***Dr. Belsito reports on day 2*** – This is the first time the Panel is reviewing a safety assessment of these four ingredients, Lactobacillus Ferment, Lactobacillus Ferment Filtrate, Lactobacillus Ferment Lysate, and Lactobacillus Ferment Lysate Filtrate. Ample data were found on these species as live bacteria (e.g., as probiotics in clinical studies, safety assessments, and case reports); however, these data were not included in the report as they are not relevant to the cosmetic ingredients reviewed herein. The main components of the ingredients reviewed in this report are not the live bacteria themselves, but byproducts of the fermentation of the bacteria (e.g., intracellular and extracellular metabolites, enzymes, peptides, teichoic acids, polysaccharides, organic acids (e.g., lactic acid), fragments of the dead bacteria). As there are many potential byproducts, the composition of these ingredients in cosmetics is unknown.

   Due to the paucity of relevant safety data for these cosmetic ingredients, a Notice to Proceed Without the Preparation of a Scientific Literature Review (NTP) was issued on November 21, 2024, requesting data to fill numerous gaps. Since issuance of the NTP, data have been submitted in response to these noted gaps.

   According to 2023 VCRP data and 2024 RLD, Lactobacillus Ferment is reported to have the highest number of uses (it is reported be used in 266 and 2106 formulations, respectively). All other ingredients are reported to be used in 876 formulations or less (according to 2024 RLD). The results of the concentration of use survey conducted by the Council indicate Lactobacillus Ferment also has the highest concentration of use in a leave-on formulation; it is used at up to 1.5% in makeup bases.

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

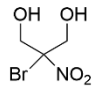
4. Dimer Dilinoleates – DR (Christina) – ***Dr. Cohen reports on day 2*** – This is the first time the Panel is reviewing a safety assessment of these 7 dimer dilinoleate ingredients that are reported to function as hair conditioning agents, skin conditioning agents, and viscosity increasing agents in cosmetics. An NTP was issued by CIR in February 2025, stating multiple data needs. Since the issuing of the NTP, some of the requested data have been received in response, and these data have been added to the report.



   According to RLD submitted to CIR in 2024, the ingredient in this group with the most reported uses is Dimer Dilinoleyl Dimer Dilinoleate; it is reported to be used in 801 formulations. Phytosteryl Isostearyl Dimer Dilinoleate has the second most reported uses in the RLD; it is reported to be used in 78 formulations. The 2023 VCRP data reported Phytosteryl/Isostearyl/Cetyl/Stearyl/Behenyl Dimer Dilinoleate to have the most reported uses, with 244 formulations, most of which were in lipsticks. The results of the concentration of use survey collected by the Council in 2025 indicate Dimer Dilinoleyl Dimer Dilinoleate is used at up to 48.7% in lipsticks and lip glosses.

   If no further data are needed, the Panel should formulate a Discussion and issue a Tentative Report.

However, if additional data are required, the Panel should be prepared to identify those needs and issue an IDA.

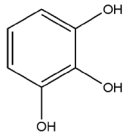
5. 2-Bromo-2-Nitropropane-1,3-Diol – DAR (Thushara) – ***Dr. Belsito reports on day 2*** – 

The Panel previously reviewed the safety of 2-Bromo-2-Nitropropane1,3-Diol in 1980. The Panel concluded that 2-Bromo-2-Nitropropane-1,3-Diol was safe as a cosmetic ingredient at concentrations up to and including 0.1% except under circumstance where its action with amines or amides can result in the formation of nitrosamines or nitrosamides. An addendum to the report was published in 1984 due to the availability of new scientific literature; the Panel reaffirmed their 1980 conclusion and further stated that the additional data suggested the possibility that on absorption, 2 Bromo-2-Nitropropane-1,3-Diol may contribute to the endogenous formation of nitrosamines in humans. The Panel previously considered a re-review of this report in 2003 after studying the data submitted and reaffirmed the conclusion, as published in 2006. In August 2024 an extensive search of the world's literature was performed for studies dated 2000 forward related to 2-Bromo-2-Nitropropane-1,3-Diol. After reviewing that information at the meeting in September 2024, the Panel decided to reopen its safety assessment.

   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 in 2023 and 2025, the maximum reported concentration of use is 0.05% (in leave-on skin cleansing hand wipes, eye makeup removers, and disposable wipes); in 2003, the maximum reported concentration of use was 0.1%.

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

1. Pyrogallol – TAR (Christina) – ***Dr. Belsito reports on day 2*** – 

At the December 2024 meeting, the Panel determined that the data were insufficient to support safety of this hair dye ingredient. The additional data needs are:
   - Maximum concentration of use
   - Dermal irritation and sensitization at maximum concentration of use for non-hair dye uses
   - Ocular irritation data at maximum concentration of use for products used around the eyes

   Since the IDA, CIR has received an updated concentration of use survey from the Council. The survey found no uses for Pyrogallol, but suppliers indicated that Pyrogallol is a constituent of some botanical ingredients and may be incidentally found in cosmetics at low concentrations. 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.

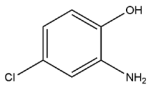
2. Cocoyl Hydrolyzed Collagens – TAR (Thushara) – ***Dr. Cohen reports on day 2*** – At the June 2024 meeting the Panel decided to reopen the safety assessment of Potassium and TEA-Cocoyl Hydrolyzed Collagen, concluding that some of the sensitization and photosensitization data included in the original report needed to be re-investigated. After reviewing the Draft Amended Report at the December 2024 meeting, the Panel decided to add 2 ingredients (Cocoyl Hydrolyzed Collagen and Sodium Cocoyl Hydrolyzed Collagen) to this safety assessment, and issued an IDA requesting the following information for all 4 ingredients:
   - 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.

Since the IDA was issued, CIR has received data and other information towards filling these insufficiencies. These include dermal irritation and sensitization of a product containing 3.2% Potassium Cocoyl Collagen; repeated insult patch test (liquid blush containing 0.1% Cocoyl Hydrolyzed Collagen); dermal and ocular irritation tests on Cocoyl Hydrolyzed Collagen; clinical safety evaluation repeated insult patch (emulsion containing 0.058% Potassium Cocoyl Hydrolyzed Collagen tested as received; summary information Potassium Cocoyl Hydrolyzed Collagen (irritation, sensitization, photosensitization data, and UV absorption spectra); and concentration of use by FDA Product category.

The Panel should carefully consider and discuss the data (or lack thereof) and be prepared to 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.

Draft Final Reports - There are 4 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. Cohen reports on day 2*** – At the December 2024 meeting, the Panel concluded that the available data are insufficient to make a determination of safety for 4-Chloro-2-Aminophenol 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:



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

Since the Tentative Amended Report was issued, CIR has received no new data. No uses have been reported for this ingredient by the RLD, VCRP, or the Council. CIR received comments from the Council on the draft Tentative Amended Report prior to the December 2024 meeting and on the Tentative Amended Report issued after the meeting; these comments have been addressed. The Panel should carefully review the Abstract, Discussion, and Conclusion, and issue a Final Amended Report.

2. *Paeonia suffruticosa* – FR (Thushara) – ***Dr. Cohen reports on day 2*** – At the December 2024 meeting, the Panel concluded that Paeonia Suffruticosa Seed Oil is safe as used in cosmetics. However, The Panel also concluded that the available data are insufficient to make a determination of safety for Paeonia Suffruticosa Bark Extract, Paeonia Suffruticosa Extract, Paeonia Suffruticosa Root Extract and Paeonia Suffruticosa (Tree Peony) Root Bark Extract under the intended conditions of use in cosmetic formulations.

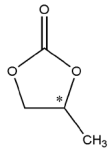
For these 4 ingredients, the Panel determined that the following data are needed to determine safety:

- For Paeonia Suffruticosa Root Bark Extract
    - Clarification on the definition, methods of manufacture, and composition as applicable to cosmetic use
    - Clarification as to whether Paeonia Suffruticosa Root Extract includes the root bark of the plant
- For Paeonia Suffruticosa Bark Extract, Paeonia Suffruticosa Extract, and Paeonia Suffruticosa Root Extract
    - Maximum concentration of use
    - Ocular irritation data (in vitro) at the maximum reported concentration of use for near the eye.
- For all 4 ingredients
    - 28-d dermal toxicity assay
        - 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

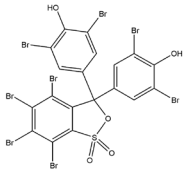
Since the December meeting, safety data on a test sample containing 1.5% Paeonia Suffruticosa Root Extract (ocular irritation and genotoxicity data) and updated use information have been received. The Panel should carefully review the Abstract, Discussion, and Conclusion and issue a Final Report.

3. Propylene Carbonate – FAR (Priya) – ***Dr. Belsito reports on day 2*** – At the March 2025 meeting, the Panel issued a Tentative Amended Report for public comment with the conclusion that Propylene Carbonate is safe in cosmetics in the present practices of use and cosmetics as described in the safety assessment, when formulated to be non-irritating.



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 Amended Report.

4. Tetrabromophenol Blue – FR (Christina) – ***Dr. Belsito reports on day 2*** – At the December 2024 meeting, the Panel concluded that Tetrabromophenol Blue is safe for use as a hair dye ingredient in the present practices of use and concentration described in this safety assessment.



Since the Tentative Report was issued, CIR has received no new data. CIR received comments from the Council on the draft Tentative Report prior to the December 2024 meeting and on the Tentative Report issued after the meeting; these comments have been addressed. The Panel should carefully review the Abstract, Discussion, and Conclusion, and issue a Final Report.

Read-Across Working-Group (RAWG) meeting items. The RAWG should confer on the following 2 items; these items are not being reviewed by the Full Panel at this meeting. Following the conclusion of this meeting, the RAWG should provide a summary document of their analysis to the CIR Executive Director, for each item, for future consideration by the Full Panel.

1. Prostaglandins – RAWG (Priya/Jinqiu) – ***RAWG items are not discussed by Teams on day 1 or reported on day 2*** - The RAWG is asked to convene at this meeting on June 9th, immediately following the presentations and prior to the beginning of the Panel Team Breakouts. As this report is not advancing (i.e., remains tabled), it will not be on the agenda for the Full Panel Session on June 10th. Instead, following the end of this meeting, the RAWG should provide a summary document of their analysis to the CIR Executive Director, for future consideration by the Full Panel.

   The safety assessment on these prostaglandin analogues as well as data on potential read-across sources have been discussed at previous CIR meetings. For the RAWG's convenience, a summary has been provided noting the relevant outcomes of the assessment at previous meetings and the prior receipt of read-across data from industry (these data were received prior to the December 2023 and June 2024 meetings).

   As the data from the previous meetings have already been reviewed by the Panel, the focus at the current meeting should be on newly received data (highlighted herein). Since the June 2024 meeting, several data files have been received from industry for both Ethyl Tafluprostamide and Isopropyl Cloprostenate, and are presented herein for consideration by the RAWG.

   While it is not being reviewed at this meeting, the Revised Draft Tentative Report of the Safety Assessment of Ethyl Tafluprostamide and Isopropyl Cloprostenate as Used in Cosmetics is included for reference. This updated report version includes all new data on Ethyl Tafluprostamide and Isopropyl Cloprostenate. It should be noted, however, that results on the ToxProfiler, ReproTracker, 3T3 NRU assay, in silico endocrine receptor/activation predictions, and QSAR predictions on hormone receptors were not included in the report; because these assays were primarily performed as a comparison to support the use of read-across ingredients. The RAWG should indicate if these data should be included in the report, and how they would like them to be presented.

Considering the historical and newly received data and other information, the RAWG should arrive at a consensus and support the leader of the RAWG in preparing a written proposal to the Full Panel for the future advancement of the report (including, e.g., status of data sufficiency, level of confidence in presented read-across strategies, remaining unresolved issue(s)). Following the conclusion of the Panel meeting, this proposal should be submitted to the Executive Director, and should also include an analysis and summarization of the discussions held by RAWG at this meeting. This document will be included in the next iteration of the report for consideration by the Full Panel at a future meeting.

2. Priorities Update – RAWG (Bart) – ***RAWG items are not discussed by Teams on day 1 or reported on day 2*** – At the March 2025 meeting, the RAWG was asked to consider, following the end of that meeting, 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, a proposal should be made for discussion with the full Panel. One grouping question that was raised at the March meeting was, should the 2 ingredients in this draft priorities list for review in 2026, Ethyl Trimethylbenzoyl Phenylphosphinate and Bis-Trimethylbenzoyl Phenylphosphine Oxide, be instead added to the currently advancing report on Trimethylbenzoyl Diphenylphosphine Oxide (which the Panel issued an IDA for at the March meeting)?

   The data requested in the IDA for the report on Trimethylbenzoyl Diphenylphosphine Oxide included: concentrations of use in non-nail products, dermal irritation and sensitization data at maximum use concentration for the skin, ocular irritation data (preferably at concentrations for products resulting in eye exposure, once received), Margin of Exposure (MOE), and phototoxicity/photosensitization data. Priya has conducted a cursory search for relevant, publicly available data on these 2 proposed add-ons. No relevant published results were found in PubMed for either ingredient; however, relevant data were found in databases such as ECHA, NICNAS, and NTIS. If the Panel determines confidence in the use of these ingredients as read-across sources to Trimethylbenzoyl Diphenylphosphine Oxide, then one or more of the above data needs might be met. The Council has initiated a survey for these 2 proposed add-ons, but we do not yet have concentration of use data thereon.

   Does the RAWG propose that Ethyl Trimethylbenzoyl Phenylphosphinate and Bis-Trimethylbenzoyl Phenylphosphine Oxide remain on the 2026 Priorities List or instead should be added to the ongoing report on Trimethylbenzoyl Diphenylphosphine Oxide?

   Does the RAWG propose any changes to any of the other groupings included in the Draft 2026 Priorities List?

   The 2026 Priorities List is scheduled to be finalized at the September 2025 meeting of the Panel. Any proposals of the RAWG will be brought to the Full Panel at that time for consideration.

Administrative Items - there are 7 administrative items.

RRsums - The Panel is being asked for editorial comment.

1. Ascorbic Acid – RRsum – (Priya) – ***Dr. Belsito reports on day 2*** – The Panel should carefully consider the extended rereview summary and finalize it.
2. Isopropanolamines – RRsum – (Priya) – ***Dr. Cohen reports on day 2*** – The Panel should carefully consider the extended rereview summary and finalize it.
3. Waxes – RRsum – (Temima) – ***Dr. Belsito reports on day 2*** – The Panel should carefully consider the extended rereview summary and finalize it.
4. Glyceryl Monoesters – with use – RRsum – (Temima) – ***Dr. Cohen reports on day 2*** – The Panel should carefully consider the rereview summary and finalize it.
5. Glyceryl Monoesters – no use – RRsum – (Temima) – ***Dr. Belsito reports on day 2*** – The Panel should carefully consider the rereview summary, which commutes the conclusion to “use not supported,” and finalize it.

Resource Document – The Panel is being asked if this is ready for posting.

6. Hair Dye Epi – Admin (Jinqiu) – ***Dr. Belsito reports on day 2*** – The most recent draft of this resource document was reviewed by the Panel at the September 2023 meeting, during which time the Panel emphasized the importance of maintaining this it as a living document with the intent to incorporate emerging epidemiological data. The Panel agreed that the conclusions should be periodically

reassessed as new information becomes available, and discussed strategies to broaden the document's public accessibility. The Panel reaffirmed its commitment to continuous surveillance of epidemiological research on the potential association between personal hair dye use and cancer risk.

The Panel is requested to review this updated draft and determine whether it should replace the current version posted on CIR's Findings & Resources Documents page.

Strategy Memo – Further expertise needed?

7. Phthalates – SM (Christina) – ***Dr. Cohen reports on day 2*** - 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 2024, CIR staff initiated an extensive literature search for studies on this ingredient dated 1999 forward. A very large number of studies was discovered, with many studies delving into research on reproductive, developmental, and endocrine effects. Many of the studies have expanded into mechanisms of action, gene expression, and other specialized areas. It may be beneficial to have an expert come in to talk to the Panel about these types of DART and endocrine studies concurrently with the Panel's first review of this amended report.

   Does the Panel, or other 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? Who? Specific topics to be addressed?

   Additionally, Dimethyl Phthalate appears to no longer be in use. Accordingly, CIR staff propose splitting off Dimethyl Phthalate into a separate re-review proposal document, wherein the Panel would have the option of issuing a use not supported conclusion via a re-review summary (should they choose not to reopen this zero-use ingredient).

   Does the Panel support the idea of having Dimethyl Phthalate in a separate re-review proposal document?

Full Panel Meeting

The Panel will consider the 4 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 rereview summaries and the resource document.

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
173rd Meeting of the Expert Panel for Cosmetic Ingredient Safety
June 9-10, 2025

Monday, June 9, 2025

8:30 AM	**WELCOME TO THE 173rd EXPERT PANEL TEAM MEETINGS**	**Drs. Bergfeld/Heldreth**
8:45 AM	**PRESENTATION – Drug vs. Cosmetic (FDA)**	**Dr. Elizabeth Petro** **Chief, Compliance Regulatory Activities Branch, FDA**
9:45 AM	**PRESENTATION – Recent studies on Isopropyl Cloprostenate**	**Dr. Jennifer Ator** **Principal Toxicologist, ToxServices LLC**
10:45AM – 12 PM	**Read-Across Working Group (RAWG)**	**Dr. Rettie**
12 PM – 1 PM	**Lunch break**	
1 PM - 5 PM	**TEAM MEETINGS**	**Drs. Belsito/Cohen**

Dr. Belsito's Team

FAR (CB)	4-Chloro-2-Aminophenol
FR (CB)	Tetrabromophenol Blue
TAR (CB)	Pyrogallol
DAR (CB)	2-Nitro-*p*-Phenylenediamine
DR (CB)	Dimer Dilinoleates
SM (CB)	Phthalates
Admin (JZ)	Hair Dye Epi
FAR (PF)	Propylene Carbonate
DR (PF)	*Lactobacillus* Ferment
DAR (PF)	Oxyquinoline
RRSum (PF)	Ascorbic Acid
RRSum (PF)	Isopropanolamines
RRSum (TN)	Waxes
RRSum (TN)	Glyceryl Monoesters – with use
RRSum (TN)	Glyceryl Monoesters – no use
DAR (TD)	2-Bromo-2-Nitropropane-1,3-Diol
TAR (TD)	Cocoyl Hydrolyzed Collagens
FR (TD)	*Paeonia suffruticosa*

Dr. Cohen's Team*

FAR (PF)	Propylene Carbonate
DR (PF)	*Lactobacillus* Ferment
DAR (PF)	Oxyquinoline
RRSum (PF)	Ascorbic Acid
RRSum (PF)	Isopropanolamines
RRSum (TN)	Waxes
RRSum (TN)	Glyceryl Monoesters – with use
RRSum (TN)	Glyceryl Monoesters – no use
FR (TD)	*Paeonia suffruticosa*
TAR (TD)	Cocoyl Hydrolyzed Collagens
DAR (TD)	2-Bromo-2-Nitropropane-1,3-Diol
Admin (JZ)	Hair Dye Epi
SM (CB)	Phthalates
DAR (CB)	2-Nitro-*p*-Phenylenediamine
DR (CB)	Dimer Dilinoleates
TAR (CB)	Pyrogallol
FR (CB)	Tetrabromophenol Blue
FAR (CB)	4-Chloro-2-Aminophenol

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 || TD: Thushara Diyabalanage || PF: Priya Ferguson || 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, June 10, 2025			
8:30 AM	**WELCOME TO THE 173rd FULL EXPERT PANEL MEETING**		**Dr. Bergfeld**
8:40 AM	Admin **MINUTES OF THE MARCH 2025 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)	4-Chloro-2-Aminophenol – ***Dr. Cohen reports***	
	FR (CB)	Tetrabromophenol Blue – ***Dr. Belsito reports***	
	FR (TD)	*Paeonia suffruticosa*-derived ingredients ***– Dr. Cohen reports***	
	FAR (PF)	Propylene Carbonate – ***Dr. Belsito reports***	
	Reports Advancing		
	DAR (PF)	Oxyquinoline – ***Dr. Cohen reports***	
	DR (PF)	*Lactobacillus* Ferment ingredients – ***Dr. Belsito reports***	
	DAR (CB)	2-Nitro-*p*-Phenylenediamine – ***Dr. Cohen reports***	
	TAR (CB)	Pyrogallol – ***Dr. Belsito reports***	
	DR (CB)	Dimer Dilinoleates – ***Dr. Cohen reports***	
	DAR (TD)	2-Bromo-2-Nitropropane-1,3-Diol – ***Dr. Belsito reports***	
	TAR (TD)	Cocoyl Hydrolyzed Collagens – ***Dr. Cohen reports***	
	Other Items		
	RRSum (PF)	Ascorbic Acid & Ascorbates – ***Dr. Belsito reports***	
	RRSum (PF)	Isopropanolamines – ***Dr. Cohen reports***	
	RRSum (TN)	Waxes – ***Dr. Belsito reports***	
	RRSum (TN)	Glyceryl Monoesters – with use – ***Dr. Cohen reports***	
	RRSum (TN)	Glyceryl Monoesters – no use – ***Dr. Belsito reports***	
	SM (CB)	Phthalates– ***Dr. Cohen reports***	
	Admin (JZ)	Hair Dye Epi Resource Paper – ***Dr. Belsito reports***	

ADJOURN – – *The next will be held virtually on Monday and Tuesday, September 8-9, 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 || TD: Thushara Diyabalanage || PF: Priya Ferguson || TN: Temima Nguyen || JZ: Jinqiu Zhu

ONE HUNDRED SEVENTY-SECOND MEETING

OF THE

EXPERT PANEL FOR COSMETIC INGREDIENT SAFETY

March 13th – 14th, 2025

Washington Marriott Georgetown
1221 22nd St 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 Cherian, MS - Senior Scientific Analyst

Thushara Diyabalanage, PhD - Scientific Analyst

Information Services
Kevin Stone Fries, MLS - Information Services Manager

Other In-Person Attendees

Name	Organization
Don Bjerke	Procter & Gamble
Carol Eisenmann	Personal Care Products Council
Linda Giles	Transcription Etc.
Allison Schafer	Procter & Gamble
Kathy Stanton	Personal Care Products Council
Josie Williams	general public

Other Vitrual Meeting Attendees

Name	Organization
Valentina Aguirre	Bioeutectics
Ayodele Ajayi	June Jacobs Labs
Nan An	FDA
Nkem Azu	VSCO
Alyssa Bellomo	Colgate-Palmolive
Lee Cowan	Nouryon Chemicals
Amanda Dysert	Kao USA
Lorraine Gallagher	Nice-Pak Products, Inc.
Lumos Li	Colgate-Palmolive
Miao Li	FDA
Janet Marcincavage	Nouryon Chemicals
Alexander Mol	Kao USA
Lauren Nardella	HBW Insight
Akira Ogasawara	Kao USA
Stefanie O'Neal	Kao USA
Shanti Pabbathi	Chanel, Inc.
Alexandra Scranton	Women's Voices for the Earth
Stephanie Wang	Colgate-Palmolive
Teresa Washington	FDA
Joanna Woo	Colgate-Palmolive
Leah Yip	general public
Merle Zimmermann	American Herbal Products Association

CHAIRPERSON'S OPENING REMARKS

Dr. Bergfeld welcomed the attendees to the 172nd meeting of the Expert Panel for Cosmetic Ingredient Safety and also welcomed the Panel's newest member, Dr. Samuel Cohen. Dr. Bergfeld noted the Panel is nearing its 50th anniversary and has reviewed over 6,200 ingredients. There are still many more ingredients to review.

The Panel reviewed 11 ingredient reports at this meeting, including 3 finals, 3 tentative reports, and 5 draft reports. Four of the 5 draft reports were reports that the Panel reopened for review. The Panel also reviewed the Inhalation Resource Document, the Margin of Exposure Resource Document, and the 2026 draft Priorities List, as well as Wave 2 data.

Dr. Bergfeld thanked the CIR staff, the Panel, 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 December 1-2, 2024 (171st) 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 from the Office of Cosmetics and Colors (OCAC) for their ongoing assistance, even in the face of organizational upheavals. Additionally, he thanked Dr. Don Bjerke, who announced his pending retirement 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 Panel member, Dr. Samuel M. Cohen, MD, PhD, Havlik-Wall Professor of Oncology in the University of Nebraska Medical Center, Department of Pathology and Microbiology. Dr. Heldreth mentioned that Dr. Cohen has already become a critical part of this Panel, and he expressed his thanks to Dr. Cohen for joining his expertise.

In addition to the ingredient dossiers under review at this meeting, Dr. Heldreth encouraged the Panel to confirm their intent for future iterations of both the Inhalation Resource Document and the MOE Resource Document by vote. He also discussed plans to update the Hair Dye Epidemiology Resource Document, in light of the newly added cancer expertise that Dr. Cohen brings.

The first of CIR's four 2025-IJT issues is 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%20Review%20(CIR)). Additionally, copies of this issue in IJT's Nxtbook format, are available here:

Feb 2025- https://www.nxtbook.com/sage/sage/ijt_cir_202502/

FINAL SAFETY ASSESSMENTS

2,4-Diaminophenoxyethanol
The Panel issued a Final Amended Report 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.

2,4-Diaminophenoxyethanol HCl and 2,4-Diaminophenoxyethanol Sulfate are reported to function as oxidative hair dye ingredients in hair coloring products. The Panel recognizes that hair dyes containing these ingredients, as coal tar hair dye products, are exempt from certain adulteration and color additive provisions of the US Federal Food, Drug, and Cosmetic Act (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.

The Panel noted that 2,4-Diaminophenoxyethanol HCl and 2,4-Diaminophenoxyethanol Sulfate have been reported to be used in eye makeup preparations. The FD&C Act mandates that color additives must be pre-market approved by the FDA for their intended use. 2,4-Diaminophenoxyethanol HCl and 2,4-Diaminophenoxyethanol Sulfate are not approved color additives in cosmetic products, and thereby, use in eye makeup products is not permitted. The Panel also noted that hair dyes, such as these ingredients, should not be applied to the eyebrows and eyelashes in that such use can result in lost or permanently damaged vision.

***p*-Phenylenediamine, *p*-Phenylenediamine HCl, and *p*-Phenylenediamine Sulfate**
The Panel issued a Final Amended Report 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 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.

The high degree of cross-reactivity between *p*-Phenylenediamine and other structurally related aromatic amines, including *p*-toluenediamine and aminophenols, poses a significant challenge in allergen avoidance. Studies indicate that a substantial proportion of *p*-Phenylenediamine-sensitized individuals exhibit concomitant reactivity to these compounds, highlighting the complexity of managing allergic contact dermatitis in this context.

Copper Gluconate
The Panel issued a Final Report 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. The Panel noted that while there is a paucity of genotoxicity data in this safety assessment, carcinogenicity data from dietary studies on Copper Gluconate are available. While pre-neoplastic lesions were observed in these studies, along with nephrotoxic effects in an oral gavage study, the concentrations at which these adverse effects were observed are much greater than those used in cosmetic formulations. The US FDA has designated Copper Gluconate as generally recognized as safe (GRAS) as a direct food ingredient. Additionally, Copper Gluconate is not a dermal irritant or dermal sensitizer in human repeated insult patch tests. The Panel considered these findings, coupled with the low concentration of use in cosmetic products and negative developmental and reproductive toxicity data, and determined that the data were sufficient to conclude on the safety of Copper Gluconate.

TENTATIVE SAFETY ASSESSMENTS

Basic Blue 7
The Panel issued a Tentative Report for public comment with the conclusion 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. In order to come to a conclusion of safety for this hair dye ingredient, the following information is required:

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

Nelumbo nucifera
The Panel issued a Tentative Report for public comment with the conclusion that the available data are insufficient to make a determination of safety for the following 14 *Nelumbo nucifera* ingredients:

Nelumbo Nucifera Callus Culture Extract
Nelumbo Nucifera Extract
Nelumbo Nucifera Flower Extract
Nelumbo Nucifera Flower/Leaf/Stem Juice
Nelumbo Nucifera Flower Oil
Nelumbo Nucifera Flower Water
Nelumbo Nucifera Germ Extract
Nelumbo Nucifera Leaf Extract
Nelumbo Nucifera Phytoplacenta Culture Extract
Nelumbo Nucifera Root Extract
Nelumbo Nucifera Root Water
Nelumbo Nucifera Seed Extract
Nelumbo Nucifera Seed Powder
Nelumbo Nucifera Stamen Extract

The Panel determined that the data needs from the Insufficient Data Announcement (IDA) issued following the December 2024 Panel meeting remain unmet. In order to come to a conclusion of safety for these ingredients, the following data are therefore needed:

- 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 (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

Octoxynols
The Panel issued a Tentative Amended Report for public comment with the conclusion that the following 25 octoxynols are safe in cosmetics in the present practices of use and concentration described in the safety assessment when formulating to be non-irritating.

Octoxynol-1	Octoxynol-12	Octoxynol-9 Carboxylic Acid
Octoxynol-3	Octoxynol-13	Octoxynol-20 Carboxylic Acid
Octoxynol-5	Octoxynol-16	Potassium Octoxynol-12 Phosphate
Octoxynol-6	Octoxynol-20	Sodium Octoxynol-2 Ethane Sulfonate
Octoxynol-7	Octoxynol-25	Sodium Octoxynol-2 Sulfate
Octoxynol-8	Octoxynol-30	Sodium Octoxynol-6 Sulfate
Octoxynol-9	Octoxynol-33	Sodium Octoxynol-9 Sulfate
Octoxynol-10	Octoxynol-40	
Octoxynol-11	Octoxynol-70	

The Panel noted that there is currently no evidence of use in categories/products of concern for this ingredient group (i.e., baby products, products used near the eyes, or vaginal products) according to 2024 RLD. In addition, the Panel suggested UV absorption (and other) data from the previously issued report on octoxynols be included in this current iteration. Lastly, the Panel discussed the low reliability of certain genotoxicity assays (e.g., unscheduled DNA synthesis); while these data are still provided in the report, they should not be relied upon to determine genotoxicity.

Propylene Carbonate
The Panel issued a Tentative Amended Report for public comment with the conclusion that Propylene Carbonate is safe in cosmetics in the present practices of use and concentration as described in the safety assessment when formulated to be non-irritating. In September 2024, an IDA was issued for lack of concentrations of use in baby products and UV absorption data. No concentrations of use in baby products were received; however, since the primary concern therein was potential irritation, the Panel's conclusion caveat to formulate products containing this ingredient to be non-irritating, mitigates this concern. UV absorption data were received and considered sufficient by the Panel to eliminate phototoxicity/photosensitization concerns.

According to 2023 FDA VCRP data, Propylene Carbonate is reported to be used in 882 total formulations. RLD 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 2022 concentration of use survey conducted by Council).

INSUFFICIENT DATA ANNOUNCEMENTS (IDA)

Butoxyethanol
The Panel issued an IDA for Butoxyethanol. The additional data needed to determine the safety of this ingredient are:

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

Kojic Acid
The Panel issued an IDA for Kojic Acid. The additional data needed to determine the safety of this ingredient are:

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

Trimethylbenzoyl Diphenylphosphine Oxide
The Panel issued an IDA for Trimethylbenzoyl Diphenylphosphine Oxide. The additional data needed to determine the safety of this ingredient are:

- Concentrations of use in non-nail products
- Dermal irritation and sensitization data at maximum use concentration for the skin
- Ocular irritation data (preferably at concentrations for products resulting in eye exposure, once received)
- MOE
- Phototoxicity/photosensitization data

Acacia senegal
The Panel issued an IDA for these 2 *Acacia senegal*-derived ingredients. The additional data needed to determine the safety of Acacia Senegal Gum and Acacia Senegal Gum Extract are:

- 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

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 reaffirmed the conclusion reached in 1 of these safety assessments (i.e., chose not to re-open the original report). A rereview summary for this safety assessment will be prepared and presented to the Panel at a future meeting.

- Beeswax, Copernica Cerifera (Carnauba) Wax, Euphorbia Cerifera (Candelilla) Wax, and Rhus Succedanea Fruit Wax - 4 ingredients

For the other previous assessment, the Panel chose not to re-open the report, but additionally chose to split the ingredients into 2 rereview summaries: 1) in one rereview summary they reaffirmed the conclusion reached in the original report of 2 in-use ingredients, but 2) in the other, which comprised 5 ingredients with no uses, they issued a new conclusion of "use not supported." The CIR Steering Committee previous amended the Priorities so that 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; the Panel exercised this new pathway for the first time herein. Thus, 2 rereview summaries for this previous safety assessment will be prepared and presented to the Panel at a future 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

OTHER DOCUMENTS

Inhalation Resource Document
The Panel reviewed the revised Inhalation Resource Document and assessed the suitability of the inhalation boilerplate (BP) language. They considered the updates and additions to accurately reflect their understanding of exposure to airborne particles and droplets resulting from the use of cosmetic sprays. The Panel examined available particle size data across various cosmetic spray categories and requested a clearer presentation of the summarized findings. Additionally, they deliberated on modifying the inhalation BP language, particularly in cases where inhalation toxicity data are absent, to better highlight potential inhalation risks associated with the use of specific cosmetic spray products. The Panel deemed these changes as editorial and agreed that the document should be posted to the CIR Resources page once the editing is complete. Once posted, stakeholders will have 60 days to comment before this version of the document is considered final.

MOE Resource Document
The Panel reviewed the updated MOE resource document and determined the preferred terminology to be used in systemic quantitative risk assessment (QRA). They conducted a comprehensive evaluation of the application and significance of the MOE approach in the safety assessment of cosmetic ingredients. Additionally, they engaged in a thorough discussion on its limitations, considering challenges, uncertainties, and areas that require further validation and characterization to enhance the scientific liability and applicability of this approach in risk assessment. The Panel decided to issue an official 60-day comment period for this document, which will be posted on CIR's website after further editorial revisions based on the meeting discussion and comments from the Council.

Draft 2026 Priorities
The CIR Procedures require preparation of the Draft 2026 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 this year; 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.

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. The Panel agreed that a concentration of use survey should be conducted for the non-fragrance uses of this ingredient, to inform their decision as to whether it will be reviewed hereby.

Groupings of ingredients, drafted by CIR Staff, were included in the document. Following the conclusion of the March meeting and prior to the June meeting, the Panel's 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.

Commitment & Credibility since 1976

Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Christina Burnett, M.S., Senior Scientific Analyst/Writer, CIR
Date: May 16, 2025
Subject: Strategy Memo for Dibutyl Phthalate, Diethyl Phthalate, and Dimethyl Phthalate

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.[2] 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 2024, CIR staff initiated an extensive literature search for studies on this ingredient dated 1999 forward. A very large number of studies was discovered, with many studies delving into research on reproductive, developmental, and endocrine effects. Many of the studies have expanded into mechanisms of action, gene expression, and other specialized areas. It may be beneficial to have an expert come in to talk to the Panel about these types of DART and endocrine studies concurrently with the Panel's first review of this amended report.

- ***Does the Panel, or other 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?***
    - ***If so, please provide specifics to be addressed by this expert in such a presentation.***

Additionally, we would like to invite any interested stakeholders to provide any support or information that would aid in the Panel's deliberations of these phthalate ingredients at this time.

While preparing the Draft Amended Report, CIR staff have noted that the 2024 RLD and 2025 concentration of use survey by the Council indicate no current uses for Dimethyl Phthalate. The 2023 VCRP also reported no uses. In 2001, 12 uses were reported to the VCRP and the maximum concentration of use reported was 2% in a hair spray. In an effort to help streamline the Panel's focus, CIR staff propose splitting off Dimethyl Phthalate into a separate re-review proposal document, wherein the Panel would have the option of issuing a use not supported conclusion via a re-review summary (should they choose not to reopen this zero-use ingredient).

- ***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?***