

ADMIN

Memo

Agenda

Minutes

EXPERT PANEL MEETING

September 26-27, 2022



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## MEMORANDUM

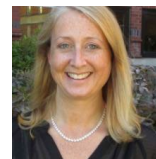
To: The Expert Panel for Cosmetic Ingredient Safety Members and Liaisons  
From: Bart Heldreth, Ph.D., Executive Director, Cosmetic Ingredient Review  
Subject: 162<sup>nd</sup> Meeting of the Expert Panel — Monday and Tuesday, September 26-27, 2022  
Date: September 1, 2022

Welcome to the third Panel Meeting of 2022! The agenda and accompanying materials for the 162<sup>nd</sup> Expert Panel Meeting, to be held on September 26-27, 2022, are now available. Please note that this meeting is on a **Monday and Tuesday**. The location is the **same** as in June – this meeting will be held virtually. Invitations (3 of them) to join the meeting will arrive separately in your email inbox. Panel members and liaisons will be registered **automatically**. However, other interested parties may register to attend in advance of the meeting at the meeting page:

<https://www.cir-safety.org/meeting/162nd-expert-panel-meeting>

The meeting agenda includes the consideration of 12 reports advancing in the review process, including 6 final reports, 2 tentative reports, and 4 draft reports. Also on the agenda, are 7 rereview documents; **in each case, the Panel is only being asked if the report should be reopened**. Additionally, there are 12 administrative items: the draft final 2023 Priorities, 3 strategy memos, a report format & SOPs review, and 7 rereview summaries. In addition, the team meetings on Day 1 will kick-off with speakers (Dr. Sylvain Mazalrey and Audrey Pokrzywa) on the topic of yeast-derived cosmetic ingredients. The speakers will be available for questions during each of the team meetings.

Hellos and goodbyes. We are now very happy to welcome world-class expert, Dr. Susan Tilton, to the Panel. Dr. Tilton brings a wealth of expertise in chemistry and toxicology, including specialized experience in bioinformatics, carcinogenicity, and inhalation toxicology. More information on Dr. Tilton, and all current Panel members, may be found at the Panel's membership page, <https://ingredientsafetyexpertpanel.org/membership/>.

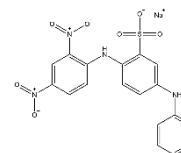


Dr. Susan Tilton

However, we are also sad to say goodbye to Dr. Dan Liebler following this meeting. Dr. Liebler has been with us since 2009, making a powerful impact on the Panel in chemistry, toxicology, and especially in the pioneering of read-across, adoption of New Approach Methodologies, and delivery of science humor 🍷 😊.

Team Meetings**Draft Report - There are 4 draft reports for review. - Sufficient data to proceed, or issue an IDA?**

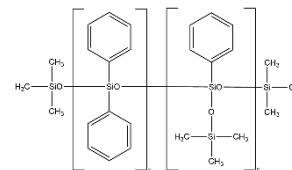
1. Acid Orange 3 – DAR (Christina) – **Dr. Belsito reports on day 2** - Acid Orange 3 was previously reviewed by the Expert Panel for Cosmetic Ingredient Safety (Panel) in a safety assessment that was published in 2000. At that time, the Panel concluded that Acid Orange 3 is safe for use in hair dye formulations at concentrations < 0.2%. In June 2022, the Panel re-opened the safety assessment for this ingredient, which functions as a hair colorant, due to it being banned for use in cosmetics by the European Commission. The Panel also noted reported uses in a non-hair dye cosmetic formulation.



According to 2022 VCRP survey data, Acid Orange 3 is used in one non-hair dye formulation: a nail polish and enamel (VCRP\_AcidOrange3\_092022). The results of the concentration of use survey provided by the Council in 2022 indicate that there are no uses for this ingredient. When the original safety assessment was published in 2000, Acid Orange 3 was reported to be used in 4 hair dye formulations (data acquired in 1997). At that time, concentrations of use were no longer reported by the FDA; however, data available from the FDA in 1984 indicate that Acid Orange 3 was used in one hair dye formulation at a concentration between 10% and 25%, and 33 uses were reported at < 1%.

Since the reopening of this report at the June meeting, no new data have been received. After reviewing these documents, if the available data are deemed sufficient to make a determination of safety, the Panel should issue a Tentative Report with a safe as used, safe with qualifications, unsafe, or split conclusion, and Discussion items should be identified. If the available data are insufficient, the Panel should issue an Insufficient Data Announcement (IDA), specifying the data needs therein.

2. Phenyl-Substituted Methicones – DR (Preethi) – **Dr. Belsito reports on day 2** – Please note that this report is presented in 3 separate pdf files. This is the first time the Panel is seeing a safety assessment of this group of 7 cosmetic ingredients. A Scientific Literature Review (SLR) was announced on April 7, 2022. However, the Panel has previously reviewed the safety of Phenyl Trimethicone, and in 1986 published the conclusion that Phenyl Trimethicone is safe as a cosmetic ingredient in the practices of use and concentration described in that safety assessment. The Panel reaffirmed this conclusion, as published in 2006.

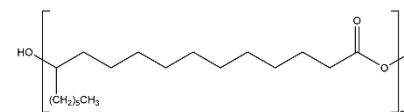


According to 2022 VCRP survey data, Phenyl Trimethicone has the greatest reported frequency of use; it is reported to be used in 781 formulations, 722 of which are leave-on products. Diphenylsiloxyl Phenyl Trimethicone is reported to be used in 269 formulations, and Diphenyl Dimethicone is reported to be used in 145 formulations. The results from concentration of use surveys conducted by the Council in 2021 and 2022 indicate that Phenyl Trimethicone has the highest reported maximum concentration of use, at 59.5% in non-coloring shampoos; it also has the highest reported maximum concentration of use in leave-on formulations, at up to 24.8% (in other makeup preparations). Use concentration data were reported for Diphenylsiloxyl Phenyl/Propyl Trimethicone in makeup bases at 5.3%, but no uses were received in the VCRP; it should be presumed there is at least one use in this category.

Following the announcement of the SLR, a significant quantity of data were received. These data include (repeated) human patch tests, irritation assays, photosensitization potential, and other endpoints.

After reviewing these documents, if the available data are deemed sufficient to make a determination of safety, the Panel should issue a Tentative Report with a safe as used, safe with qualifications, unsafe, or split conclusion, and Discussion items should be identified. If the available data are insufficient, the Panel should issue an IDA, specifying the data needs therein.

3. Polyhydroxystearic Acid – DR (Preethi) – **Dr. Cohen reports on day 2** - This is the first time the Panel is seeing a safety assessment of these 3 polymeric cosmetic ingredients. An SLR



was announced on March 29, 2022. The Panel has previously reviewed the safety of the monomers of these ingredients, namely, hydroxystearic acid (original review published in 1999; conclusion reaffirmed in 2015) and lactic acid (original report published in 1998; conclusion reaffirmed in 2017).

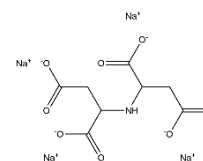
According to 2022 VCRP survey data, Polyhydroxystearic Acid is reported to be used in 265 formulations, of which 116 uses are in lipsticks, and Polylactic Acid is reported to be used in 18 formulations. Results from a 2021 concentration of use survey, conducted by the Council, indicate Polyhydroxystearic Acid has the highest reported concentration of use; it is used at up to 14.2% in lipsticks. Polylactic Acid is reported to be used at up to 5% in skin cleansing products. Poly(3-Hydroxyoctanoic Acid) is not reported to be in use according to the VCRP and industry survey.

Following the announcement of the SLR, data were submitted. These data include chemistry, and various skin studies.

After reviewing these documents, if the available data are deemed sufficient to make a determination of safety, the Panel should issue a Tentative Report with a safe as used, safe with qualifications, unsafe, or split conclusion, and Discussion items should be identified. If the available data are insufficient, the Panel should issue an IDA, specifying the data needs therein.

4. Trisodium Ethylenediamine Disuccinate – DR (Priya) – **Dr. Cohen reports on day**

**2** - This is the first time the Panel is reviewing these 2 ingredients. The SLR was announced on June 2, 2022. Since the issuing of the SLR, no unpublished data were received; comments have been received and addressed.



According to the 2022 VCRP survey data, Trisodium Ethylenediamine Disuccinate is used in 228 formulations (68 leave-on formulations and 160 rinse-off formulations) and Tetrasodium Iminodisuccinate is used in 9 formulations (4 leave-on formulations and 5 rinse-off formulations). The results of the concentration of use survey conducted by the Council in 2021 indicate that the reported maximum concentration of use is 0.64% Trisodium Ethylenediamine Disuccinate in tonics, dressings, and other hair grooming aids; the greatest reported maximum concentration of use in products intended for dermal contact is 0.56% in moisturizing products. No concentration of use data were reported for Tetrasodium Iminodisuccinate.

After reviewing these documents, if the available data are deemed sufficient to make a determination of safety, the Panel should issue a Tentative Report with a safe as used, safe with qualifications, unsafe, or split conclusion, and Discussion items should be identified. If the available data are insufficient, the Panel should issue an IDA, specifying the data needs therein.

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

1. Clays – TAR (Christina) – **Dr. Cohen reports on day 2** – At the March 2022 meeting, the Panel determined that the data were insufficient to determine the safety of the 7 clay ingredients. The additional data needs are:



- Particle size distribution (mean and range) on all ingredients, except Bentonite
- Chronic inhalation data on all ingredients, except Attapulgate and Kaolin
- Human dermal irritation and sensitization data at maximum use concentrations

A significant quantity of data were received since the issuance of the IDA. These data include chemistry, skin irritation and sensitization, and ocular data. No chronic inhalation toxicity data were received.

Some of the data in this report are inclusive of the ingredient illite (which is a group of clay-sized micas that have a higher lattice water content and lower potassium content than mica). The US Geological Survey classifies illite as a clay; however, it uses the term “micaceous minerals” to describe it. Currently, there are 59 uses reported to the VCRP for illite and it is used at up to 0.02% in leave-on products (hair tonics and dressings) and at up to 3.8% in rinse-off products (skin cleansing products). **Does the Panel feel that this ingredient should be added to this naturally-sourced clays report?**

According to the updated concentration of use survey conducted by the Council, Kaolin has the highest concentration of use in a leave-on formulation; it is used at up to 53.2% in manicuring preparations. This is approximately the same as the previously reported maximum use concentration for Kaolin. The maximum use concentration for Bentonite in a leave-on product has decreased slightly. Currently it is reported to be used at up to 8% in skin care preparations. Previously, it was reported to be used at up to 15% in skin care preparations. Maximum use concentrations in leave-on products for the remaining ingredients either decreased slightly or were not reported.

The Women's Voices for the Earth (WVE) has provided some additional information about impurities of crystalline silica in Kaolin and Hectorite, which were identified from the websites of market products of several suppliers. WVE suggested caveats be made to avoid the application of Kaolin and Hectorite in cosmetic formulations that may be incidentally inhaled. The information from US Silica Company on calcined kaolin was not included in the report. Based on the product description compared to current data on method of manufacturing, it is not certain that this data refers to the ingredient Kaolin as found in the *Dictionary*. Likewise, information from American Colloid Company on "Hectorite" was not included as the description of the product lists Bentonite as a synonym and gives the CAS # for Bentonite, not Hectorite. It cannot be ascertained to which ingredient this information actually refers. The remaining impurities data have been incorporated into the report and highlighted to aid the Panel's review.

The WVE memo also includes some information relevant to nanoclay usage in cosmetics, which was identified from a report written by a nanotechnology research company (StatNano). This report claimed that, based on the data covered by Nanotechnology Products Database (NPD), 4% of the global nanoclay market is associated with cosmetic applications. Specifically, nanoclay has been used as cosmetic additives for lipsticks, eyeliners, and toothpaste. It should be noted that such reporting categories do not include any sprayable product type, thus mitigating the health concerns on incidental inhalation, which was raised by WVE in their comments. However, it should also be noted the NPD database that presented the statistical data was established by the same company (StatNano) that wrote the report. Therefore, it warrants further validation on the exact share percentage of cosmetics that use nanoclays in the global nanoclay market (e.g., the StatNano report stated 4% of the global nanoclay market is shared by cosmetics). Nonetheless, the information regarding the application of nanoclay in relevant cosmetic product categories has been incorporated into the report under the Cosmetic Use section for the Panel's consideration.

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

2. *Rosa centifolia* – TR (Regina) – **Dr. Belsito reports on day 2** – After reviewing the Draft Report at the March 2022 meeting, an IDA on the 12 *Rosa centifolia*-derived ingredients was issued with the following data needs:



- Method of manufacturing
- Composition and impurities data for all ingredients except flower and bud ingredients
- Dermal toxicity (28-day dermal)
  - If positive, other toxicological endpoints (e.g., developmental and reproductive toxicity, genotoxicity, carcinogenicity, etc.) may be needed

Data were received in response to some of these needs since the issuance of the IDA. These data include method of manufacture, composition, genotoxicity, and skin toxicity.

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

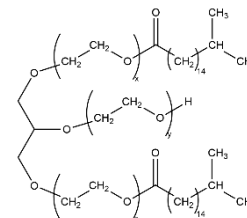
**Draft Final Reports - There are 6 Draft Final Reports for consideration. - Review these drafts, especially the rationales provided in the Discussion sections, and issue these as Final Reports, as appropriate.**

1. Diatomaceous Earth – FR (Christina) – **Dr. Cohen reports on day 2** – At the March 2022 meeting, the Panel issued a Tentative Report with the conclusion that Diatomaceous Earth is safe in cosmetics in the present practices of use and concentration as described in the safety assessment.



Since the issuance of the Tentative Report, CIR has received no new unpublished data. Comments on the Tentative Report have been received and addressed. After carefully reviewing the Abstract, Discussion, and Conclusion, the Panel should be prepared to issue a Final Report.

2. Fatty Ester End-Capped Alkoxylates – FR (Christina) – **Dr. Belsito reports on day 2** – At the June 2022 meeting, the Panel issued a Tentative Report with the conclusion that PEG/PPG-8/3 Diisostearate is safe in cosmetics in the present practices of use and concentration described in the safety assessment. However, the Panel also concluded that the available data are insufficient to make a determination of safety for the remaining 13 fatty ester end-capped alkoxylated ingredients under the intended conditions of use in cosmetic formulations. The additional data needed to determine safety for these 13 cosmetic ingredients are:

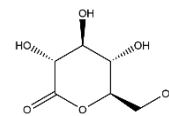


- Method of manufacture
- Composition and impurities

Since the June meeting, CIR has received method of manufacturing, composition, and impurities data for PEG-15 Butylene Glycol Diisostearate, PEG-10 Glyceryl Diisostearate, PEG-20 Glyceryl Diisostearate, PEG-30 Glyceryl Diisostearate, PEG-60 Glyceryl Diisostearate, and PEG-4 Glyceryl Distearate. No method of manufacturing, composition, or impurities data have been received for PEG-15 Glyceryl Diisostearate, PEG-12 Glyceryl Dimyristate, PEG-12 Glyceryl Dioleate, PEG-3 Glyceryl Distearate, PEG-12 Glyceryl Distearate, PEG-23 Glyceryl Distearate, or PEG-4 Polyglyceryl-2 Distearate. No additional data were received and no formal comments were received from the Council. The new data have been incorporated into the report.

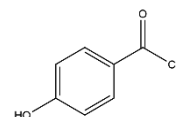
The Panel should carefully consider the Abstract, Discussion, and Conclusion presented in this report. If these are satisfactory, the Panel should issue a Final Report.

3. Glycolactones – FR (Priya) – **Dr. Belsito reports on day 2** – At the March 2022 meeting, the Panel issued a Tentative Report for public comment with the conclusion that Gluconolactone is safe as used in cosmetics in the present practices of use and concentration as described in the safety assessment. The Panel also concluded that the available data are insufficient to make a determination that the remaining ingredients (i.e., Galactonolactone, Glucarolactone, Glucoheptonolactone, and Ribonolactone, none of which are reported to be in use) are safe under the intended conditions of use in cosmetic formulations. To conclude on the safety, the Panel requires impurities data for these ingredients, and cosmetic-specific method of manufacturing data for Glucarolactone and Glucoheptonolactone.



Since the issuing of the Tentative Report, no new unpublished data were received. Comments were received and addressed. The Panel should carefully consider the Abstract, Discussion, and Conclusion, and be prepared to issue a Final Report.

4. Hydroxyacetophenone – FR (Preethi) – **Dr. Belsito reports on day 2** – At the March 2022 meeting, the Panel issued a Tentative Report for public comment with the conclusion that Hydroxyacetophenone is safe in cosmetics in the present practices of use and concentration described in the safety assessment.



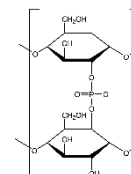
Since the issuing of the Tentative Report, no new unpublished data were received. Comments were received and addressed. The Panel should carefully consider the Abstract, Discussion, and Conclusion, and be prepared to issue a Final Report.

5. *Portulaca oleracea* – FR (Preethi) – **Dr. Cohen reports on day 2** – At the March 2022 meeting, a revised Draft Tentative Report was presented to the Panel. The Panel acknowledged the confirmed use of whole *Portulaca oleracea* as a food, and that fact, coupled with negative findings in human dermal irritation and sensitization studies on the whole plant extract, mitigated systemic toxicity concerns. The Panel also acknowledged the presence of potentially sensitizing constituents in these ingredients (namely, terpenes). Accordingly, the Panel issued a Tentative Report for public comment with the conclusion that these 4 *Portulaca oleracea*-derived ingredients are safe in cosmetics in the present practices of use and concentration described in the safety assessment when formulated to be non-sensitizing.



Since the issuing of the Tentative Report, no new unpublished data were received. Comments were received and addressed. The Panel should carefully consider the Abstract, Discussion, and Conclusion, and be prepared to issue a Final Report.

6. Starch Phosphates – FR (Regina) – **Dr. Cohen reports on day 2** – At the March 2022 meeting, the Panel issued a Tentative Report for public comment with the conclusion that the 4 starch phosphate ingredients reviewed in the safety assessment are safe in cosmetics in the present practices of use and concentration described in this safety assessment.



Since the issuing of the Tentative Report, the following unpublished data regarding Hydroxypropyl Starch Phosphate were received from the Council and have been added to the Draft Final Report:

- *Salmonella typhimurium*-*Escherichia coli*/mammalian-microsome reverse mutation assay
- Primary dermal irritation test
- Primary eye irritation test
- Skin sensitization study in guinea pigs, Buehler method

Comments were received and addressed. The Panel should carefully consider the Abstract, Discussion, and Conclusion, and be prepared to issue a Final Report.

#### **Abbreviated Rereviews – There are 7 rereview documents – In each case, the Panel is only being asked if the report should be reopened.**

1. Chloroxylenol – RR (Priya) – **Dr. Belsito reports on day 2** – The Panel first published a review of the safety of Chloroxylenol in 1985, with the conclusion that this ingredient is safe in the present practices of use, as described in the safety assessment. This conclusion was re-affirmed, as published in 2006. Because it has been at least 15 years since the previous rereview was published, in accordance with CIR Procedures, the Panel should consider whether the safety assessment of Chloroxylenol should be reopened. An exhaustive search of the world's literature was performed for studies dated 2000 forward.

New studies were found for several toxicological endpoints (acute dermal, inhalation, and oral toxicity, subchronic and chronic dermal toxicity, DART, genotoxicity, carcinogenicity, dermal irritation, dermal sensitization, and ocular irritation). Of note are a positive mutagenicity assay and a positive mouse local lymph node assay. In addition, several case reports were found reporting hypersensitization and/or hyper- and depigmentation following exposure to Chloroxylenol. The frequency of Chloroxylenol has slightly increased from 43 to 51 total uses, and the maximum concentration of use has remained the same at 0.5%.

The Panel should carefully review the historical overview, comparison of original and new use data, the search strategy used, a synopsis of notable new data for each ingredient or ingredient group, and the use table. If upon review of the new studies and updated use data the Panel determines that a re-review is warranted, a Draft Amended Report will be presented at an upcoming meeting. If instead the Panel determines that the report should not be reopened, a draft rereview summary, conforming to the original conclusion, will be presented at an upcoming meeting.

2. Erythorbic Acid – RR (Preethi) – **Dr. Cohen reports on day 2** – The Panel first published a review of the safety of Erythorbic Acid and Sodium Erythorbate in 1999, with the conclusion that these ingredients are safe for use as cosmetic ingredients in the present practices of use described in the safety assessment. Ascorbyl Palmitate, Ascorbyl Dipalmitate, and Ascorbyl Stearate, which were included in the original review, were added to a grouping of ethers and esters of ascorbic acid, for which a safety assessment was published in 2017; accordingly, these 3 ingredients are not included in this rereview.

Because it has been at least 15 years since the final report was published, in accordance with CIR Procedures, the Panel should consider whether the safety assessment of Erythorbic Acid and Sodium Erythorbate should be re-opened. An exhaustive search of the world's literature was performed for studies dated 1994 forward. A historical overview, comparison of original and new use data, search strategy, and relevant data found are enclosed herein. One notable finding is a local lymph node assay performed in female mice using Sodium Erythorbate at up to 25% in propylene glycol.

Also included for your review is a table of current and historical use data. Generally, there has been a decrease in frequency of use since the last review. In 2022, FDA VCRP data indicate that Erythorbic Acid has 300 reported uses, 298 of which are in hair coloring formulations. Of note, Sodium Erythorbate was reported to be used in hair coloring preparations at > 50% in 1984; in 2022, the maximum reported concentration of use is 0.3 % in hair dyes and colors. There were no reported uses of either ingredient in products applied near the eye in the original assessment; there is 1 reported use of Erythorbic Acid in this use category in 2022.

If upon review of the new studies and updated use data the Panel determines that a rereview is warranted, a Draft Amended Report will be presented at an upcoming meeting. If instead the Panel determines that the report should not be reopened, a draft rereview summary, conforming to the original conclusion, will be presented at an upcoming meeting.

3. Glyceryl Diesters – RR (Preethi) – **Dr. Belsito reports on day 2** – The Panel first published a review of the safety of these 17 Glyceryl Diester ingredients in 2007, with the conclusion that these ingredients are safe as cosmetics in the present practices of use and concentrations described in the safety assessment provided that the content of 1,2-diester is not high enough to induce epidermal hyperplasia. Glyceryl Dimyristate was originally a part of this group but has since been reviewed with Myristic Acid ingredients. Thus, this ingredient is not rereviewed herein.

Because it has been 15 years since the final report was published, in accordance with CIR Procedures, the Panel should consider whether the safety assessment of these Glyceryl Diesters should be re-opened. An exhaustive search of the world's literature was performed for studies dated 2002 forward. Notable findings include dosages for FDA-approved use of Glyceryl Dibehenate and Glyceryl Distearate as inactive ingredients in oral capsule formulations (at up to 5.7 and 39.2 mg, respectively) and regulations on diglycerides as food additives. Additionally, acute and repeated dose (90-d) oral toxicity studies, oral developmental and reproductive toxicity studies of diacylglycerol oil in rats and dogs, and 2-yr studies on the dietary effect of diacylglycerol oil upon carcinogenicity/tumor promotion in mice and rats were found.

Frequency of use of the in-use ingredients has generally increased since the last review. Of note, Glyceryl Stearate Citrate, which previously had no reported uses, is now reported to be used in 164 formulations. Two ingredients, Glyceryl Distearate and Glyceryl Stearate Citrate, are now reported to be used in baby products; none of the glyceryl diesters were previously reported for use in that product category. There have been no significant increases in concentration of use.

If upon review of the new studies and updated use data the Panel determines that a rereview is warranted, a Draft Amended Report will be presented at an upcoming meeting. If instead the Panel determines that the report should not be reopened, a draft rereview summary, conforming to the original conclusion, will be presented at an upcoming meeting.

4. Hexamidine – RR (Priya) – **Dr. Cohen reports on day 2** – The Panel first published a review of the safety of Hexamidine and Hexamidine Diisethionate in 2007, with the conclusion that these ingredients are safe at concentrations up to 0.1%. Because it has been 15 years since this report was published, in accordance with CIR Procedures, the Panel should consider whether the safety assessment of Hexamidine and Hexamidine Diisethionate should be re-opened. An exhaustive search of the world's

literature was performed for studies dated 2000 forward.

New studies were found for several toxicological endpoints (e.g., acute oral toxicity, genotoxicity, dermal irritation and sensitization, ocular irritation). Of note are hypersensitivity case reports following Hexamidine exposure, and positive patch test results to Hexamidine in atopic patients.

The frequency of use of Hexamidine Diisethionate has increased from 38 to 52, according to 2002 and 2022 VCRP data, respectively. The concentration of use of this ingredient has remained the same ( $\leq 0.1\%$ ). There were previously and currently no reported uses for Hexamidine.

If upon review of the new studies and updated use data the Panel determines that a rereview is warranted, a Draft Amended Report will be presented at an upcoming meeting. If instead the Panel determines that the report should not be reopened, a draft rereview summary, conforming to the original conclusion, will be presented at an upcoming meeting.

5. Mink Oil – RR (Regina) – **Dr. Belsito reports on day 2** – The Panel first published a review on the safety of Mink Oil in 1998, with an insufficient data conclusion. Subsequently, the Panel's data needs were met, and in 2005, a Final Amended Report was published with the conclusion that Mink Oil is safe as a cosmetic ingredient in the practices of use and concentration described in the safety assessment.

Because it has been at least 15 years since the previous report was published, in accordance with CIR Procedures, the Panel should consider whether the safety assessment of Mink Oil should be re-opened. An exhaustive search of the world's literature was performed for studies dated 2000 forward. No relevant published data were found.

Since the Final Amended Report was issued, there is one new use category reported in 2022 (hair-coloring). The frequency of use has decreased, from 100 reported uses in 2001 to 32 uses in 2002, and the maximum concentration of use for Mink Oil has gone from 3% in 2001 to 0.1% in 2022.

If upon review of the new studies and updated use data the Panel determines that a rereview is warranted, a Draft Amended Report will be presented at an upcoming meeting. If instead the Panel determines that the report should not be reopened, a draft rereview summary, conforming to the original conclusion, will be presented at an upcoming meeting.

6. Octyldodecyl Stearoyl Stearate – RR (Regina) – **Dr. Cohen reports on day 2** – The Panel previously issued an insufficient data conclusion on Octyldodecyl Stearoyl Stearate, and a Final Report with this conclusion was published in 2001. Subsequently, the Panel's data needs were met, and a Final Amended Report with the following conclusion was published in 2005: Octyldodecyl Stearoyl Stearate is safe as a cosmetic ingredient in the practices of use and concentration described in this safety assessment.

Because it has been at least 15 years since the Final Amended Report was published, in accordance with CIR Procedures, the Panel should consider whether the safety assessment of Octyldodecyl Stearoyl Stearate should be reopened. An exhaustive search of the world's literature was performed for studies dated 2000 forward. It should be noted that this search for safety test data on Octyldodecyl Stearoyl Stearate did not reveal any new relevant information.

The reported use frequency of this ingredient increased from 105 to 605 formulations. Some trends of note are an increase in incidental ingestion and mucous membrane exposure from 1 to 48 uses, as well as eye area use from 35 in 2005 to 322 in 2022. The highest use concentration currently reported is in lipstick (28%).

If upon review of the new studies and updated use data the Panel determines that a rereview is warranted, a Draft Amended Report will be presented at an upcoming meeting. If instead the Panel determines that the report should not be reopened, a draft rereview summary, conforming to the original conclusion, will be presented at an upcoming meeting.

7. Sodium Lauryl Sulfoacetate – RR (Christina) – **Dr. Belsito reports on day 2** – The Panel first published a review of the safety of Sodium Lauryl Sulfoacetate in 1987 with the conclusion that this ingredient is safe as a cosmetic ingredient in the present practices of use and concentration. The Panel reaffirmed this conclusion in a rereview that was published in 2006.

Because it has been at least 15 years since the first rereview was published, in accordance with CIR Procedures, the Panel should consider whether the safety assessment of Sodium Lauryl Sulfoacetate should be re-opened. An exhaustive search of the world's literature was performed for studies dated 2004 forward. No relevant published data were found.

Since the initial rereview was considered, the frequency of use has increased slightly from 68 to 87 uses. In 2004, the maximum concentration of use for this ingredient was 4% in leave-on products, 5% in rinse-off products, and 21% in products diluted for use. Concentration of use data for 2022 indicate that Sodium Lauryl Sulfoacetate is used at up to 2.5% in leave-on products (foot powders), up to 10.2% in rinse-off products (pre-shave lotions), and up to 8.4% in products diluted for use (bubble baths).

If upon review of the new studies and updated use data the Panel determines that a rereview is warranted, a Draft Amended Report will be presented at an upcoming meeting. If instead the Panel determines that the report should not be reopened, a draft rereview summary, conforming to the original conclusion, will be presented at an upcoming meeting.

**Administrative Items - there are 7 rereview summaries (presented in 1 document), 3 strategy memos, a report formats & SOPs document, and the 2023 Priorities document.**

1. N,N-Bis(2-Hydroxyethyl-p-Phenylenediamine Sulfate – RRsum – (Christina) – **Dr. Cohen reports on day 2** – The Panel should carefully consider the rereview summary and finalize it.
2. Glycol Stearate – RRsum – (Regina) – **Dr. Belsito reports on day 2** – The Panel should carefully consider the rereview summary and finalize it.
3. Polyacrylamide – RRsum – (Preethi) – **Dr. Cohen reports on day 2** – The Panel should carefully consider the rereview summary and finalize it.
4. Cottonseed – RRsum – (Preethi) – **Dr. Belsito reports on day 2** – The Panel should carefully consider the rereview summary and finalize it.
5. PPG Stearyl Ethers – RRsum – (Priya) – **Dr. Cohen reports on day 2** – The Panel should carefully consider the rereview summary and finalize it.
6. Amyl Acetates – RRsum – (Priya) – **Dr. Belsito reports on day 2** – The Panel should carefully consider the rereview summary and finalize it.
7. PEG Soy Sterols – RRsum – (Priya) – **Dr. Cohen reports on day 2** – The Panel should carefully consider the rereview summary and finalize it.
8. Use Tables – SM (Monice) – **Dr. Cohen reports on day 2** – As discussed in June, it is becoming readily apparent that duration and type of exposure can no longer be accurately determined based on the product category. For example, shampoos, which are currently classified in current Use Tables as liquid rinse-off formulations, can actually be spray leave-on formulations (e.g., dry shampoo). Although the intended area of exposure can be surmised with some confidence, how the product is applied (e.g., spray) and the expected duration of exposure (i.e., leave-on or rinse-off) can be presumed, but not truly known.

A proposed format for the Use Table is once again being presented to the Panel, in which all reported product categories (for both frequency and concentration of use) as received from the VCRP and Council survey are included for each ingredient. At the last meeting, the Panel voiced concern that duration and exposure were not included in the proposed format. As stated earlier, attempting to include duration of exposure, or how the product is applied (e.g., spray), could be misleading and incorrect. However, it does seem valid to indicate the likely exposure site (e.g., skin, eye area, etc.). Accordingly, a column identifying the likely exposure site has been added to the proposed table.

**Please be prepared to discuss the proposed Use Table format, as well as any other suggestions that you may have.**

9. Report Format & SOPs – Admin – (Monice) – **Dr. Belsito reports on day 2** – CIR reports follow a standard format. In that we have several new members of the Panel, the outline that is used is being provided to help familiarize everyone with that format. Additionally, there is boilerplate language that has been developed over the years that is used regularly in reports issued by the Panel, as well as certain standard operating procedures (SOPs). In addition to the “boilerplates” and SOPs, in some instances background regarding these common matters is also provided. [Please note: This document is used as a reference by CIR staff, and as such, there are links to files in the guidance document that are only accessible internally; therefore, please know that as you review this Guidance document, these links are not accessible.]

**These documents are provided for informational purposes. However, if there are concerns or edits to propose, the Panel should demonstrate consensus for any changes.**

10. Low FOU Rereviews – SM (Monice) – **Dr. Belsito reports on day 2** – As noted above for the 7 rereview documents, “because it has been at least 15 years since the first rereview was published, in accord with CIR Procedures, the Panel should consider whether the safety assessment of [report name] should be re-opened.” **CIR is asking the Panel and the CIR SSC whether, in their opinions, that simply the knowledge of a lack of reported use, or very low use, could be a reason to not re-open reports that have reached the end of this 15-yr clock?** If so, a rereview summary would be developed explicit to that fact. (As a reminder, if any interested party believes a decision is incorrect, they may petition to have that decision amended.)

**Also, if in fact a “low” number of uses is a valid reason to not re-open an assessment, what would that cut-off be?** Please note, considering that hair dyes typically have low reported FOU, it should be considered whether they are an exception.

11. Yeast – SM (Priya) – **Dr. Belsito reports on day 2** – In February 2022, data were received suggesting the use of various genus and species of yeasts in the preparation of Yeast Extract, other than *Saccharomyces cerevisiae*. These include the following:

- *Candida oleophila*
- *Candida magnoliae*
- *Candida saitoana*
- *Debaryomyces nepalensis*
- *Metschnikowia agaves*
- *Metschnikowia pulcherrima*
- *Metschnikowia reukaufii*
- *Pichia anomala*
- *Pichia heedii*
- *Pichia minuta*
- *Pichia naganishii*
- *Saccharomyces cerevisiae*

Because of these new data, and the broad and uninformative definition of Yeast in the Dictionary, CIR staff issued a strategy memo at the March 2022 meeting and asked the Panel if the report should continue to only review the safety of *Saccharomyces cerevisiae*-derived yeast ingredients, or if other species of yeast (e.g., *Pichia anomala*) should be included in the document.

Subsequently, at the March 2022 meeting, the Panel suggested the preparation of another strategy memo, to include all yeast ingredients currently listed in the *Dictionary*, along with notations of whether or not these ingredients (or their corresponding species) are used in foods, as well as their frequency of use. In addition, the Panel requested information from industry verifying which species of yeast are used in the manufacturing of Yeast and Yeast Extract. No new information has been received. However, speakers are scheduled to present at this meeting.

**The CIR staff is asking the Panel for guidance; after listening to the presentation and reviewing the list of yeast ingredients provided herein, should:**

1. ***this report continue to only review the safety of Saccharomyces cerevisiae-derived yeast ingredients, which would be explained in the document, and only data on Saccharomyces cerevisiae-derived ingredients be included?***  
Or
  2. ***should all yeast ingredients provided in the Dictionary with both food/GRAS and/or 2022 frequency of use data (as indicated in the list provided herein,) be included?***  
Or
  3. ***should all yeast ingredients provided in the Dictionary, regardless of food use or 2022 frequency of use data (as indicated in the list provided herein), be included?***
12. Priorities – Admin (Bart) – ***Dr. Cohen reports on day 2*** – The 2023 Draft Priority List was presented to the Panel in March 2022, and these priorities are now before the Panel again for finalization. A hair dye, HC Blue No. 15, has been proposed for addition to the list. Additionally, the grouping of prostaglandin ingredients on the list should be discussed. The Panel will vote to finalize the 2023 Priority List.

### **Full Panel Meeting**

The Panel will consider the 6 reports to be issued as final safety assessments, followed by the remaining reports advancing in the process (including the Tentative Reports and Draft Reports). In addition, a consensus should be reached for the 7 rereview documents, the 7 rereview summaries, the 3 strategy memos, report format & SOPs, and the finalization of the 2023 Priorities.

Please remember, the meeting starts at 8:30 am on day 1 and day 2. It is likely that the full Panel session will conclude before lunch on day 2.

Looking forward to seeing you all (virtually)!

# Agenda

## 162<sup>nd</sup> Meeting of the Expert Panel for Cosmetic Ingredient Safety

### September 26<sup>th</sup> – 27<sup>th</sup>, 2022

Virtual via Microsoft Teams

Monday, September 26, 2022

8:30 AM	WELCOME TO THE 162 <sup>nd</sup> EXPERT PANEL TEAM MEETINGS	Drs. Bergfeld/Heldreth
8:45 AM	PRESENTATION – Yeast-derived ingredients (virtual)	Silab (France)
9:45 AM	TEAM MEETINGS	Drs. Cohen/Belsito

Dr. Belsito's Team*		Dr. Cohen's Team	
SM (PC)	Yeast-derived ingredients	Admin (BH MF)	Priorities
FR (CB)	Fatty Ester End-Capped Alkoxylates	RRsum (BH MF)	RR Summaries (all)
FR (CB)	Diatomaceous Earth	SM (PC)	Yeast-derived ingredients
TAR (CB)	Clays	FR (PC)	Glycolactones
DAR (CB)	Acid Orange 3	DR(PC)	Trisodium Ethylenediamine Disuccinate
RR (CB)	Sodium Lauryl Sulfoacetate	RR (PC)	Chloroxylenol
FR (RT)	Starch Phosphates	RR (PC)	Hexamidine
TR (RT)	<i>Rosa centifolia</i>	FR (PR)	Hydroxyacetophenone
RR (RT)	Mink Oil	FR (PR)	<i>Portulaca oleracea</i>
RR (RT)	Octyldodecyl Stearoyl Stearate	DR (PR)	Polyhydroxystearic Acid
Admin (MF BH)	Report Format & SOPs	DR (PR)	Phenyl-Substituted Methicones
SM (MF BH)	Use Tables	RR (PR)	Glyceryl Diesters
SM (MF BH)	Low FOU Re-reviews	RR (PR)	Erythorbic Acid
FR (PC)	Glycolactones	FR (CB)	Fatty Ester End-Capped Alkoxylates
DR(PC)	Trisodium Ethylenediamine Disuccinate	FR (CB)	Diatomaceous Earth
RR (PC)	Chloroxylenol	TAR (CB)	Clays
RR (PC)	Hexamidine	DAR (CB)	Acid Orange 3
FR (PR)	Hydroxyacetophenone	RR (CB)	Sodium Lauryl Sulfoacetate
FR (PR)	<i>Portulaca oleracea</i>	FR (RT)	Starch Phosphates
DR (PR)	Polyhydroxystearic Acid	TR (RT)	<i>Rosa centifolia</i>
DR (PR)	Phenyl-Substituted Methicones	RR (RT)	Mink Oil
RR (PR)	Glyceryl Diesters	RR (RT)	Octyldodecyl Stearoyl Stearate
RR (PR)	Erythorbic Acid	Admin (MF BH)	Report Format & SOPs
Admin (BH MF)	Priorities	SM (MF BH)	Use Tables
RRsum (BH MF)	RR Summaries (all)	SM (MF BH)	Low FOU Re-reviews

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

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

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

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

Tuesday, September 22, 2022		
8:30 AM	WELCOME TO THE 162 <sup>nd</sup> FULL EXPERT PANEL MEETING	Dr. Bergfeld
8:40 AM	Admin MINUTES OF THE JUNE 2022 EXPERT PANEL MEETING	Dr. Bergfeld
9:00 AM	DIRECTOR'S REPORT	Dr. Heldreth
9:10 AM	FINAL REPORTS, REPORTS ADVANCING TO THE NEXT LEVEL, OTHER ITEMS	
Final Reports		
FR (PR)	Hydroxyacetophenone – <i>Dr. Belsito reports</i>	
FR (PR)	<i>Portulaca oleracea</i> – <i>Dr. Cohen reports</i>	
FR (PC)	Glycolactones – <i>Dr. Belsito reports</i>	
FR (RT)	Starch Phosphates – <i>Dr. Cohen reports</i>	
FR (CB)	Fatty Ester End-Capped Alkoxylates – <i>Dr. Belsito reports</i>	
FR (CB)	Diatomaceous Earth – <i>Dr. Cohen reports</i>	
Reports Advancing		
DAR (CB)	Acid Orange 3 – <i>Dr. Belsito reports</i>	
TAR (CB)	Clays – <i>Dr. Cohen reports</i>	
TR (RT)	<i>Rosa centifolia</i> – <i>Dr. Belsito reports</i>	
DR (PR)	Polyhydroxystearic Acid – <i>Dr. Cohen reports</i>	
DR (PR)	Phenyl-Substituted Methicones – <i>Dr. Belsito reports</i>	
DR (PC)	Trisodium Ethylenediamine Disuccinate – <i>Dr. Cohen reports</i>	
Other Items		
RR (PC)	Chloroxylenol – <i>Dr. Belsito reports</i>	
RR (PC)	Hexamidine – <i>Dr. Cohen reports</i>	
RR (PR)	Glyceryl Diesters – <i>Dr. Belsito reports</i>	
RR (PR)	Erythorbic Acid – <i>Dr. Cohen reports</i>	
RR (RT)	Mink Oil – <i>Dr. Belsito reports</i>	
RR (RT)	Octyldodecyl Stearoyl Stearate – <i>Dr. Cohen reports</i>	
RR (CB)	Sodium Lauryl Sulfoacetate – <i>Dr. Belsito reports</i>	
RRsum (CB BH MF)	<i>N,N</i> -Bis(2-Hydroxyethyl)- <i>p</i> -Phenylenediamine Sulfate Stearate – <i>Dr. Cohen reports</i>	
RRsum (RT BH MF)	Glycol Stearate – <i>Dr. Belsito reports</i>	
RRsum (PR BH MF)	Polyacrylamide – <i>Dr. Cohen reports</i>	
RRsum (PR MF BH)	Cottonseed – <i>Dr. Belsito reports</i>	
RRsum (PC BH MF)	PPG Stearyl Ethers – <i>Dr. Cohen reports</i>	
RRsum (PC MF BH)	Amyl Acetates – <i>Dr. Belsito reports</i>	
RRsum (PC BH MF)	PEGs Soy Sterol – <i>Dr. Cohen reports</i>	
SM (MF)	Low FOU Re-reviews – <i>Dr. Belsito reports</i>	
SM (MF)	Use Tables – <i>Dr. Cohen reports</i>	
Admin (MF)	Report Format & SOPs – <i>Dr. Belsito reports</i>	
Admin (BH)	Priorities – <i>Dr. Cohen reports</i>	
SM (PC)	Yeast-derived ingredients – <i>Dr. Belsito reports</i>	

**ADJOURN** – The next meeting will be held in-person on **December 5 - 6, 2022** at the Melrose Hotel, 2430 Pennsylvania Avenue, 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 // SM: Strategy Memo // Admin: Administrative item

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

ONE HUNDRED SIXTY-FIRST MEETING  
OF THE  
EXPERT PANEL FOR COSMETIC INGREDIENT SAFETY

June 16-17, 2022

Microsoft Teams Virtual Meeting

Expert Panel Members

Wilma F. Bergfeld, M.D., Chairperson

Donald V. Belsito, M.D., Teamleader

David E. Cohen, M.D., Teamleader

Curtis D. Klaassen, Ph.D.

Daniel C. Liebler, Ph.D.

Allan E. Rettie, Ph.D.

David Ross, Ph.D.

Ronald C. Shank, Ph.D.

Thomas J. Slaga, Ph.D.

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

Liaison Representatives

Consumer

Thomas Gremillion, J.D.

Industry

Alex Kowcz, M.B.A.

Government

Prashiela Manga, Ph.D.

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Adopted (Date)

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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 - Senior Scientific Analyst

Preethi S. Raj, MS - Senior Scientific Analyst

Regina Tucker –Scientific Analyst

**Information Services**

Kevin Stone Fries, MLS - Information Services Manager

**Other Meeting Attendees**

<b><i>Name</i></b>	<b><i>Organization</i></b>
Jean Anjos	Presperse Corporation
Jay Ansell	Personal Care Products Council
Karen Assanome	Givaudan
Wafaa Ayad	Church Dwight, Inc.
Buitrago Basilio	unidentified
Sabrina Behnke	TRI-K Industries
Nadine Bewry	Sanofi
Don Bjerke	Procter & Gamble
Richard Brown	Wyo-Ben, Inc.
Sumita Butani	R + F
Liwen Chen	US FDA
Vivek Dadhanian	Bath & Body Works
Carol Eisenmann	Personal Care Products Council
Howard Epstein	EMD Surface Solutions
Christine Mazza Ferreira	unidentified
Rocio Garcia	Revlon
Eduardo Gonzalez	Victoria's Secret & Co.
Ludwick Gorczyca	Cogate-Palmolive
Khusbu Jain	REN Skincare
Sandra James-Yi	Nu Skin Enterprises
Alexandro Juarez	MANE
Martha Elena Leal	Mary Kay, Inc.
Ekaterine Kovziridze	TRI-K Industries
Neringa Kontrimiene	Presperse Corporation
Christopher Tilman Krueger	Beiersdorf, Inc.
Zydnia Madera	E.T. Browne Drug Company, Inc.
Natasha Malhi	REN Skincare
Maxwell Mangrum	KaMin LLC
Sharlee More	Cardno ChemRisk
Jeffery Nicolai	J Nicolai Law
Kimberly Norman	Personal Care Products Council
Edmund O'Brien	L'Oreal USA S/D, Inc.
Vanessa Oliveira	Boehringer Ingelheim
Gbemi Oyeti	unidentified
Shanti Pabbathi	CHANEL
Elizabeth Petro	US FDA
Krista Merker Reilly	Personal Care Products Council
Sonia Sandoval	E.T. Browne Drug Company, Inc.
Shripal Sharma	Imerys
Brenda Shinyashiki	Edgewell Personal Care
Janet Summers	Sanofi
Michael Wyatt	US FDA
Hong Xie	US FDA
Janet Zang	US FDA
Merle Zimmerman	AHPA
Gloria Zuclich	Keystone Industries

## **CHAIRPERSON'S OPENING REMARKS**

Dr. Bergfeld welcomed the attendees to the 161<sup>st</sup> meeting of the Expert Panel for Cosmetic Ingredient Safety. She announced the retirement of Dr. Ronald Shank from the Panel. She expressed her gratitude for his years of service to the Panel and stated that everyone would sorely miss him. On behalf of the Panel, she wished him well in his retired life.

Dr. Bergfeld then welcomed two new Panel members, Drs. Allan Rettie and David Ross. She appreciated their willingness to jump right into discussions during the review of ingredients during the team meetings. Dr. Bergfeld also expressed her appreciation towards CIR staff, CIR directors, the CIR Scientific and Support Committee, and the Panel for all their continuing efforts, support, and research.

Dr. Bergfeld stated that the Panel would review 11 ingredient reports, including 4 reports on botanical ingredients, along with several administrative items. The administrative items included discussion of a new format for cosmetic use tables, and the potential of accelerating review of prostaglandins, kojic acid, and aluminum. The Panel was also to review a document concerning "generally recognized as safe" (GRAS) designations and how these relate with cosmetic ingredient safety considerations. Dr. Bergfeld noted that comments were received from Women's Voices of the Earth on the GRAS document and on inhalation and airbrush boilerplate language. CIR staff prepared responses to the comments that the Panel would review.

Additionally, the Panel would discuss the new presentation of 7 abbreviated rereviews, including hair dyes. There currently is a backlog of rereviews, with a few hundred ingredients in the queue. The new presentation will hopefully allow the Panel to quickly review newly available data and determine if the Panel needs to reassess any conclusions on safety.

## **APPROVAL OF MINUTES**

The minutes of the March 7-8, 2022 (160<sup>th</sup>) Expert Panel meeting were approved.

## **DIRECTOR'S REPORT**

Dr. Heldreth remarked on the great fortune to have two amazing new Panel members, Drs. Allan Rettie and David Ross, join at this meeting. There was a consensus that they did a splendid job.

Dr. Heldreth stated that he knows Dr. Ron Shank would rather kiss his horse and ride off into the sunset without fanfare, but that all of the Panel and CIR Staff were going to miss this cowboy. Dr. Shank completed his bachelors and doctorate at MIT, achieving the 1st doctorate there in toxicology. He continued his education as a postdoctoral fellow at the Medical Research Council Laboratories in Surrey, England. He returned to MIT as a professor for a time, but then rode out west to the University of California, Irvine, where he served as professor, director, chair, and emeritus professor. Dr. Shank continued on to achieve many accolades, but Dr. Heldreth's favorite is that he joined this Panel in 1984. Thirty-eight years of distinguished serve, wow! Dr. Heldreth just wanted to say thank you Ron, we have learned so much from you. He also noted that we all will miss seeing Ron and Cathy (Ron's wonderful spouse) at these meetings. He wish him all the best in his retirement.

Dr. Heldreth reiterated how fortunate it is to have such an amazing group of clinicians and scientists on this Panel. He noted that every member of this Panel is deserving of many accolades. Indeed, Dr. Bergfeld, after receiving the Master Dermatologist award in 2012, has this year been awarded the Master Clinician award by the Cleveland Clinic.

The CIR Staff have also been busy. Dr. Jinqui Zhu recently added to the alphabet soup following his name; he had PhD, DABT, ERT, but now he has also achieved DCST, which is the Chinese equivalent of the American board of toxicology diplomat status. And CIR's newest staff member, Regina Tucker, graduated with her Master of Science degree in skin biology, while writing the reports presented at this meeting.

Although we have one more of these virtual meetings in September, Dr. Heldreth noted how he is looking forward to seeing everyone in-person in December.

## **FINAL SAFETY ASSESSMENTS**

### **Acryloyloxyethyl Phosphorylcholine Polymers**

The Panel issued a Final Report with the conclusion that the following 8 ingredients are safe in cosmetics in the present practices of use and concentrations described in the safety assessment.

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

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

The Panel considered the available data to be adequate to determine safety for the use of these ingredients as reported to be used in cosmetics. The Panel's respiratory exposure resource document (<https://www.cir-safety.org/cir-findings>) notes that airbrush delivery systems present a potential safety concern, and

that no data are available for consumer habits and practices thereof. As a result of deficiencies in these critical data needs, the risk and safety of cosmetic ingredients applied by airbrush delivery systems cannot be assessed by the Panel. Therefore, the Panel has found the data insufficient to support the safe use of cosmetic ingredients applied via an airbrush delivery system.

### Barley

The Panel issued a Final Report with the conclusion that the following 5 barley-derived ingredients are safe in cosmetics in the present practices of use and concentrations described in this safety assessment.

Hordeum Distichon (Barley) Seed Flour\*  
Hordeum Vulgare Seed Extract  
Hordeum Vulgare Seed Flour

Hordeum Vulgare Seed Water\*  
Hordeum Vulgare Sprout Extract\*

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

The Panel noted that the barley seed- and sprout-derived ingredients that are reviewed in this safety assessment are found in foods that are consumed daily, and daily exposure from food use would result in much greater systemic exposures than those from use in cosmetic products. This fact, coupled with negative findings in human dermal irritation and sensitization studies on whole plant extracts and seed extracts, led the Panel to

determine that barley seed- and sprout-derived ingredients are safe for use in cosmetic products.

However, the Panel also concluded that the available data are insufficient to make a determination of safety on the following 11 barley-derived ingredients:

Hordeum Distichon (Barley) Extract  
Hordeum Vulgare Extract  
Hordeum Vulgare Flower/Leaf/Stem Juice\*\*  
Hordeum Vulgare Juice\*\*  
Hordeum Vulgare Leaf Extract  
Hordeum Vulgare Leaf Juice

Hordeum Vulgare Leaf Powder\*\*  
Hordeum Vulgare Leaf/Stem Powder\*\*  
Hordeum Vulgare Powder\*\*  
Hordeum Vulgare Root Extract  
Hordeum Vulgare Stem Water\*\*

*\*\*There are currently no uses reported for these ingredients.*

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

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

The Panel's respiratory exposure resource document (<https://www.cir-safety.org/cir-findings>) notes that airbrush delivery systems present a potential safety concern, and that no data are available for consumer habits and practices thereof. As a result of deficiencies in these critical data needs, the safety of cosmetic ingredients applied by airbrush delivery systems cannot be assessed by the Panel. Therefore, the Panel has found the data insufficient to support the safe use of cosmetic ingredients applied via an airbrush delivery system.

### Glucosamine

The Panel issued a Final Report with the conclusion that the following 4 ingredients are safe in the present practices of use and concentration as described in the safety assessment when formulated to be non-irritating.

Acetyl Glucosamine  
Glucosamine

Glucosamine HCl  
Glucosamine Sulfate\*

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

The safety of these ingredients is supported by available in chemico/in vitro sensitization data, clinical sensitization data, a lack of case reports, systemic toxicity data, and the safe use of these ingredients as dietary supplements and debulking agents.

The Panel's respiratory exposure resource document (<https://www.cir-safety.org/cir-findings>) notes that airbrush delivery systems present a potential safety concern, and that no data are available for consumer habits and practices thereof. As a result of deficiencies in these critical data needs, the safety of cosmetic ingredients applied by airbrush delivery systems cannot be assessed by the Panel. Therefore, the Panel has found the data insufficient to support the safe use of cosmetic ingredients applied via an airbrush delivery system.

### Glyceryl Acrylates

The Panel issued a Final Report with the conclusion that the following 4 ingredients are safe in cosmetics in the present practices of use and concentrations described in the safety assessment.

Caprylyl Glycol/Glycerin/Polyacrylic Acid Copolymer  
Glyceryl Acrylate/Acrylic Acid Copolymer

Glyceryl Polyacrylate  
Glyceryl Polymethacrylate

The Panel's respiratory exposure resource document (<https://www.cir-safety.org/cir-findings>) notes that airbrush delivery systems present a potential safety concern, and that no data are available for consumer habits and practices thereof. As a result of deficiencies in these critical data needs, the safety of cosmetic ingredients applied by airbrush delivery systems cannot be assessed by the Panel. Therefore, the Panel has found the data insufficient to support the safe use of cosmetic ingredients applied via an airbrush delivery system.

#### Radish Root

The Panel issued a Final Report with the conclusion these 7 radish root-derived ingredients are safe as used in the present practices of use and concentration described in the safety assessment when formulated to be non-sensitizing.

Lactobacillus/Radish Root Ferment Extract Filtrate\*  
Lactobacillus/Radish Root Ferment Filtrate  
Leuconostoc/Radish Root Ferment Filtrate  
Leuconostoc/Radish Root Ferment Lysate Filtrate\*

Raphanus Sativus (Radish) Root Extract  
Raphanus Sativus (Radish) Root Juice\*  
Raphanus Sativus (Radish) Root Powder\*

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

The Panel considered the available data to be adequate to determine safety for the use of these ingredients as reported to be used in cosmetics. Safety of these ingredients is further supported by the root portion of the *Raphanus sativus* plant being consumed as food, and that foods fermented with lactic acid and *Leuconostoc* bacterial strains have generally recognized as safe (GRAS) status, further mitigating potential systemic toxicity concerns.

The Panel's respiratory exposure resource document (<https://www.cir-safety.org/cir-findings>) notes that airbrush delivery systems present a potential safety concern, and that no data are available for consumer habits and practices thereof. As a result of deficiencies in these critical data needs, the safety of cosmetic ingredients applied by airbrush delivery systems cannot be assessed by the Panel. Therefore, the Panel has found the data insufficient to support the safe use of cosmetic ingredients applied via an airbrush delivery system.

#### Sage

The Panel issued a Final Report with the conclusion that the following 6 *Salvia officinalis* (sage)-derived ingredients are safe in cosmetics in the present practices of use and concentration described in the safety assessment when formulated to be non-sensitizing.

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

Salvia Officinalis (Sage) Leaf Powder\*  
Salvia Officinalis (Sage) Leaf Water  
Salvia Officinalis (Sage) Oil

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

Systemic and dermal toxicity concerns were mitigated by the GRAS status of *Salvia officinalis* (sage) leaves and negative findings from dermal irritation and sensitization studies for leaf-derived ingredients, respectively.

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

Salvia Officinalis (Sage) Extract  
Salvia Officinalis (Sage) Flower/Leaf/Stem Extract\*\*  
Salvia Officinalis (Sage) Flower/Leaf/Stem Juice\*\*

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

*\*\* There are currently no uses reported for these ingredients.*

In the absence of additional data, including a 28-day dermal toxicity data for the *Salvia Officinalis* (Sage) Flower/Leaf/Stem Extract or Root Extract, or the whole plant, the safety of these ingredients could not be determined. Additionally, the Panel discussed the occasional challenge of ascertaining which parts of the *Salvia officinalis* plant were used in the methods of manufacture described in the assessment. The Panel determined that general descriptions of 'aerial' parts being used is not sufficient to confirm the use of flowers or stems to produce these ingredients.

The Panel's respiratory exposure resource document (<https://www.cir-safety.org/cir-findings>) notes that airbrush delivery systems present a potential safety concern, and that no data are available for consumer habits and practices thereof. As a result of deficiencies in these critical data needs, the safety of cosmetic ingredients applied by airbrush delivery systems cannot be assessed by the Panel. Therefore, the Panel has found the data insufficient to support the safe use of cosmetic ingredients applied via an airbrush delivery system.

#### Zeolites

The Panel issued a Final Amended Report with the conclusion that the following 6 zeolite ingredients are safe in cosmetics in the present practices of use and concentration described in the safety assessment.

Ammonium Silver Zeolite\*  
Gold Zeolite\*

Silver Copper Zeolite\*  
Titanium Zeolite\*

## Zeolite

## Zinc Zeolite

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

The Panel noted that erionite is a naturally-occurring fibrous material that is carcinogenic to humans and animals, and is significantly more structurally similar to asbestos than the zeolite ingredients discussed in this report (i.e., the superstructures of the zeolites in this report comprise layered sheets, while those of erionite (and by comparison, asbestos) are fibrous). The Panel stressed that the cosmetics industry should continue to use current good manufacturing processes (cGMPs) to ensure erionite is not present in cosmetic formulations.

The Panel also expressed concern about the presence of heavy metals and free metal ions in zeolite ingredients. The metals in Ammonium Silver Zeolite, Gold Zeolite, Silver Copper Zeolite, Titanium Zeolite, and Zinc Zeolite would have limited metal exchange into solution due to the nature of the zeolite framework. The zeolites are also not likely to absorb through the skin. Although other heavy metals (e.g., lead, nickel, mercury, etc.) may be present during mining, those should be removed through processing. Accordingly, the Panel stressed that the cosmetics industry should continue to use the necessary procedures to limit these impurities in the ingredients before blending into cosmetic formulations.

The Panel's respiratory exposure resource document (<https://www.cir-safety.org/cir-findings>) notes that airbrush delivery systems present a potential safety concern, and that no data are available for consumer habits and practices thereof. As a result of deficiencies in these critical data needs, the safety of cosmetic ingredients applied by airbrush delivery systems cannot be assessed by the Panel. Therefore, the Panel has found the data insufficient to support the safe use of cosmetic ingredients applied via an airbrush delivery system.

### **TENTATIVE SAFETY ASSESSMENTS**

#### **Fatty Esters End-Capped Alkoxyates**

The Panel issued a Tentative Report for public comment with the conclusion that PEG/PPG-8/3 Diisostearate is safe cosmetics in the present practices of use and concentration described in this safety assessment.

The Panel noted the lack of developmental and reproductive toxicity (DART) and genotoxicity studies for fatty ester end-capped alkoxyated ingredients. However, the Panel also noted these ingredients are large molecules (> 1600 Da) and are not likely to absorb readily through the skin. These factors, coupled with the favorable safety profile and lack of structural features associated with genotoxicity, mitigated the need for DART and genotoxicity data.

However, the data are insufficient to make a determination of safety for the following 13 fatty ester end-capped alkoxyate:

PEG-15 Butylene Glycol Diisostearate**	PEG-12 Glyceryl Dioleate**
PEG-10 Glyceryl Diisostearate**	PEG-3 Glyceryl Distearate
PEG-15 Glyceryl Diisostearate**	PEG-4 Glyceryl Distearate**
PEG-20 Glyceryl Diisostearate**	PEG-12 Glyceryl Distearate
PEG-30 Glyceryl Diisostearate**	PEG-23 Glyceryl Distearate**
PEG-60 Glyceryl Diisostearate**	PEG-4 Polyglyceryl-2 Distearate**
PEG-12 Glyceryl Dimyristate	

*\*\* There are currently no uses reported for these ingredients.*

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

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

The Panel's respiratory exposure resource document (<https://www.cir-safety.org/cir-findings>) notes that airbrush delivery systems present a potential safety concern, and that no data are available for consumer habits and practices thereof. As a result of deficiencies in these critical data needs, the safety of cosmetic ingredients applied by airbrush delivery systems cannot be assessed by the Panel. Therefore, the Panel has found the data insufficient to support the safe use of cosmetic ingredients applied via an airbrush delivery system.

#### **Fatty Ethers**

The Panel issued a Tentative Report for public comment with the conclusion that the following 8 ingredients are safe as used in the present practices of use and concentration described in the safety assessment.

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

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

Dicaprylyl Ether has 255 reported uses and Distearyl Ether has 6 reported uses; the Panel discussed the absence of method of manufacturing data for ingredients with the highest reported frequencies of use. The Panel noted, however, the data stating that Dicaprylyl Ether and Distearyl Ether were tested at ≥

99.1% purity. Negative DART data, as well as negative genotoxicity data, a lack of structural alerts, and data demonstrating lack of dermal absorption, mitigated systemic toxicity concerns. Irritation and sensitization study data results further assured the Panel of the dermal safety of these ingredients.

The Panel's respiratory exposure resource document (<https://www.cir-safety.org/cir-findings>) notes that airbrush delivery systems present a potential safety concern, and that no data are available for consumer habits and practices thereof. As a result of deficiencies in these critical data needs, the safety of cosmetic ingredients applied by airbrush delivery systems cannot be assessed by the Panel. Therefore, the Panel has found the data insufficient to support the safe use of cosmetic ingredients applied via an airbrush delivery system.

### **Ginger**

The Panel issued a Tentative Report for public comment with the conclusion that the following 7 Zingiber officinale (ginger)-derived ingredients are safe as used in the present practices of use and concentration as described in the safety assessment, when formulated to be non-sensitizing.

Zingiber Officinale (Ginger) Rhizome Extract  
Zingiber Officinale (Ginger) Root\*  
Zingiber Officinale (Ginger) Root Extract  
Zingiber Officinale (Ginger) Root Juice\*

Zingiber Officinale (Ginger) Root Oil  
Zingiber Officinale (Ginger) Root Powder  
Zingiber Officinale (Ginger) Water

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

The Panel found the available data to be sufficient to conclude on the safety for Zingiber Officinale (Ginger) Water, as this ingredient, according to manufacturers, is reported to be prepared via the distillation of ginger roots.

However, the Panel determined that the data are insufficient to make a determination of safety for the following non-root Zingiber officinale (ginger)-derived ingredients:

Zingiber Officinale (Ginger) Leaf Cell Extract Zingiber Officinale (Ginger) Extract\*\*

*\*\* There are currently no uses reported for this ingredient.*

In order evaluate safety, the Panel requested the following data:

- Method of manufacturing, composition, and impurities data for Zingiber Officinale (Ginger) Leaf Cell Extract
  - If the composition of Zingiber Officinale (Ginger) Leaf Cell Extract notably differs from the root-derived ginger ingredients, the following are needed:
    - Systemic toxicity data (28-d dermal toxicity, genotoxicity, developmental/reproductive toxicity, and carcinogenicity data)
    - Dermal irritation/sensitization data
- Irritation and sensitization data on Zingiber Officinale (Ginger) Extract at the maximum concentration of use

The Panel's respiratory exposure resource document (<https://www.cir-safety.org/cir-findings>) notes that airbrush delivery systems present a potential safety concern, and that no data are available for consumer habits and practices thereof. As a result of deficiencies in these critical data needs, the safety of cosmetic ingredients applied by airbrush delivery systems cannot be assessed by the Panel. Therefore, the Panel has found the data insufficient to support the safe use of cosmetic ingredients applied via an airbrush delivery system.

### **INSUFFICIENT DATA ANNOUNCEMENTS**

#### **Phytosteryl Glutamates**

The Panel issued an Insufficient Data Announcement (IDA) for these 3 phytosterol glutamate ingredients:

Phytosteryl/Behenyl/Octyldodecyl Lauroyl Glutamate  
Phytosteryl/Behenyl/Octyldodecyl/Isostearyl Lauroyl Glutamate  
Phytosteryl/Octyldodecyl Lauroyl Glutamate

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

- Method of manufacturing data
- Impurities data
- 28-day dermal toxicity data
  - If positive, other toxicity data, including DART, genotoxicity, and carcinogenicity data, may be needed
- Irritation and sensitization data for Phytosteryl/Octyldodecyl Lauroyl Glutamate at maximum concentration of use
- Ocular irritation data, if available

### **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 9 previous assessments for re-review. The Panel determined that the following two reports should be reopened.

- Acid Orange 3 – 1 ingredient

- Amino Cresols – 6 ingredients

In contrast, the Panel reaffirmed the conclusions reached for the following 7 safety assessments (choosing to no re-open the original reports).

- Amyl Acetates
- *N,N*-Bis(2-Hydroxyethyl)-*p*-Phenylenediamine Sulfate
- Cottonseed Glycerides
- Glycol Stearate
- PEGS Soy Sterol
- Polyacrylamide
- PPGs Stearyl Ethers

## **STRATEGY MEMOS**

### **Prostaglandins/Kojic Acid/Aluminum**

**Prostaglandins** – at the March Panel meeting, representatives from the FDA were requested to evaluate whether the safety evaluation of products containing prostaglandin ingredients is exclusively within the purview of FDA Drugs, or if the use of such ingredients could be considered within the parameters of cosmetic use. It was determined that for some products containing prostaglandins, drug claims are not made, and therefore, those ingredients could be registered in the VCRP. Accordingly, prostaglandins will be considered at the September meeting for inclusion on the 2023 Priority List.

**Kojic Acid** – according to the standard 15-year re-review clock, the safety of this ingredient should be reconsidered in 2025. The Panel was asked if the re-review should be accelerated based on the European Commission Scientific Committee on Consumer Safety opinion, issued in March, that Kojic Acid was deemed not safe when used as a skin lightening agent in cosmetic products at concentrations of up to 1%, due to concerns related to potential “endocrine disrupting” properties. The Panel determined to accelerate this re-review.

**Aluminum Hydroxide** – according to the standard 15-year re-review clock, the safety of these ingredient should be reconsidered in 2031. The Panel was asked if the re-review should be accelerated because aluminum was selected by ACDS as the “Allergen of the Year.” Because the issue concern for aluminum is in with use in vaccines, not cosmetics, the Panel determined to not accelerate this re-review.

### **Use Table Format**

The Panel reviewed proposed changes to the Use Table format that is utilized in each report. As a result of their discussions, the Panel has requested that a letter be submitted by CIR to the FDA requesting updates to the VCRP product categories. The requested updates would provide the Panel with additional information regarding exposure. No updates to the use table format were finalized at this meeting.

### **GRAS Food Status Discussion**

The Panel discussed how food and GRAS status should be utilized in the safety assessments. The Panel agreed the draft white paper contributes to develop a weight of evidence (WoE) decision-making approach for considering GRAS status in the safety evaluation of cosmetic ingredients; however, they determined that the document would be better suited as an internal SOP for CIR Staff (i.e., not to be issued as a white paper/resource document). The Panel deliberated as to how to utilize GRAS as an assessment factor in accessing the systemic toxic potential of cosmetic substances. The Panel noted the recognition of GRAS status should relate to the conditions of intended use, and the differences of route exposure between cosmetic and food ingredients (topical vs. oral) warrant careful consideration. The Panel requested formal comments from the US FDA on the document and would reconsider the document with such additional relevant information at an upcoming meeting.

### **Airbrush Boilerplate Discussion**

The Panel discussed the airbrush boilerplate language that has been proposed for addition in all reports. It was the consensus of the Panel that insufficiencies affecting the ability of the Panel to address and conclude on the safety of cosmetic ingredients as used in airbrush delivery systems should be included in the Discussion of all reports. The Panel also edited some of the language proposed by the CIR staff for inclusion in the Cosmetic Use section of each report. The Panel members expressed great concern that they are not being informed of ingredients that are used in cosmetic formulations that are intended for use with airbrush delivery systems, and queried the FDA about adding a category to the VCRP specifically identifying airbrush use. An FDA representative informed the Panel that there is a specific process that is required for any changes to the VCRP. CIR Staff were tasked with communicating further with the FDA about such a potential change.