ADMIN

Memo
Agenda
Minutes

EXPERT PANEL MEETING
December 2 - 3, 2024

Cosmetic Ingredient Review

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MEMORANDUM

To: The Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Bart Heldreth, Ph.D., Executive Director, Cosmetic Ingredient Review
Subject: 171st Meeting of the Panel — Monday and Tuesday, December 2nd - 3rd, 2024
Date: November 8, 2024

Welcome to the final Panel Meeting of 2024! The agenda and accompanying materials for the 171st Expert Panel Meeting, to be held on December 2nd - 3rd, 2024, are now available. ***The location is different from our meeting in September*** – and 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:

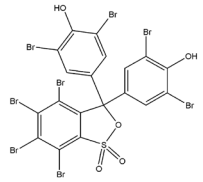
https://www.cir-safety.org/meeting/171st-expert-panel-meeting

The meeting agenda includes the consideration of 8 reports advancing in the review process, including 2 draft final reports, 2 draft tentative reports, and 4 draft reports (2 of which are re-opened reviews). Also on the agenda are 2 previous reports proposed for rereview; ***for these proposed rereviews, the Panel is only being asked if the reports should be reopened.*** Additionally, 2 rereview summaries are on the agenda for editorial review. There are also 3 administrative items, including a strategy memo on Fatty Amphocarboxylates (***with requests for both the RAWG and the full Panel***), a new iteration of the Inhalation Resource Document (including updated boilerplate language), and a new Resource Document for Margin of Exposure (MOE). Additionally, Day 1 will start with a presentation regarding how we have incorporated the FDA's Registration and Listing Data (RLD) into these reports.

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 *p*-Phenylenediamine and Inositol.) ***Submissions received on non-final reports, after the issuance of the Wave 2 supplement on November 22nd, will be held back until the next Panel review of those reports.***

Draft Reports - There are 4 draft reports for review. Sufficient data to proceed, or issue an Insufficient Data Announcement (IDA)?

1. Tetrabromophenol Blue – DR (Christina) – ***Dr. Cohen reports on day 2*** – This is the first time the Panel is reviewing a safety assessment on this ingredient. The Scientific Literature Review (SLR) was issued by CIR on October 2, 2024.



This ingredient is reported to function as a hair colorant in cosmetic formulations. In 2023, Tetrabromophenol Blue was added to the 2024 Priorities List for cause as the European Union's Scientific Committee on Consumer Safety (SCCS) had concluded that the data were insufficient to determine safety. The Hair Color Technical Committee supported the inclusion of Tetrabromophenol Blue on the 2024 Priorities List. Since the Priorities List was finalized, additional data were submitted to the SCCS and their opinion has been updated to safe in oxidative and non-oxidative hair coloring products at a final on-head concentration of up to 0.2%.

According to the RLD that CIR received in 2024, Tetrabromophenol Blue is reported to be used in 40 hair coloring preparations. In 2023, Tetrabromophenol Blue was reported to be used in 2 formulations according to the VCRP, i.e., 1 hair lightener with color and 1 hair bleach. ***Because there are numerous differences in the ways the data for the VCRP and the RLD were collected and processed, it is not appropriate to contrast data from the VCRP and RLD to determine a trend in frequency of use.*** The results of the concentration of use survey conducted by the Council in 2023 and updated in 2024 indicate Tetrabromophenol Blue is used at a maximum of 0.0025% in hair dyes and colors.

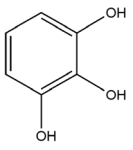
If no further data are needed to reach a conclusion of safety, the Panel should formulate a Discussion and issue a Tentative Report. However, if additional data are required, the Panel should be prepared to identify those needs and issue an IDA.

2. Potassium Cocoyl Hydrolyzed Collagen – DAR (Thushara) – ***Dr. Belsito reports on day 2*** – The Panel first published a Final Report on the Safety Assessment of Potassium-Coco-Hydrolyzed Animal Protein and Triethanolamine-Coco-Hydrolyzed Animal Protein in 1983. The Panel concluded that Potassium-Coco-Hydrolyzed Animal Protein and Triethanolamine-Coco-Hydrolyzed Animal Protein are safe as cosmetic ingredients in the present practices of use, as described in that report. The names of these two ingredients as listed in the web-based *International Cosmetic Ingredient Dictionary and Handbook* (*Dictionary*) have subsequently changed, and are now Potassium Cocoyl Hydrolyzed Collagen and TEA-Cocoyl Hydrolyzed Collagen, respectively. The Panel previously considered a rereview of this report in 2002 and reaffirmed the 1983 conclusion, as published in 2005. In June 2024, the Panel concluded that some of the sensitization and photosensitization data included in the original report need to be re-investigated and decided to re-open the safety assessment.

A comprehensive literature search conducted in April 2024 and subsequent searches performed in October 2024 did not find any new data. Based on 2023 FDA VCRP data and RLD received in 2024, it is evident that the use of these ingredients has decreased substantially since the last re-review. For instance, according to 2023 VCRP data, Potassium Cocoyl Hydrolyzed Collagen is used in 2 formulations, and TEA-Cocoyl Hydrolyzed Collagen has no reported uses; in 2001, these ingredients were used in 64 and 20 formulations, respectively. RLD indicated that Potassium Cocoyl Hydrolyzed Collagen has 32 uses whereas TEA-Cocoyl Hydrolyzed Collagen has 3 applications. According to the Council survey that was conducted in 2022, no concentrations of use were reported for either ingredient; in 2001, Potassium Cocoyl Hydrolyzed Collagen was reported to be used at a maximum concentration of 20% (in non-coloring shampoos) and TEA-Cocoyl Hydrolyzed Collagen was reported to be used at a maximum concentration of 1% (in bubble baths).

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. Pyrogallol – DAR (Christina) – ***Dr. Cohen reports on day 2*** – The original review of Pyrogallol was published in 1991 with the conclusion that "Pyrogallol is safe as a cosmetic ingredient in the present practices of use and concentration." A rereview was initiated in 2007; the re-review was subsequently tabled at the June 2007 Panel meeting to await the findings of the National Toxicology Program (NTP) 2-year carcinogenicity study. In March



2024, since it had been at least 15 years since the initial rereview was presented, the Panel was presented with a 2nd rereview of Pyrogallol with the NTP study results and additional relevant studies that have become available since the Panel's last review. The Panel reopened this safety assessment to incorporate the findings of the NTP studies and the additional relevant data, and to finally publish the amended rereview.

Since the March meeting, no new unpublished data have been received. RLD that were received have been incorporated. According to 2024 RLD, Pyrogallol is reported to be used in 19 formulations, in such product categories as eye makeup preparations, manicuring preparations, and hair coloring preparations. The 2023 VCRP survey data reported Pyrogallol to be used in 1 "other" hair coloring product. In 2006 and in 1989, Pyrogallol was reported to be used in 11 and 42 hair dyes and colors, respectively. The maximum concentration of use range reported in the original safety assessment was < 0.1 - 5% in hair dyes and colors; however, no uses were reported by the Council in surveys conducted in 2006 or in 2023.

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

4. *Nelumbo nucifera* – DR (Thushara) – ***Dr. Belsito reports on day 2*** – This is the first time the Panel is reviewing a safety assessment on these ingredients. The SLR was issued by CIR on October 2, 2024. This report reviews the safety of 14 *Nelumbo nucifera*-derived ingredients. Among them, one, Nelumbo Nucifera Flower Oil, is not included in the *Dictionary*. It had reported uses in 2023 in the VCRP database and in 2024 in RLD and is thus included in this review.

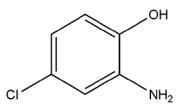
According to 2023 VCRP survey data, Nelumbo Nucifera Flower Extract was reported to be used in 200 formulations, 151 of which are presumed to be leave-on formulations. All other in-use ingredients were reported to be used in 25 formulations or less. The results of the concentration of use survey conducted by the Council in 2022 indicate that Nelumbo Nucifera Root Extract has the highest maximum reported concentration of use; it is reported to be used at up to 0.2% in foundations. Based on RLD of 2024, Nelumbo Nucifera Flower Extract is used in 544 formulations, which includes one air brush application on leg and body parts.

Summary Information for an extract of *Nelumbo nucifera* (lotus) flowers in isostearyl isostearate (extraction solvent), an extract of *Nelumbo nucifera* (lotus) flowers in propanediol and glycerin (extraction solvents) with a *Nymphaea caerulea* flower extract, and Nelumbo Nucifera Germ Extract has also been received since the SLR was announced, and have been incorporated into the report.

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

Draft Tentative Reports - There are 2 draft tentative reports for consideration. Issue a tentative conclusion?

1. 4-Chloro-2-Aminophenol – TAR (Christina) – ***Dr. Belsito reports on day 2*** – At the June 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
- 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 IDA, CIR has received no new data. No uses have been reported for this ingredient by the FDA RLD, FDA VCRP, or the Council. 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.

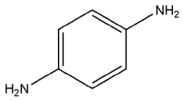
2. *Paeonia suffruticosa* – TR (Thushara) – ***Dr. Cohen reports on day 2*** – At the June 2024 meeting, the Panel determined that the data were insufficient to the support safety of these ingredients. The additional data requested are:

- 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 included the root bark of the plant
- For Paeonia Suffruticosa Seed Oil
  - Clarification of ingredient constituents
- 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 ingredients
  - 28-d dermal toxicity assay
    - If positive, data on systemic toxicity endpoints (e.g. developmental and reproductive toxicity)
  - Genotoxicity data
- For all ingredients, except Paeonia Suffruticosa Root Extract
  - Dermal irritation and sensitization data

Since the IDA was issued, CIR received a human repeated-insult patch test on a lotion containing 0.0015% Paeonia Suffruticosa Root Extract. 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 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 2 Draft Final Reports for consideration. Review these drafts, especially the rationale provided in the Discussion sections, and issue final reports, as appropriate.

1. *p*-Phenylenediamine – FAR (Christina) – ***Dr. Belsito reports on day 2*** – At the June 2024 meeting, the Panel issued a Revised Tentative Amended Report with the conclusion that *p*-Phenylenediamine, *p*-Phenylenediamine HCl, and *p*-Phenylenediamine Sulfate are safe for use as hair dye ingredients in the present practice of use and concentration described in the safety assessment. However, the Panel also concluded that these ingredients are unsafe for use in dermal coloring applications, specifically noting unsafe use in temporary black henna tattoos.



The RLD have been incorporated into this report. According to these data, *p*-Phenylenediamine is reported to be used in 6480 formulations (with the majority of the uses (5502) reported in hair dyes and colors), *p*-Phenylenediamine HCl is used in 25 hair coloring preparations, and *p*-Phenylenediamine Sulfate was used in 45 hair coloring preparations. Notably, *p*-Phenylenediamine is still reported as being used in eye makeup preparations, but it is now also reported to be used in non-coloring hair preparations and skin care preparations.

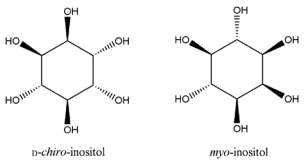
Furthermore, while there are numerous differences in the ways the VCRP and the RLD were collected and processed which make comparing the two data sets difficult, it should be noted that there is a hair coloring preparation product category that was not historically associated with hair dyes, i.e., eyelash and eyebrow dyes. The RLD reported that *p*-Phenylenediamine has 51 such uses. As noted in the Use section and the Discussion, the FDA and the Panel have stated that coal tar hair dyes should not be used for dyeing eyelashes and eyebrows. The safety assessment currently includes wording about

color additive provisions and non-acceptable uses. Please confirm that the current language in the report is adequate to address the new reported uses in product categories outside of hair coloring preparations.

Since the June meeting, no unpublished data have been received for this report. However, additional published case and retrospective studies, including a case report on allergic contact dermatitis following the administration of a permanent tattoo, have been added to the safety assessment and are highlighted to aid in the Panel's review. Comments provided by the Council on the Revised Tentative Amended Report have been addressed. Additionally, comments provided by the Women's Voice for the Earth on the Revised Tentative Amended Report and a response addressing these comments are also included in this report package.

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

2. Inositol – FR (Priya) – ***Dr. Cohen reports on day 2*** – At the June 2024 meeting, the Panel reviewed the Draft Report of this ingredient and issued a Tentative Report for public comment with the conclusion that Inositol is safe in cosmetics in the present practices of use and concentration described in the safety assessment.



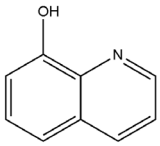
D-*chiro*-inositol *myo*-inositol

It should be noted that updated concentration of use data have been received from the Council. This ingredient is now reported to be used at up to 4% in face and neck preparations; it was previously reported to be used at up to 2% in this product category in 2022. In addition, the RLD have been included in the report alongside 2023 FDA VCRP data. Inositol is reported to be used in 212 and 1167 total formulations according to VCRP data and RLD, respectively.

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

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

1. Oxyquinoline – RR (Priya) – ***Dr. Belsito reports on day 2*** - The Panel first published a review of the safety of Oxyquinoline and Oxyquinoline Sulfate in 1992. The Panel concluded that there were insufficient data to conclude on the safety of these ingredients. In 2006, the Panel published a Final Amended Report on these ingredients, and 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, please note that 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.



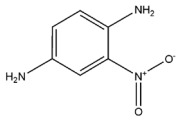
In October 2024, an extensive search of the world's literature was performed for studies dated 2001 forward. A historical overview, comparison of original and new use data, the search strategy used, and a synopsis of notable new data are enclosed herein.

In 2002, Oxyquinoline and Oxyquinoline Sulfate were reported to be used in 4 formulations (at up to 0.1%) and 7 formulations (at up to 0.1%), respectively. According to 2023 FDA VCRP data, Oxyquinoline and Oxyquinoline Sulfate were reported to be used in 1 formulation and 19 formulations, respectively. Also according to 2023 data, Oxyquinoline Sulfate is reported to be used in 2 lipstick formulations. 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%).

Ample new data have been found since the last iteration of the report. Of note are the developmental and reproductive toxicity assays, as toxicity was seen; no reproductive and developmental toxicity assays were included in the original report. Also of note are dermal sensitization assays suggesting that these ingredients

may be sensitizers.

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

2. 2-Nitro-*p*-Phenylenediamine – RR (Christina) – ***Dr. Cohen reports on day 2*** – 

The Panel first published a review of the safety of 2-Nitro-*p*-Phenylenediamine and 4-Nitro-*o*-Phenylenediamine in 1985. The Panel concluded that these ingredients are skin sensitizers for guinea pigs. Information in this report and in the report on *p*-phenylenediamine suggests that these ingredients have potential for human sensitization. For those persons not sensitized, the Panel concludes that 2-Nitro-*p*-Phenylenediamine and 4-Nitro-*o*-Phenylenediamine are safe as hair dye ingredients at the current concentration of use. The Panel previously considered a re-review of this report in 2003 and reaffirmed the 1985 conclusion, as published in 2006.

In October 2024, an extensive search of the world's literature was performed for studies dated 2002 forward. A historical overview, comparison of original and new use data, the search strategy used, and a synopsis of notable new data are enclosed herein.

In 2023 FDA VCRP data, 2-Nitro-*p*-Phenylenediamine was reported to have 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 2022 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.

The VCRP data in 2023 reported 3 uses in hair dyes and colors; 22 uses in hair dyes and colors were reported in 2002. The maximum concentration of use range reported in 2003 was 0.1 - 0.2% in hair dyes and colors. In 2022, the maximum concentration of use for 4-Nitro-*o*-Phenylenediamine was reported to be slightly increased, at 0.33% in hair dyes and colors.

Many new studies have been identified in the published literature. Several studies were identified in which 4-Nitro-*o*-Phenylenediamine was used as a positive control in antimutagenic studies of different botanical compounds; however, these studies were not included in the new data table as the original report and the first re-review contained multiple studies that established the mutagenic effect of 4-Nitro-*o*-Phenylenediamine in Ames tests.

It should be noted that at the time the original report was written, no restrictions for the use of 2-Nitro-*p*-Phenylenediamine or 4-Nitro-*o*-Phenylenediamine in cosmetic products were in effect in Europe; however, European regulations regarding cosmetic ingredients now categorize 2-Nitro-*p*-Phenylenedaimine in Annex II, the list of substances prohibited in cosmetic products, and 4-Nitro-*o*-Phenylenediamine in Annex III, the list of substances which cosmetic products must not contain except subject to the restrictions laid down. In an opinion published in 2006, the SCCP determined that 4-Nitro-*o*-Phenylenediamine does not pose a risk to the health of the consumer when used in oxidative hair dye products at a maximum on-head concentration of 0.5%. The SCCP calculated an MOS of 357.

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

Administrative Item - there are 5 administrative items.

RRsums - The Panel is being asked for editorial comment.

1. Castor Oil – RRsum – (Monice) – ***Dr. Belsito reports on day 2*** – The Panel should carefully consider the rereview summary and finalize it.
2. PEG Stearates – RRsum – (Monice) – ***Dr. Cohen reports on day 2*** – The Panel should carefully consider the rereview summary and finalize it.

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

3. Inhalation – Admin (Jinqiu) – ***Dr. Belsito reports on day 2*** – The Panel last published an update of this document to the CIR website at the December 2021 meeting. Subsequent revisions were made at

the December 2023 meeting to incorporate additional particle size data in some types of propellant-based sprays, such as dry shampoos in powdered galenic formulations.

The Panel should review the revised Document to assess the relevance and applicability of the inhalation BP, and update it as necessary to align with their understanding of exposure to airborne particles/droplets from the use of spray products, and issue the document to replace the currently posted version. If there are concerns that are not adequately addressed, the Panel should determine the necessary revisions and the extent to which further modifications are required.

4. MOE – Admin (Jinqiu) – ***Dr. Cohen reports on day 2*** - On May 6, 2024, the CIR Science and Support Committee (CIR SSC) submitted a comment on the differentiation between the terms MOE and Margin of Safety (MOS). The Panel noted that MOS and MOE are often used interchangeably in the scientific literature, and highlighted the importance of transparency in determining Point of Departure (POD) and the application of uncertainty or extrapolation factors in exposure assessments and calculations of protective margins. The Panel further requested the definitions used in Quantitative Risk Assessment (QRA) be easily accessible through a resource document on the CIR website.

   Additionally, after reviewing the comments on quantitative systemic risk assessments, submitted by the CIR SSC on February 7, 2024, the Panel agreed that the decision to include a systemic QRA in reports should be determined on a case-by-case basis. In cases where MOE is considered inappropriate, the Panel requested that an explanation should be provided in the discussion to ensure transparency and clarity. The Panel acknowledged that the calculation of an MOE can vary depending on endpoints of concern and should be established based on valid PODs (e.g., NOAELs and LOAELs), which should be identified and substantiated by the data included in CIR report.

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

Strategy Memo – The RAWG and the Full Panel are being asked separate questions.

5. Fatty Amphocarboxylates – SM (Priya) – ***Drs. Cohen and Rettie-(providing the Panel input from the RAWG) report on day 2*** - At the June 2024 meeting, the Panel reviewed the Revised Draft Report on the 11 fatty amphocarboxylates, along with justification tables on potential read-across substances, and issued an IDA. In order to conclude on the safety of these ingredients, the Panel requested 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 and fatty acid compositions)
   - Sensitization data on Sodium Lauroamphoacetate at maximum use concentration
   - Sensitization data on Disodium Lauroamphodiacetate at maximum use concentration

   Since the issuing of the IDA, quantitative structure-activity relationship (QSAR) skin sensitization predictions on C12 diacetate 1, C12 diacetate 2, C12 monoacetate 1, and C12 monoacetate 2 have been received from the REACH Amphoacetates Consortium. In addition, the Consortium stated that a prenatal developmental toxicity study in rabbits performed using C8-18 (diacetate form) is currently underway and would likely be finalized by the end of April 2025. Accordingly, the Consortium proposed that the Expert Panel table this assessment until June 2025 to ensure all information has been received prior to the next review of this report.

   The Read-Across Working-Group (RAWG) is thus being asked (we have set aside 30 minutes following lunch on Day 1 for the RAWG to discuss these data):

   1. Are the QSAR skin sensitization predictions on C12 diacetate 1, C12 diacetate 2, C12 monoacetate 1, and C12 monoacetate 2 appropriate for inclusion in the report? Do these data help to fill the stated gaps for sensitization of Sodium Lauroamphoacetate and/or Disodium Lauroamphodiacetate?

   The full Panel is being asked (as an agenda item in each breakout team):

   2. Would the Panel like to table this report, as proposed by the Consortium, to allow for all information to be received prior to the next review of this report? What is the Panel's deadline for receiving these data?

Full Panel Meeting

The Panel will consider the 2 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 2 rereview documents, 2 rereview summaries, inhalation and MOE resource documents, and the strategy memo.

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

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

Agenda
171st Meeting of the Expert Panel for Cosmetic Ingredient Safety
December 2 – 3, 2024

Monday, December 2, 2024		
9:30 AM EST	**WELCOME TO THE 171st EXPERT PANEL TEAM MEETINGS**	**Drs. Bergfeld/Heldreth**
9:45 AM	**PRESENTATION – FDA Registration and Listing Data**	**Dr. Heldreth**
10:30 AM - 12 PM	**TEAM MEETINGS**	**Drs. Belsito/Cohen**
12 PM – 1 PM	**Lunch break**	
1 PM – 1:30 PM	**Read-Across Working Group (RAWG)**	**Dr. Rettie**
1:30 PM - 6 PM	**TEAM MEETINGS (continued)**	**Drs. Belsito/Cohen**

Dr. Belsito's Team

FAR (CB)	*p*-Phenylenediamine
TAR (CB)	4-Chloro-2-Aminophenol
DAR (CB)	Pyrogallol
DR (CB)	Tetrabromophenol Blue
RR (CB)	2-Nitro-*p*-Phenylenediamine
RRSum (BH|MF)	Castor Oil
RRSum (BH|MF)	PEG Stearates
TR (TD)	*Paeonia suffruticosa*
DR (TD)	*Nelumbo nucifera*
DAR (TD)	Potassium Cocoyl Hydrolyzed Collagen
FR (PC)	Inositol
RR (PC)	Oxyquinoline
SM (PC)	Fatty Amphocarboxylates
Admin (JZ)	MOE Resource Paper
Admin (JZ)	Inhalation Resource Paper

Dr. Cohen's Team*

TR (TD)	*Paeonia suffruticosa*
DR (TD)	*Nelumbo nucifera*
DAR (TD)	Potassium Cocoyl Hydrolyzed Collagen
FR (PC)	Inositol
RR (PC)	Oxyquinoline
SM (PC)	Fatty Amphocarboxylates
Admin (JZ)	MOE Resource Paper
Admin (JZ)	Inhalation Resource Paper
RRSum (MF|BH)	Castor Oil
RRSum (MF|BH)	PEG Stearates
FAR (CB)	*p*-Phenylenediamine
TAR (CB)	4-Chloro-2-Aminophenol
DAR (CB)	Pyrogallol
DR (CB)	Tetrabromophenol Blue
RR (CB)	2-Nitro-*p*-Phenylenediamine

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

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

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

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

Tuesday, December 3, 2024			
9:30 AM EST	**WELCOME TO THE 171st FULL EXPERT PANEL MEETING**		**Dr. Bergfeld**
9:40 AM	Admin **MINUTES OF THE SEPTEMBER 2024 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		
	FR (PC)	Inositol – ***Dr. Cohen reports***	
	FAR (CB)	*p*-Phenylenediamine – ***Dr. Belsito reports***	
	Reports Advancing		
	DR (CB)	Tetrabromophenol Blue – ***Dr. Cohen reports***	
	TAR (CB)	4-Chloro-2-Aminophenol – ***Dr. Belsito reports***	
	DAR (CB)	Pyrogallol – ***Dr. Cohen reports***	
	DR (TD)	*Nelumbo nucifera*-derived ingredients – ***Dr. Belsito reports***	
	TR (TD)	*Paeonia suffruticosa*-derived ingredients – ***Dr. Cohen reports***	
	DAR (TD)	Potassium Cocoyl Hydrolyzed Collagen – ***Dr. Belsito reports***	
	Other Items		
	SM (PC)	Fatty Amphocarboxylates – ***Dr. Cohen reports***	
	RR (PC)	Oxyquinoline – ***Dr. Belsito reports***	
	RR (CB)	2-Nitro-*p*-Phenylenediamine – ***Dr. Cohen reports***	
	RRsum (MF)	Castor Oil – ***Dr. Belsito reports***	
	RRsum (MF)	PEG Stearates – ***Dr. Cohen reports***	
	Admin (JZ)	Inhalation Resource Paper – ***Dr. Belsito reports***	
	Admin (JZ)	MOE Resource Paper – ***Dr. Cohen reports***	

ADJOURN – *The next will be held in-person on **March 13 -14, 2025** (Thursday & Friday) at the Marriott Georgetown Hotel, 1221 22nd Street, NW, Washington, DC. Please check the CIR website for details as the meeting approaches*

On the basis of all data and information submitted, and after following all of the Procedures (https://www.cir-safety.org/supplementaldoc/cir-procedures), the Expert Panel shall determine whether each ingredient, under each relevant condition of use, is safe, safe with qualifications, 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

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ONE HUNDRED SEVENTIETH MEETING

OF THE

EXPERT PANEL FOR COSMETIC INGREDIENT SAFETY

September 30 - October 1, 2024

Westin Georgetown
2350 M 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

Curtis D. Klaassen, Ph.D.

Allan E. Rettie, Ph.D.

David Ross, Ph.D.

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

Susan Tilton, Ph.D.

Liaison Representatives

Consumer

Courtney Griffin, J.D.

Industry

Alex Kowcz, M.B.A.

Government

Hong Xie, Ph.D.

Jannavi Srinivasan, Ph.D.

Prashiela Manga, Ph.D.

Janet Zang, Ph.D.

_____
Adopted (Date)

_____
Wilma F. Bergfeld, M.D.

CIR Staff

Administration
Bart Heldreth, PhD - Executive Director

Monice Fiume, MBA - Senior Director

Carla Jackson - Administrative Coordinator

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

Analysis
Christina L. Burnett, MSES - Senior Scientific Analyst

Priya Cherian, MS - Senior Scientific Analyst

Thushara Diyabalanage, PhD–Senior Scientific Analyst

Information Services
Kevin Stone Fries, MLS - Information Services Manager

Other In-Person Meeting Attendees

Name	***Organization***
Don Bjerke	Procter & Gamble
Carol Eisenmann	Personal Care Products Council
Kimberly Norman	Personal Care Products Council
Allison Schafer	Procter & Gamble
Kathy Stanton	Personal Care Products Council
Homer Swei	Environmental Working Group

Other Vitrual Meeting Attendees

Name	**Organization**
Ayodele Ajayi	June Jacobs Labs
Nadine Bewry	Opella
Anne Corriou	Givaudan
Jose Flores	Eastman LAR Distribution
Lama Hamieh	Dr. Burgener
Annie James	Henkel Corp.
Cici Jiang	Yatsen
Miao Li	FDA
Kris Miles	The Honey Pot Co.
John Milligan	The Honey Pot Co.
Lauren Nardella	HBW Insight
Robin Newkold	Inolex
Jeffrey Nicolai	J. Nicolai Law Firm
Carrie Ohalloran	The Honey Pot Co.
Thaisa Oliveira	Avanzza
Stefanie O'Neal	Kao USA, Inc.
Soo Jin Park	LG H&H USA, Inc./The Avon Co.
Yang Qiongli	Yatsen Holding Ltd.
Vasundhara Raut	Hindustan Unilever
Charmaine Rodriques	LVMH
Barbara Schmitt	Evonik
Jan Summers	Opella
Liza Van Den Eede	Eastman
Amparo Villarreal	Independiente
Joseph Wang	MasterGlam
Zemin Wang	FDA
Teresa Washington	FDA
Sun Wen	Yatsen Global
Leah Yip	Public observer

CHAIRPERSON'S OPENING REMARKS

Dr. Bergfeld welcomed the attendees to the 170th meeting of the Expert Panel for Cosmetic Ingredient Safety. At this meeting, Dr. Bergfeld noted that the Panel reviewed 11 ingredient reports, including 7 finals, 1 tentative, 3 draft reports, and 5 re-reviews. The Panel also reviewed the 2025 priorities and an inhalation boilerplate. Dr. Bergfeld expressed gratitude that wave 2 submissions were minimal. Dr. Bergfeld also thanked the CIR staff for their continuing work in presenting high-quality documents to the Panel and the Personal Care Products Council and CIR Science and Support Committee for their helpful input.

Dr. Bergfeld acknowledged the receipt of the new US FDA Registration and Listing Data (RLD) and expressed interest in how the new data will be incorporated into the safety assessments in the future.

APPROVAL OF MINUTES

The minutes of the June 3-4, 2024 (169th) Expert Panel meeting were approved.

DIRECTOR'S REPORT

Dr. Heldreth thanked the members of and liaisons to the Panel for their tireless efforts to protect consumers. He also thanked colleagues at the Office of Cosmetics and Colors for their assistance in understanding the US FDA RLD, which CIR received in response to an FOIA request this summer. While CIR had grown accustomed to the VCRP data received in the past, which were ingredient-centric, the RLD will take some processing to be useful to CIR and the Panel, as these data are product-centric. Dr. Heldreth was confident that CIR could parse out all of the information needed therein and run some quality control to ensure quality and confidence in the output.

Additionally, Dr. Heldreth announced a call for nominations for a new member of the Panel. Specifically, the Panel is seeking to add an expert in carcinogenesis, mutagenesis, genotoxicity, and tumorigenesis. Nominees must have no financial conflicts of interest; a copy of the Panel's conflict of interest statement may be found on their website https://ingredientsafetyexpertpanel.org/conflict-of-interest-statement. Nominations may be sent directly to Dr. Heldreth at heldretb@cir-safety.org.

FINAL SAFETY ASSESSMENTS

4-Amino-*m*-Cresol

The Panel issued a Final Amended Report with the conclusion that 4-Amino-*m*-Cresol is safe for use as a hair dye ingredient in the present practices of use and concentration described in the safety assessment. The Panel previously reviewed this ingredient as part of a larger group of amino-cresol hair dyes; however, because the Panel determined that data for those amino cresol hair dye ingredients could not be read-across the group, re-reviews of each hair dye included in that original 2004 report were presented as individual stand-alone reports, including this one.

4-Amino-*m*-Cresol 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 Food, Drug, and Cosmetic (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 4-Amino-*m*-Cresol absorbs slowly through the skin and has low concentrations of use. Additionally, a margin of exposure (MOE) calculation yielded a result greater than 100, which is generally considered to be protective. The Panel considered these findings, coupled with the short exposure time as a rinse-off product, and determined that the data are sufficient to conclude that 4-Amino-*m*-Cresol is safe as a hair dye ingredient in the present practices of use and concentration described in the report.

Lanolin Ingredients

The Panel issued a Final Amended Report with the conclusion that the following 9 lanolin-derived ingredients are safe in cosmetics in the present practices of use and concentration described in the safety assessment:

Acetylated Lanolin
Acetylated Lanolin Alcohol
Hydrogenated Lanolin
Hydroxylated Lanolin
Lanolin
Lanolin Acid
Lanolin Alcohol
Lanolin Oil
Lanolin Wax

The Panel discussed the "lanolin paradox" where Lanolin may cause allergic contact dermatitis when applied to damaged skin, but allergenicity does not appear in these apparently sensitized patients when Lanolin is applied to normal, healthy skin in patch tests. The rate of allergic reactions to Lanolin is extremely low in the general population, and sensitization can be further reduced when Lanolin is ultra-refined to reduce the amount of free Lanolin Alcohol. The Panel expressed concern regarding heavy metals that may be present in these ingredients. They stressed that the cosmetics industry should continue to use the necessary procedures to minimize impurities in cosmetic formulations according to limits set by the FDA and EPA. The Panel was also 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 infectious agents (e.g., prions), and/or biologically-derived impurities.

Toluene

The Panel issued a Final Amended Report with the conclusion that Toluene is safe for use in nail products at concentrations up to 20%. No uses are reported for Toluene according to 2023 US FDA VCRP data; however, according to a concentration of use survey performed in 2023 and updated in 2024, Toluene is used at

up to 20% in nail polish and enamel. (It should be presumed that there is at least one use for every category for which a concentration is reported.) Additionally, the Panel noted the presence of Toluene at low concentrations in non-nail products (e.g., hair conditioners). Because these concentrations are considered to be residual amounts/impurities, and not the intentional addition of Toluene in cosmetic products, the Panel reviewed the use of Toluene in only nail products. The safety of this ingredient in nail products was supported by a lack of irritation and sensitization in human assays and conservative MOE calculations (based on both neuropathological and developmental and reproductive toxicity endpoints) yielding values greater than 100.

MIBK

The Panel issued a Final Amended Report concluding that MIBK is safe as used in nail polish removers and as an alcohol denaturant in cosmetics in the present practices of use and concentration described in the safety assessment. At the December 2023 meeting, the Panel concluded that MIBK is safe as used in nail care products and as an alcohol denaturant in nail polish removers. However, at the March 2024 meeting, due to the absence of recent use information regarding the broad area of nailcare, the Panel decided to issue a more restrictive conclusion, reaffirming their previous conclusion as issued in 2004. The Panel concluded that MIBK is safe as used in nail polish removers (as opposed to nail care products) and as an alcohol denaturant in cosmetics in the present practices of use and concentrations described in this safety assessment. Since no current concentrations of use are reported, it is expected that this ingredient would be used at concentrations comparable to those reported in the 2004 safety assessment.

BHA

The Panel issued a Final Amended Report with the conclusion that BHA is safe in cosmetics in the present practices of use and concentration as described in the safety assessment. A safety assessment on BHA was first published in 2005, with a conclusion of safe as a cosmetic ingredient in the present practices of use (as described in the safety assessment); that conclusion was reaffirmed, as published in 2006. A re-review was initiated at the June 2023 Panel meeting to evaluate the potential endocrine and reproductive effects of BHA at high doses and to provide an updated assessment of the safety of this ingredient. With regard to any concern for potential endocrine and reproductive effects of BHA at high doses, the Panel considered the developmental and reproductive toxicity and endocrine studies presented in the amended report. The Panel stated that any observed developmental and reproductive, endocrine, androgenic, and estrogenic effects were seen primarily in cell systems and at concentrations far in excess of those derived from cosmetic exposures, thus mitigating any concerns.

The *International Cosmetic Ingredient Dictionary and Handbook* (Dictionary) defines BHA as a mixture of *tert*-butylated 4-hydroxyanisole isomers which consists chiefly of 3-*tert*-butyl-4-hydroxyanisole with lesser amounts of 2-*tert*-butyl-4-hydroxyanisole. Thus, data found on BHA in both isomeric forms were included in this assessment.

***t*-Butyl Alcohol**

The Panel issued a Final Amended Report with the conclusion that *t*-Butyl Alcohol is safe in cosmetics in the present practices of use and concentration described in the safety assessment. The initial safety assessment of *t*-Butyl Alcohol was published in 2005, with a conclusion of safe as used in cosmetic products. A re-review was initiated at the September 2023 Panel meeting to evaluate developmental and reproductive toxicity effects, to update the previous discussion of carcinogenicity, and to rectify the erroneous test concentration reported in an HRIPT in the original assessment.

The Panel asserted they were in agreement with their previous review, which stated that the developmental effects of *t*-Butyl Alcohol were likely secondary to maternal toxicity and that the effects on learning development were attributable to *t*-Butyl Alcohol in maternal milk and were not an *in utero* effect. Additionally, the Panel discussed the carcinogenicity studies and determined that the weight-of-evidence does not support a carcinogenic effect. Also, the Panel determined that a negative guinea pig maximization test mitigated the need for confirmatory sensitization data at maximum concentration of use. Finally, it was noted that *t*-Butyl Alcohol showed low potential for dermal absorption and bioaccumulation.

Pentapeptide Ingredients

The Panel issued a Final Report with the conclusion that Myristoyl Pentapeptide-4, Palmitoyl Pentapeptide-4, and Pentapeptide-4 (KTTKS and KTSKS sequences) are safe in cosmetics in the present practices of use and concentration described in the safety assessment. The amino acid sequence of the pentapeptide portion of these ingredients can vary; one sequence is lysine-threonine-threonine-lysine-serine (i.e., Lys-Thr-Thr-Lys-Ser, or, KTTKS), and the other is Lys-Thr-Ser-Lys-Ser (or KTSKS). According to the *Dictionary*, Palmitoyl Pentapeptide-4 is associated with the Pal-KTTKS and Pal-KTSKS sequences; Pentapeptide-4 and Myristoyl Pentapeptide-4 are only associated with the KTTKS amino acid sequence.

Data on Palmitoyl Pentapeptide-4 demonstrated limited dermal absorption, and log p values received for all 3 ingredients indicated that the dermal penetration of Myristoyl Pentapeptide-4 would be less than Palmitoyl Pentapeptide-4. Thus, the Panel found the data sufficient to conclude on the safety of Palmitoyl Pentapeptide-4, Myristoyl Pentapeptide-4, and Pentapeptide-4 when these ingredients are comprised of one of either the KTTKS or KTSKS sequences. The Panel noted the lack of developmental and reproductive toxicity and carcinogenicity data; however, the low reported maximum concentration of use for these ingredients, the limited percutaneous absorption evidenced in vitro, the negative genotoxicity studies, and negative results obtained in response to a formulation containing 0.12% Palmitoyl Pentapeptide-4 (Pal-KTSKS) in an estrogen agonist assay mitigated the need for such data.

TENTATIVE SAFETY ASSESSMENTS

2,4-Diaminophenoxyethanol

The Panel issued a Tentative Amended Report for public comment with the conclusion that 2,4-Diaminophenoxyethanol HCl and 2,4-Diaminophenoxyethanol Sulfate are safe for use as hair dye ingredients in the present practices of use and concentration described in the safety assessment.

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

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.

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.

Copper Gluconate

The Panel issued a Tentative Report for public comment with the conclusion that Copper Gluconate is safe for use as a cosmetic ingredient in the present practices of use and concentration described in the safety assessment. 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 some carcinogenic effects 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.

INSUFFICIENT DATA ANNOUNCEMENTS

Basic Blue 7

The Panel issued an IDA for Basic Blue 7. The following information is required to determine the safety of this ingredient:

- 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
- Dermal irritation and sensitization data

Propylene Carbonate

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

- Ultraviolet light (UV) absorption data
    - If a UV absorption λ_{max} is evident, phototoxicity/photosensitization data are needed
- Concentration of use in baby products

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 previous assessments for re-review. The Panel determined that the following report should be reopened; a Draft Amended Report will be presented to the Panel for this ingredient at a later meeting.

- 2-Bromo-2-Nitro-1,3-Propanediol – 1 ingredient

The Panel reaffirmed the conclusions reached for 2 of these safety assessments (i.e., chose to not re-open the original reports). A re-review summary for each of these safety assessments will be presented to the Panel at an upcoming meeting.

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

The Panel determined that the new data for the following 2 reports was significant, but would ultimately not change the conclusion of their original safety assessment in each case. The Panel would like the CIR Steering Committee to consider a new type of report output, which falls somewhere in between a re-review summary and a full, amended report, to showcase significant new data. Accordingly, the Panel tabled these reports to await a response from the CIR Steering Committee.

- Ascorbic Acid – 6 ingredients
- Isopropanolamines – 4 ingredients

Inhalation BP

The Panel discussed the factors involved in evaluating the safety of incidental inhalation of particles/droplets from cosmetics and the necessary context for applying the inhalation boilerplate (BP) in the report. The Panel requested the inhalation BP be updated, along with the Respiratory Exposure Resource Document to clarify the rationale for these updates, and to more accurately reflect the Panel's understanding of exposure to airborne particles/droplets from various cosmetic sprays and the associated health risks. The current Respiratory Exposure Resource Document is available at the CIR Findings page, https://www.cir-safety.org/cir-findings. A draft update of this document, including this inhalation BP, will be presented at a future meeting.

Priorities

There are 18 reports docketed, covering 32 ingredients, on the 2024/2025 Final Priorities List. While the priority list includes only the lead ingredients, groupings of ingredients for reports can be found on the CIR Findings page. Reports previously prioritized and on the CIR docket (including Dimer Dilinoleate, *Lactobacillus* ferment ingredients, *Salix alba* (willow)-derived ingredients, HC Blue No. 1, *Pelargonium graveolens*-derived ingredients, *Houttuynia cordata*-derived ingredients, Sigesbeckia Orientalis Extract, *Centaurea cyanus* flower-derived ingredients, and Sodium Hydrosulfite), as well as an extensive number of re-reviews of previous assessments, will supplement the total number of reports/ingredients to be assessed in 2024/2025, and beyond. Rereviews to potentially be considered for reopening during 2024/2025, based on time passed since last assessment, include:

2-Nitro-p- & 4-Nitro-o-Phenylenediamine
Aloe-derived ingredients
Butylene Glycol, etc.
Capsaicin, etc.
Dimethicone Copolyol ingredients
Ethyl Methacrylate
Fossil & Synthetic Waxes (e.g., Ozokerite)
Glyceryl Monoesters
Glycyrrhetinic Acid, etc.
Maleic Acid
Methacrylic Acid
p-Methylaminophenol & Sulfate
Niacinamide & Niacin
Oryza sativa (rice)-derived ingredients
Oxyquinoline & Oxyquinoline Sulfate
PEGs Laurate
Sodium & Ammonium Lauryl Sulfate
Sodium p-Chloro-m-Cresol, etc.
Stearyl Alcohol, etc.
Tosylamide/Formaldehyde Resin
Urea
Waxes (e.g., Candelilla)

Thus, interested parties are again encouraged to submit pertinent data to CIR as soon as possible for use in the development of the Scientific Literature Reviews (SLR), and to participate in meetings of the Panel, for the ingredients on the 2024/2025 Final Priorities List. Although the specific data needs vary for each safety assessment, the following are typical data that the Panel reviews for each safety assessment. The Panel also implores stakeholders to make use of, and submit, new/non-animal approach methodologies (NAMs), along with an appropriate level of support to induce confidence that the use of such methodologies is protective.

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

For the review of natural complex substances (NCS), including botanical or animal derived ingredients, the additional data needed include: species, organism part, extraction method, solvent, and data on component chemical characterization. It is important that these data are specific for the ingredient(s) as used in cosmetics.

2024/2025 Final Priorities List

Ingredient	Frequency of Use (FOU) - VCRP Data Year: 2023
For cause	
Cannabidiol	32
Trimethylbenzoyl Diphenylphosphine Oxide	127
Tetrabromophenol Blue	2
Per FOU (VCRP)	
Polyacrylate-13	**265**
Polygonum Cuspidatum Root Extract	**245**
Xylitylglucoside	**213**
Phytosphingosine	**210**
Sodium Hyaluronate Crosspolymer	**207**
Polyacrylate Crosspolymer-6	**205**
Trimethylpentanediyl Dibenzoate	**202**
Tosylamide/Epoxy Resin	**189**
Carnosine	**184**
Madecassoside	**182**
Propolis Extract	**179**

Sophora Flavescens Root Extract	**179**
Curcuma Longa (Turmeric) Root Extract	**177**
Lonicera Japonica (Honeysuckle) Flower Extract	**175**
Perfluorohexylethyl Triethoxysilane	**172**