Enclosed are the agenda and accompanying materials for the 121st CIR Expert Panel Meeting to be held Monday and Tuesday, December 12-13, 2011 at the Madison Hotel, 1177 Fifteenth Street, NW, Washington, DC 20005. Phone: (202) 862-1600. Fax: (202) 785-1255.

The agenda includes consideration of 17 ingredient groups, along with further refinement of the inhalation toxicity and cosmetic aerosols background and approval of two re-review summaries from September. We will also hear the final piece to Dr. Julie Skare’s hair dye presentation – hair dye chemistry. Kevin Fries will introduce the new CIR website.

Schedule and hotel accommodations

We will reserve rooms for the nights of Sunday, December 11th and Monday, December 12th at the Madison. If you have any travel problems, please contact me on my cell phone at 301-512-7846.

Team meetings

Re-review summaries - buff book 1 - you’ll be able to review the re-review summaries of 4-Chlororesorcinol and Glutaral.

New re-reviews – there are 2 new 1996 safety assessments to re-review and make a determination on the need to reopen.

1. Methyldibromo Glutaronitrile – in 1996, this preservative was found safe as used in rinse-off products and safe at < 0.025% in leave-on products. Lots of additional published studies on sensitization have become available (representative studies are summarized in the re-review document), NTP has completed a dermal toxicity study using rodents, and the SCCP has found this preservative to be unsafe for use in cosmetics. Uses reported in the VCRP are up, but use concentrations in leave-on products are below our limit and concentrations in rinse-off products are low. Do we need to modify our conclusion?

2. Polyvinyl Acetate - in 1996, an amended safety assessment was published with the conclusion that this ingredient is safe as a cosmetic ingredient in the present practices of use. No new relevant published studies on toxicology or irritation and sensitization have become available, although uses and use concentrations have increased, changing the meaning of “present practices of use.”

Draft reports - there are 6 reports under green cover. For each of these 6 reports, if we have all the data we need, we can issue a tentative report. If not, we should ask for whatever additional data are needed.

1. Ammonium Hectorites - the scientific literature review was announced in October, 2011. Comments and unpublished data have been received from industry and incorporated into the report. The hectorite clays moiety in these ingredients previously was reviewed by the Panel in the magnesium aluminum silicate report. A copy of that report is included in the book for item 6 (synthetic fluorophlogopites) because they also are substantially comprised of magnesium aluminum silicate. Are the data on magnesium aluminum silicate useful in supporting ammonium hectorite ingredients? Are additional data needed to complete this safety assessment?

2. Dialkyl Hydroxysuccinates – the scientific literature review was announced in August, 2011. These ingredients have a succinic acid core (a four carbon, alkyl diacid) that is either mono hydroxy substituted (ie, malic acid) or di-hydroxy substituted (ie, tartaric acid). Comments and unpublished data have been received from industry and incorporated into the report. Are additional data needed to complete this safety assessment?

3. Galactomannans – the scientific literature review for a group of 18 legume polysaccharides, commonly called galactomannans, was announced in September, 2011. We received a good deal of unpublished data. Are additional data needed to complete this safety assessment?
4. Ginseng root-derived ingredients - the scientific literature review for ginseng was announced in June, 2011. This safety assessment only addresses ingredients derived from ginseng root and does not include other plant parts. Ginseng root-derived ingredients have almost 650 uses, so the focus on root-derived deals with most of what is in use. Comments and unpublished data have been received from industry and incorporated into the report. Are additional data needed to complete this safety assessment?

5. Polyquaternium-22 and polyquaternium-29 - a scientific literature review notice (explaining that there were no published studies available for these ingredients) was announced in August, 2011. Unpublished data received during the 60-day comment period are summarized in the draft report. Are additional data needed to complete this safety assessment?

6. Synthetic Fluorphlogopite - the scientific literature review was announced in August, 2011. Unpublished data (material specs for synthetic fluorphlogopite; HRIPT test; and concentration of use data) were received from industry and incorporated into the report. One of the fundamental building blocks of synthetic fluorphlogopite is magnesium aluminum silicate, which previously was reviewed by the Panel with the conclusion that they are safe in cosmetic products as long as the products were formulated to be non-respirable. Are the data on magnesium aluminum silicate useful in supporting ammonium hectorite ingredients? Are additional data needed to complete this safety assessment?

Draft tentative reports – There are 4 reports under pink cover. The Panel should issue a tentative safety assessment for each of these.

1. Citric Acid – at the September meeting, an insufficient data announcement was issued to ask for an HRIPT on citric acid at a concentration of 35%, the highest reported leave-on concentration, and inhalation toxicity data, if available. It turns out that the 35% concentration that was reported as a leave-on formulation is actually a foot soak that is diluted prior to use. Now, the highest reported leave-on use concentration for citric acid is 4% and we have an HRIPT on a cuticle cream that contains 4% citric acid. The Panel should form a conclusion, finalize the discussion section, and issue a tentative safety assessment.

2. Ethanolamines group – back in September, the Panel agreed to have CIR prepare, for Panel review, a tentative amended safety assessment for ethanolamine that adds 12 ethanolamine salts and concludes that the entire group is safe in the present practices of use and concentration when formulated to be non-irritating. No additional data have been submitted by industry. At this meeting, the Panel should review this package and try to finalize the discussion and conclusion, and issue a tentative amended safety assessment for public comment.

3. Ethanolamides group – this is the final piece to come out of the re-review of MEA, DEA, and TEA to split and update those reports (see item 2 above) and create the companion reports on amide forms. Back in September, the Panel agreed to have CIR prepare, for Panel review, a tentative amended safety assessment for isostearamide, myristamide, and stearamide MEA and to add 47 additional ethanolamides. The Panel should review this package and try to form a conclusion, finalize the discussion section, and issue a tentative amended safety assessment.

4. Alkyl PEG Sulfoxuccinates – back in September, the Panel issued an insufficient data announcement requesting dermal absorption, mammalian genotoxicity, and inhalation toxicity (if available) data. Only mammalian genotoxicity data were received to date. While the issue of inhalation toxicity may be addressed by discussing aerosol particle sizes and the entirety of the toxicology information available, information on the dermal penetration of these ingredients is not available. While these are not low molecular weight ingredients, the molecular weight is not so high that dermal penetration is precluded. The Panel should consider issuing a tentative safety assessment with the conclusion that the available data are insufficient to support the safety of these ingredients.

Draft final reports - there are 5 reports under blue cover. After reviewing these drafts, especially the rationale in the discussion section, the Panel should issue them as final reports.

1. Alkyl Glyceryl Ethers – a tentative report with a safe in the present practices of use and concentration conclusion was issued in September. Comments and additional data were received during the 60-day comment period and the draft final report has been revised to include these data. The Panel should review the discussion to make certain that it reflects the rationale for a safe in the present practices of use and concentration conclusion and issue a final safety assessment.

2. 2-Amino-4-Hydroxyethylaminoanisole - back in September, the Panel issued a tentative report for the hair dye ingredients, 2-Amino-4-Hydroxyethylaminoanisole and 2-Amino-4-Hydroxyethylaminoanisole Sulfate, with the conclusion that these ingredients are safe for use in hair dye formulations, noting that, were the free base to be used in the future, the expectation is that it would be used at concentrations similar to the sulfate salt. The Panel also cautioned that these ingredients should not be used in products in which N-nitroso compounds are formed. No new data have been found or received. The Panel should review the discussion to confirm that it presents the rationale for the conclusion, and issue a final safety assessment.
3. Decyl Glucoside and Other Alkyl Glucosides – at the September meeting, the Panel issued a tentative safety assessment with a conclusion of safe in the present practices of use and concentration when formulated to be non-irritating. No additional data have been received. Comments on the tentative safety assessment on decyl glucoside and other alkyl glucosides as used in cosmetics were received from the Council, and these comments have been addressed. The Panel should review the discussion to confirm that it presents the rationale for the conclusion, and issue a final safety assessment.

4. Pentaerythrityl Tetraesters – the report was tabled at the September Panel meeting because of uncertainty in the “present practices of use and concentration.” Industry has clarified that products containing up to 50% pentaerythrityl tetraethylhexanoate are NOT in spray products. The Panel should review the discussion (newly revised to reflect the new information re usage) to confirm that it presents the rationale for the conclusion, and issue a final safety assessment.

5. Sodium Lauriminodipropionate – at the September meeting, the Panel concluded that the available data were insufficient to make a determination of safety for lauriminodipropionic acid and its sodium salts. The current use concentration data were not available for lauriminodipropionic acid and the disodium salt. This finding was related more to an artifact of timing of receipt of data than on an actual absence of data. Since the meeting, we have received the results of the Council’s concentration of use survey. There are no reported use concentrations for lauriminodipropionic acid and its disodium salt. Now that we know that, we can use our standard approach: “Were the ingredients 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 sodium lauriminodipropionate.” The Panel should carefully review the discussion, confirm that the discussion presents the rationale for the conclusion, and issue a final amended safety assessment.

Inhalation Toxicity and Cosmetic Aerosols, etc. – The September meeting focused a great deal of attention on the question of inhalation toxicity vis-à-vis cosmetic aerosols, pump sprays, and powders. The presentation by Dr. Rothe added a great deal to our understanding, as did the separate discussions about inhalation toxicity in each of several reports on the agenda. Dr. Boyer has included Dr. Rothe’s slides and excerpts from each part of the meeting in which aerosols/inhalation toxicity were discussed. Using all of that background, Dr. Boyer has revised the overview document to more fully present the science as we now know it. We are thinking that this overview document should be treated like we do hair dye epidemiology --- namely, post the document on the web site and refer to it in reports as needed.

Based on the Panel discussion, it was also clear that, while some boilerplate language is appropriate, it appears as if that language may have to be tailored to each individual report based on the toxicity data available for inhalation and other routes of exposure. The task at this meeting is to finalize this document, at least at this point in time, so that it can be posted on the CIR website and linked to specific ingredient safety assessments when appropriate.

**Full Panel Meeting**

Remember, the breakfast buffet will open at 7:30 am and the meeting starts at 8:00 am on day 2.

The Panel will consider the 5 reports to be issued as final safety assessments, followed by the rest of the reports advancing in the process and the remaining items on the agenda.

It is likely that the full Panel session will conclude late in the morning on day 2, so plan your travel accordingly. Have a safe journey.
# 121st Cosmetic Ingredient Review Expert Panel Meeting

**December 12-13, 2011**

**Madison Hotel**  
1177 Fifteenth Street, NW  
Washington, DC 20005  
Phone: (202) 862-1600  
Fax: (202) 785-1255  
http://www.loewshotels.com

## Monday, December 12

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<td>8:00 am</td>
<td>CONTINENTAL BREAKFAST</td>
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<td>8:30 am</td>
<td>WELCOME TO THE 121ST EXPERT PANEL TEAM MEETINGS</td>
<td>Drs. Bergfeld/Andersen</td>
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<td>9:00 am</td>
<td>CIR website presentation</td>
<td>Kevin Fries</td>
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<td>Chemistry of Hair Dyes</td>
<td>Dr. Julie Skare</td>
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<td>10:00 am</td>
<td>TEAM MEETINGS</td>
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<td>Dr. Marks' Team</td>
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**NOTE:** The order of presentation and discussion of each topic will be maintained. However, the scheduled times may be accelerated or delayed depending upon the time required for the Expert Panel to complete its review of each subject.
Tuesday, December 13

7:30 am  CONTINENTAL BREAKFAST

8:00 am  WELCOME TO THE 121st FULL CIR EXPERT PANEL MEETING

8:15 am  MINUTES OF THE September, 2011 EXPERT PANEL MEETING  Dr. Bergfeld

8:25 am  DIRECTOR'S REPORT  Dr. Andersen

8:45 am  FINAL REPORTS, REPORTS ADVANCING TO THE NEXT LEVEL, RE-REVIEW, and OTHER DISCUSSION ITEMS

Final Reports

Blue (CB)  2-amino-4-hydroxyethylaminoanisole - Dr. Marks reports
Blue (CB)  sodium lauriminoiodipropionate group - Dr. Belsito reports
Blue (LB)  pentaerythrityl tetraesters - Dr. Marks reports
Blue (WJ)  alkyl glyceryl ethers - Dr. Belsito reports
Blue (MF)  decyl glucoside group - Dr. Marks reports

Reports Advancing

Pink (MF)  citric acid - Dr. Belsito reports
Pink (MF)  ethanolamines - Dr. Marks reports
Pink (MF)  ethanalamides - Dr. Belsito reports
Pink (WJ)  alkyl PEG sulfosuccinates - Dr. Marks reports

Green (WJ)  galactomannans - Dr. Belsito reports
Green (WJ)  polyquaternium-22 and polyquaternium-39 - Dr. Marks reports
Green (LB)  ginseng root-derived ingredients - Dr. Belsito reports
Green (LB)  dialkyl hydroxyxuccinates - Dr. Marks reports
Green (LB)  ammonium hectorites - Dr. Belsito reports
Green (LB)  synthetic fluorphlogopites - Dr. Marks reports

Re-Reviews

Buff (CB)  methyl dibromo glutaronitrile – re-review - Dr. Belsito reports
Buff (CB)  polyvinyl acetate – re-review - Dr. Marks reports

Other Discussion Items

Buff (IB)  aerosol/Inhalation toxicity - Dr. Belsito reports
Buff 1 (FAA)  approval of re-review summaries - 4-chlororesorcinol and glutaral - Dr. Marks reports

ADJOURN - Next meeting Monday and Tuesday, March 5-6, 2012

NOTE: The order of presentation and discussion of each topic will be maintained. However, the scheduled times may be accelerated or delayed depending upon the time required for the Expert Panel to complete its review of each subject.
ONE HUNDRED TWENTIETH MEETING

OF THE

EXPERT PANEL

September 26-27, 2011

The Madison Hotel

Washington, D.C.

Expert Panel Members

Wilma F. Bergfeld, M.D., Chair
Donald V. Belsito, M.D.
Ronald A. Hill, Ph.D.
Curtis D. Klaassen, Ph.D.
Daniel C. Liebler, Ph.D.
James G. Marks, Jr., M.D.
Ronald C. Shank, Ph.D.
Thomas J. Slaga, Ph.D.
Paul W. Snyder, D.V.M., Ph.D.

Liaison Representatives

Consumer
Rachel Weintraub, Esq.

Industry
John Bailey, Ph.D.

Government
Linda Katz, MD., M.P.H.

Adopted (Date)

Wilma F. Bergfeld, M.D.
Others Present at Meeting

F. Alan Andersen  CIR
David Andrews  Environmental Working Group
Yuteka Aoki  Kanebo
Nancy Beck  PCRM
Lillian Becker  CIR
Ivan Boyer  CIR
Robert Bronaugh  FDA
Christina Burnett  CIR
Jon Busch  American Chemistry Council
J. Cerusu  West
Rosemary Cook  FDA
Kapal Dewa  FDA
Carol Eisenmann  The Council
Monice Fiume  CIR
Kevin Fries  CIR
Robert Golden  Tox Logic
Irene Gram  ACR
Don Havery  FDA
Bart Heldreth  CIR
Carla Jackson  CIR
Wilbur Johnson, Jr.  CIR
Pam Kloepper-Sans  Procter & Gamble
Dennis Laba  Presperse
Ann M. Mason  ACC
Tim McCarthy  J N Consumer
Kinji Mori  Kanebo
John Pestano  Environmental Working Group
Thomas Re  L’Oreal USA
Diego Rua  FDA
Julie Skare  Procter & Gamble
Jian Song  Walter Reed AIR
David Steinberg  Steinberg & Associates
Jane Vergnes  ISP
CHAIRMAN’S OPENING REMARKS

The 120th meeting of the CIR Expert Panel was called to order by Dr. Bergfeld at 8:30 a.m. on Tuesday, September 27, 2011. This year marks the 35th Anniversary of the Cosmetic Ingredient Review (CIR), and Dr. Bergfeld noted that the CIR program has been very successful. Having served on the Panel for many years, she said that the maturation of the Panel in terms of what it has been able to accomplish has superseded what she envisioned many years ago as a new Panel member. Dr. Bergfeld then recalled the wonderful Anniversary celebration hosted by Dr. Andersen on yesterday evening and her comment that, seemingly, the ongoing task of reviewing cosmetic ingredients will never end. She added that doing this job at such a high level of quality would not have been possible without support from the Personal Care Products Council, CIR staff, CIR Science and Support Committee, and the esteemed CIR Expert Panel. Dr. Bergfeld extended a sincere thank you to these organizations/committees for 35 wonderful years of success and also congratulated Dr. Andersen for a job well done. Dr. Andersen was also congratulated for having received the 2011 Alumni Fellow Award from the Pennsylvania State University. This is one of the most prestigious awards given by Penn State. Dr. Andersen was very appreciative of Dr. Bergfeld’s comments.

Dr. Bergfeld stated that 16 ingredient reports were reviewed in Teams on the preceding day, and congratulated the CIR staff for the excellent condition of each report. Furthermore, the Panel listened to a presentation on inhalation exposure assessment by Dr. Helga Rothe, with Procter & Gamble.

APPROVAL OF MINUTES

The minutes of the June 27-28, 2011 CIR Expert Panel meeting were unanimously approved, with corrections.

DIRECTOR’S REPORT

♦ Dr. Andersen mentioned that the CIR Compendium, a compilation of all abstracts, discussions, and conclusions from CIR Final Safety Assessments, continues to expand. The 35th Anniversary edition of the Compendium will be issued this year.
♦ The process of developing a new CIR website is nearing completion.
♦ The search for a new CIR Deputy Director is ongoing, and it is anticipated that this position will be filled prior to the December Panel meeting.
♦ The manuscript for the final Special Issue of CIR Final Safety Assessments (total of 8) to be published in the *International Journal of Toxicology* has been submitted for publication. Therefore, CIR’s commitment to have 3 sets of journal publications this year will be met.

APPROVAL OF FINAL REPORTS

**Benzyl Alcohol and Benzoic Acid and Its Salts and Benzyl Ester**

Benzyl alcohol, benzoic acid, sodium benzoate, calcium benzoate, magnesium benzoate, potassium benzoate, and benzyl benzoate are safe in the present practices of use and concentration as given in this amended safety assessment.

This report focuses on new inhalation toxicity data because concern over inhalation toxicity potential was the issue that prompted development of this amended safety assessment. The original 2001 final safety assessment contains a complete presentation of data regarding acute and repeat dose toxicity, genotoxicity, reproductive and developmental toxicity and clinical data initially used to evaluate the safety of benzyl alcohol, benzoic acid, and sodium benzoate in cosmetic products.

**Crosslinked Alkyl Acrylates**

Crosslinked Alkyl Acrylates are safe for use in cosmetics in the present practices of use and concentration, provided they are not polymerized in benzene. Acrylates/C10-30 Alkyl Acrylate Crosspolymer may be polymerized in benzene, and the available data are insufficient to make a determination of safety for this ingredient.

The CIR Expert Panel reasoned that that these polymers are not expected to pass through the stratum corneum. Systemic toxicity, reproductive and developmental toxicity, genotoxicity, and carcinogenicity were not expected endpoints with topical application of
products containing these ingredients, because significant dermal absorption is not expected. Additionally, the amount of residual monomer that would be available was low, as were the concentrations of use for these ingredients.

For ingredients polymerized in benzene, however, concern was expressed that residual benzene could be present. A residual benzene risk assessment was submitted and additional risk assessment calculations were provided by CIR staff to address this issue. However, the Panel was concerned that many factors regarding residual benzene in Acrylates/C10-30 Alkyl Acrylate Crosspolymer (the only crosspolymer for which benzene is reported to be a solvent) were still uncertain. Potential cancer risks should be assessed based on factors such as the amount of residual benzene present in the ingredient, the ingredient concentration of use, and the cancer slope factors for benzene, and the usage patterns of cosmetics containing those ingredients.

This final safety assessment includes the 23 crosslinked alkyl acrylates in the list below:

Acrylates/C10-30 Alkyl Acrylate Crosspolymer
Acrylates/C12-13 Alkyl Methacrylates/Methoxyethyl Acrylate Crosspolymer*
Acrylates Crosspolymer
Acrylates/Ethylhexyl Acrylate Crosspolymer
Acrylates/Ethylhexyl Acrylate/Glycidyl Methacrylate Crosspolymer*
Acrylates/PEG-4 Dimethacrylate Crosspolymer*
Acrylates/Steareth-20 Methacrylate Crosspolymer
Acrylates/Vinyl Isodecanoate Crosspolymer
Acrylates/Vinyl Neodecanoate Crosspolymer
Allyl Methacrylate/Glycol Dimethacrylate Crosspolymer*
Allyl Methacrylates Crosspolymer
Butyl Acrylate/Glycol Dimethacrylate Crosspolymer*
C8-22 Alkyl Acrylates/Methacrylic Acid Crosspolymer*
Glycol Dimethacrylate/Vinyl Alcohol Crosspolymer*
Lauryl Methacrylate/Glycol Dimethacrylate Crosspolymer
Lauryl Methacrylate/Sodium Methacrylate Crosspolymer
Methacrylic Acid/PEG-6 Methacrylate/PEG-6 Dimethacrylate Crosspolymer*
PEG/PPG-5/2 Methacrylate/Methacrylic Acid Crosspolymer*
Potassium Acrylates/C10-30 Alkyl Acrylate Crosspolymer*
Sodium Acrylates Crosspolymer-2
Sodium Acrylates/C10-30 Alkyl Acrylate Crosspolymer
Sodium Acrylates/Vinyl Isodecanoate Crosspolymer*
Stearyl/Lauryl Methacrylate Crosspolymer*

*Were the ingredients not in current use (as indicated by *) 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.

**Diethanolamine (DEA) and Its Salts**

Diethanolamine (DEA) and its 16 salts listed below are safe in the present practices of use and concentration as given in this amended safety assessment, when formulated to be non-irritating, except that these ingredients should not be used in cosmetic products in which N-nitroso compounds can be formed.

The CIR Expert Panel decided to not include DEA-Lauraminopropionate in this amended safety assessment. Since the lauraminopropionate moiety was driving the need for additional data for this ingredient, this ingredient is best addressed with sodium lauraminopropionate.

The ingredients included in this amended safety assessment are:
Diethanolamine
Diethanolamine Bisulfate
DEA-C12-13 Alkyl Sulfate*
DEA-C12-15 Alkyl Sulfate*
DEA-C12-13 Pareth-3 Sulfate*
DEA-Cetyl Sulfate*
DEA-Cocoamphodipropionate
DEA-Dodecylbenzenesulfonate*
DEA-Isostearate*
DEA-Laureth Sulfate
DEA-Lauryl Sulfate
DEA-Linoleate
DEA-Methyl Myristate Sulfonate*
DEA-Myreth Sulfate*
DEA-Myristate*
DEA-Myristyl Sulfate*
DEA Stearate

*Were the ingredients not in current use (as indicated by *) 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.

DEA Amides

The 33 DEA amides listed below are safe in the current practices of use and concentration as given in this amended safety assessment, when formulated to be non-irritating and when the levels of free DEA do not exceed those considered safe in the CIR safety assessment of DEA and its salts, except that these ingredients should not be used in cosmetic products in which N-nitroso compounds can be formed.

The CIR Expert Panel was concerned with levels of free diethanolamine (DEA) that could be present as an impurity in these ingredients, since it was the opinion of the Panel that evidence of carcinogenic activity reported in National Toxicology Program’s studies of diethanolamides was attributable to the presence of free DEA. The Panel stated that the levels of free DEA must not exceed those considered safe by the Panel, as stated in the current report on free DEA. The Panel was also concerned that the amount of free DEA present as an impurity could be nitrosated to form carcinogenic N-nitroso compounds.

The ingredients included in this amended safety assessment are:

Almondamide DEA*
Apricotamide DEA*
Avocadamide DEA*
Babassuamide DEA*
Behenamide DEA*
Capramide DEA
Cocamide DEA
Cornamide DEA*
Cornamide/Cocamide DEA*
Hydrogenated Tallowamide DEA*
Isostearamide DEA
Lanolinamide DEA*
Lauramide DEA
Lauramide/Myristamide DEA
Lecithinamide DEA*
Linoleamide DEA
Minkamide DEA*
Myristamide DEA
Myristamide DEA
Oleamide DEA
Olivamide DEA*
Palm Kernelamide DEA
Palmamide DEA*

*Were the ingredients not in current use (as indicated by *) 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.

Formaldehyde and Methylene Glycol

Formaldehyde and methylene glycol are safe for use in cosmetics when formulated to ensure use at the minimal effective concentration, but in no case should the formalin concentration exceed 0.2% (w/w), which would be 0.074% (w/w) calculated as formaldehyde or 0.118% (w/w) calculated as methylene glycol. Additionally, formaldehyde and methylene glycol are safe in the present practices of use and concentration in nail hardening products. However, formaldehyde and methylene glycol are unsafe in the present practices of use and concentration in hair smoothing products. This is a final amended safety assessment.

After reviewing the comments and additional data received, the CIR Expert Panel determined that the available data now were sufficient to support the safety of these ingredients in nail hardeners and that editorial changes should be made to address the

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1 Formalin is an aqueous solution wherein formaldehyde (gas) has been added to water to a saturation point, which is typically 37% formaldehyde (w/w). Because of the equilibrium between formaldehyde and methylene glycol in aqueous solution, formalin contains both formaldehyde and methylene glycol.
The additional data provided confirmed the current use concentration of formaldehyde/methylene glycol in the 1 – 2% range in nail hardeners (one product tested had a value of 2.2%). Given the rapid reaction on the nail surface and the use of nail hardeners at room temperature, the Expert Panel did not consider that formaldehyde/methylene glycol at 1 – 2% in nail hardeners would present a risk of sensory irritation to the eyes, nose, or throat of users. The Panel did note that the present practices of use of nail hardeners do include instructions that admonish users to limit application of the material to the nail, allow it to dry fully, and to not get the material on the skin.

The Panel remained concerned about sensory irritation adverse reports consistent with measured air levels of formaldehyde in salons using hair smoothing products (aka hair straightening products) containing formaldehyde/methylene glycol. Additional use studies were done to demonstrate that exposure to formaldehyde could be minimized with proper procedures and use of personal ventilation devices. The Panel acknowledged that formaldehyde levels in air samples were lower in these most recent data compared to data submitted earlier, but proper safety procedures, including positioning of personal ventilation devices, were not uniformly followed.

In concept, therefore, limits on the concentration of formaldehyde/methylene glycol in hair smoothing products, control of the amount of product applied, use of temperature lower than 450 °F, and approaches to mandate adequate ventilation, are among the steps that could be taken to ensure that these products could be used safely in the future. However, in the present practices of use and concentration (on the order of 10% formaldehyde/methylene glycol, heating to 450 °F, inconsistent ventilation, resulting in many reports of adverse effects), hair smoothing products containing formaldehyde and methylene glycol are unsafe.

The Panel adopted a suggestion to include limits for formalin concentration because formalin is what formulators actually add to cosmetic products. Formalin is an aqueous solution typically containing 37% (w/w) formaldehyde. Because of the equilibrium between formaldehyde and methylene glycol in aqueous solution, formalin contains both formaldehyde and methylene glycol.

While retaining the concept that formaldehyde and methylene glycol should be used only at the minimal effective concentration, the Panel stated that in no case should the formalin concentration exceed 0.2% (w/w), which would be 0.074% (w/w) calculated as formaldehyde or 0.118% (w/w) calculated as methylene glycol. While these numbers appear to be disparate, they are not. The value of 0.074% (w/w) of formaldehyde simply reflects that formalin typically contains 37% formaldehyde (0.2% (w/w) formalin multiplied by 0.37 = 0.074% (w/w) formaldehyde). The value of 0.118% (w/w) for methylene glycol simply reflects the difference in molecular weight between formaldehyde and methylene glycol. These are editorial changes intended to better communicate to the reader.

The best term to convey the dynamic equilibrium between formaldehyde and methylene glycol in aqueous media was addressed in comments. The Panel reasoned that the term “formaldehyde equivalents” best captures the idea that methylene glycol is continuously converted to formaldehyde, and vice versa, even at equilibrium, which can be easily shifted by heating, drying, and other conditions to increase the amount of formaldehyde. Any other term would not distinguish the rapid, reversible formaldehyde/methylene glycol equilibrium from the slow release of formaldehyde resulting from so-called formaldehyde releaser preservatives (e.g., diazodinyl urea). Such formaldehyde releaser preservatives are not addressed in this safety assessment. The formaldehyde releasers may continue to be safely used in cosmetics at the levels established in their individual CIR safety assessments.

**Silylates and Surface Modified Siloxysilicates**

Silica silylate, silica dimethyl silylate, trimethylsiloxyxilicate, and trifluoropropylidemethyl/trimethylsiloxyxilicate are safe for use in the present practices of use and concentration when formulated and delivered in the final product to be non-irritating and non-sensitizing to the respiratory tract.

Information provided by ingredient suppliers confirmed that inhalation toxicity studies of silylates used particles that were sheared to create respirable particles. The CIR Expert Panel determined that the finding of granulomas in animal studies was not relevant to the ingredient as provided by suppliers to be used in cosmetics. Information provided by suppliers indicated that silylate particles aggregate and further agglomerate to form large particles.

**Triethanolamine (TEA) and TEA-containing Ingredients**

Triethanolamine (TEA) and the 31 TEA-containing ingredients listed below are safe in the current practices of use and concentration as given in this amended safety assessment, when formulated to be non-irritating, except that these ingredients should not be used in cosmetic products in which nitroso compounds can be formed.

The CIR Expert Panel was concerned with levels of free diethanolamine (DEA) that could be present as an impurity in these ingredients, and included in the discussion a statement to the effect that levels of free DEA must not exceed those considered safe by
the Panel, as given in the current report on DEA. The Panel also discussed that tertiary alkyl amines such as TEA do not react with N-nitrosating agents directly to form N-nitroso compounds, but they can act as precursors in nitrosamine formation by undergoing nitrosative cleavage. The resulting secondary amine can then be N-nitrosated to products that may be carcinogenic.

Triethanolamine (TEA)  
Magnesium/TEA-Coco-Sulfate*  
Sodium/TEA C12-13 Pareth-3 Sulfate*  
TEA-C10-15 Alkyl Sulfate*  
TEA-C11-15 Alkyl Sulfate*  
TEA-C12-13 Alkyl Sulfate*  
TEA-C12-14 Alkyl Sulfate*  
TEA-C12-15 Alkyl Sulfate*  
TEA-C11-15 Pareth Sulfate*  
TEA-C12-13 Pareth-3 Sulfate*  
TEA-Canolate*  
TEA-Cocoate  
TEA-Coco-Sulfate*  
TEA-Glyceryl Dimaleate*  
TEA-Hydrochloride  
TEA-Hydrogenated Cocoate*  
TEA-Isostearate  
TEA-Lactate  
TEA-Laurate  
TEA-Laurate/Myristate*  
TEA-Laureth Sulfate  
TEA-Lauryl Sulfate  
TEA-Myristate  
TEA-Oleate*  
TEA-Oleyl Sulfate*  
TEA-Palmitate  
TEA-PEG-3 Cocamide Sulfate*  
TEA-Sorbate*  
TEA-Stearate  
TEA-Sulfate  
TEA-Tallate*  
TEA-Undecylenate*  

*Were the ingredients not in current use (as indicated by *) 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.

Tentative Safety Assessments and Tentative Amended Safety Assessments

Decyl Glucoside and Other Alkyl Glucosides

A tentative safety assessment with a conclusion of safe in the present practices of use and concentration when formulated to be non-irritating was issued for decyl glucoside and the 16 alkyl glucosides listed below.

The CIR Expert Panel received updated concentration of use information for alkyl glucoside ingredients, clarifying, for example that certain high use concentrations were for rinse-off products and not leave-on products. Reported use concentrations were also determined to refer to the active ingredient. Based on this new information, the Panel was satisfied that data demonstrate an absence of dermal sensitization at the highest reported concentrations of use in leave-on products. In addition, there was no evidence of other toxicity of these ingredients.

The ingredients included in this tentative safety assessment are:

Decyl Glucoside  
Arachidyl Glucoside  
Butyl Glucoside*  
C10-16 Alkyl Glucoside*  
C12-18 Alkyl Glucoside*  
C12-20 Alkyl Glucoside  
C20-22 Alkyl Glucoside*  
Caprylyl/Capryl Glucoside  
Caprylyl Glucoside  
Cetearyl Glucoside  
Coco-Glucoside  
Ethyl Glucoside  
Isostearyl Glucoside*  
Lauryl Glucoside  
Myristyl Glucoside  
Octyldodecyl Glucoside*  
Undecyl Glucoside*  

*Were ingredients in this group not in current use (as indicated by *) to be used in the future, the expectation is that they would be used at concentrations comparable to others in this group.

Alkyl Glyceryl Ethers

A tentative safety assessment with a conclusion of safe in the present practices of use and concentration was issued for ethylhexylglycerin, caprylyl glycerol ether, glyceryl capryl ether, chimyl alcohol, batyl alcohol, glyceryl allyl ether, glyceryl lauryl ether, isodecyl glyceryl ether, isostearyl glyceryl ether, and oleyl glyceryl ether.
Because these ingredients can be used in products that may be aerosolized, the CIR Expert Panel discussed the issue of potential inhalation toxicity. In the absence of sufficient safety test data to evaluate this endpoint, the Panel noted that 95 – 99% of particles produced in cosmetic aerosols are not respirable. Coupled with the low potential exposures in the breathing zone and concentrations at which the ingredients are used, this information suggest that inhalation would not be a significant route of exposure that might lead to systemic toxic effects.

The Panel acknowledged the evidence of percutaneous absorption of ethylhexylglycerin through rabbit skin in vivo. A review of the available data revealed: an absence of genotoxicity in studies using ethylhexylglycerin, chimyl alcohol, batyl alcohol, and glyceryl allyl ether; an absence of reproductive and developmental toxicity in oral studies using ethylhexylglycerin; no skin irritation/sensitization in studies using ethylhexylglycerin and chimyl alcohol; and no phototoxicity/photoallergenicity in studies using ethylhexylglycerin.

However, the Panel did note the skin penetration enhancement effect of isostearyl glyceryl ether, and that this effect should be taken into consideration when formulating cosmetic products that contain alkyl glyceryl ethers.

2-Amino-4-Hydroxyethylaminoanisole and 2-Amino-4-Hydroxyethylaminoanisole Sulfate

A tentative safety assessment with a conclusion of safe as hair dye ingredients in the present practices of use and concentration was issued for 2-amino-4-hydroxyethylaminoanisole and 2-amino-4-hydroxyethylaminoanisole sulfate, except that these ingredients should not be used in hair dye products in which N-nitroso compounds can be formed.

The CIR Expert Panel reviewed the data that were largely provided by the Personal Care Products Council’s Hair Coloring Technical Committee on 2-amino-4-hydroxyethylaminoanisole sulfate. The Panel noted that the sulfate salt has 94 uses in hair dye products at concentrations up to 1.5% after dilution, but that no uses or use concentrations were reported for the parent compound.

Sodium Lauriminodipropionate, Lauriminodipropionic Acid, and Disodium Lauriminodipropionate

A tentative safety assessment with a conclusion that the available data were insufficient to support the safety of these ingredients was issued. The CIR Expert Panel noted that current use concentration data were not available for 2 of these 3 ingredients and requested that current concentration of use data be provided.

This finding is related more to an artifact of timing of receipt of data than on an actual absence of data. The Panel expects to receive the results of an industry survey before this report is again considered. If those use concentration data are consistent with the currently available use concentration data, the Panel would expect to issue a final amended safety assessment.

Insufficient Data Announcements

Citric Acid group

The CIR Expert Panel issued an insufficient data announcement for these ingredients.

Citric acid and some of its salts and/or esters are generally recognized as safe (GRAS) direct food additives. Since these ingredients have been shown to be safe for ingestion, the report focused on their dermal toxicity. Citric acid is reported to be used at up to 35% in leave-on products, but sensitization data at that concentration were not available. A human repeat insult patch test with 35% citric acid was requested.

The Panel also noted that inhalation toxicity data were not presented in this report, and Citric Acid is used in a number of formulations that could involve incidental inhalation. The Panel has requested inhalation toxicity data, if available.

As reviewed by the Panel, the report included a group of Glycol Mono-, Di-, and Triesters. Since very little toxicity data were available for those esters, the Panel deleted these ingredients from the safety assessment.
The 33 ingredients now included in this safety assessment are:

Citric Acid

Inorganic Salts
Aluminum Citrate
Calcium Citrate
Copper Citrate
Diammonium Citrate
Disodium Cupric Citrate
Ferric Citrate
Magnesium Citrate
Manganese Citrate
Monosodium Citrate
Potassium Citrate
Sodium Citrate
Zinc Citrate

Alkyl Mono-, Di-, and Triesters
Isodecyl Citrate
Isopropyl Citrate
Stearyl Citrate
Dilauryl Citrate
Distearyl Citrate
Tributyl Citrate
Tri-C 12-13 Alkyl Citrate
Tri-C14-15 Alkyl Citrate
Tricaprylyl Citrate
Triethyl Citrate
Triethyhexyl Citrate
Trihexyldecyl Citrate
Trisocetyl Citrate
Triisopropyl Citrate
Trilauryl Citrate
Triocytldodecyl Citrate
Trioleyl Citrate
Triisostearyl Citrate
Tristearyl Citrate
Ethyl Citrates

Alkyl PEG Sulfosuccinates

The CIR Expert Panel issued an insufficient data announcement for these ingredients.

The Panel requested dermal absorption data and noted that, if significant dermal absorption occurs, reproductive and developmental toxicity data may be needed. The Panel acknowledged that disodium laureth sulfosuccinate was not genotoxic in a bacterial assay, but requested mammalian genotoxicity data. A statement to the effect that vapor generated from the heating of components of disodium laureth sulfosuccinate or chemicals that are similar to disodium laureth sulfosuccinate may cause irritation of mucous membranes and the upper respiratory tract is included in a material safety data sheet, suggested that some information regarding inhalation toxicity was available. The Panel requested all available inhalation toxicity data on alkyl PEG sulfosuccinates.

The Panel considered a request to add Disodium Lauryl Sulfosuccinate to the report, but concluded that this ingredient was not an alkyl PEG ether and should not be included. For the same reason, the Panel agreed that trisodium sulfosuccinate should be removed from the safety assessment.

The 18 alkyl PEG sulfosuccinates in this safety assessment are:

Disodium Laureth Sulfosuccinate,
Disodium Laureth-6 Sulfosuccinate,
Disodium Laureth-9 Sulfosuccinate,
Disodium Laureth-12 Sulfosuccinate,
Disodium Deceth-5 Sulfosuccinate,
Disodium Deceth-6 Sulfosuccinate,
Re-Reviews

4-Chlororesorcinol – not reopened

The CIR Expert Panel reaffirmed the original conclusion and determined to not reopen the safety assessment of 4-chlororesorcinol.

In 1996, the Panel concluded that 4-chlororesorcinol was safe for use in hair dye formulations. The Panel reviewed new data that was published in the opinion released by the European Commission’s Scientific Committee on Consumer Safety (SCCS) in 2010, which determined that this ingredient was not a health risk, apart from sensitization, at a maximum concentration of 2.5%. The Panel noted that use of 4-chlororesorcinol in hair dyes has increased from 33 uses to 210 and that the current use concentration is up to 2%, which is higher than the 1% concentration previously reported on but below the SCCS limit.

Glutaral – not reopened

The Expert Panel reaffirmed the original conclusion, emphasized the original finding that glutaral should not be used in aerosolized products, and did not reopen the safety assessment of glutaral.

In 1996, the CIR Expert Panel concluded that glutaral was safe for use at concentrations up to 0.5% in rinse-off products; however, the data were insufficient to determine the safety of glutaral in leave-on products. The Panel also concluded that glutaral should not be used in aerosolized products. Since that original conclusion, numerous studies have been published, including a 2-year NTP inhalation toxicity study. While the number of uses for glutaral has decreased from 60 to 13, this ingredient is currently being used in what could be an aerosol product and in leave-on products. Glutaral was also reported to be used in non-coloring hair products.

The Panel received clarification that this use of glutaral is incidental and that glutaral is not added to the products for functional use, but may be present as an impurity at 6 x 10-6% in non-coloring hair products. Additionally, while glutaral did not cause cancerous lesions in the 2-year NTP inhalation toxicity study, several studies have found that this ingredient can damage the upper respiratory tract in animals.

HC Red No. 1 – re-review summary

The CIR Expert Panel approved the re-review summary with the addition of mention of hair dye epidemiology data.

Other report decisions – Ethanolamine and Ethanolamides

The CIR Expert Panel was presented with a two-part re-review document on ethanolamine and ethanolamides. Part I included ethanolamine and related ethanolamine-containing ingredients; and Part II included ethanolamides. The Panel determined that these two groups of ingredients should be brought back to the Panel as separate draft tentative amended reports for review, and they may be presented at the December meeting.

The Panel determined that the draft amended report of ethanolamine-containing ingredients will include the following 13 ingredients:

- Ethanolamine
- Ethanolamine HCl
- MEA-Sulfite
- MEA-Benzoate
- MEA-Salicylate
- MEA-Cocoate
- MEA-Tallowate
- MEA Undecylenate
- MEA-Laureth-6 Carboxylate
- MEA PPG-6 Laethyl-7 Carboxylate
- MEA-PGP-8-Stearoth-7 Carboxylate
- MEA-Lauryl Sulfate
- MEA-Laureth Sulfate

The Panel determined that the draft amended report of ethanolamides will include the following 49 ingredients:

- Acetamide MEA*
- Azelamide MEA
Babassuamide MEA
Behenamide MEA
C16-22 Acid Amide MEA
Cocamide MEA*
Cocamide Methyl MEA
Cocamidopropyl Betainamide MEA Chloride
Deoxyphytantriyl Palmitamide MEA
Hexylloxodecanamide MEA
Hexylloxodecanamide MEA Phosphate
Hydroxyethyl Pantethenamide MEA
Hydroxypropyl Bisisostearamide MEA
Hydroxypropyl Bislauramide MEA
Hydroxypropyl Bispalmitamide MEA
Hydroxypropyl Bisstearaminide MEA
Hydroxypropyl Bisstearamide MEA
Hydroxystearamide MEA
Isostearamide MEA*
Lactamide MEA
Lauramide MEA
Linoleamide MEA
Myristamide MEA*
Myristoyl/Palmitoyl/Oxostearamide/Arachamide MEA
Oatamide MEA
Oleamide MEA
Oliveamide MEA
Palm Kernelamide MEA
Palmamide MEA
Palmitamide MEA
Pantothenamide MEA
Peanutamide MEA
Ricinoleamide MEA
Stearamide MEA*
Stearamide MEA Stearate
Stearamidoethyl Ethanolamine
Sunfloweramide MEA
Tallowamide MEA
Trideceth-2 Carboxamide MEA
Undecylenamide MEA
PEG-2 Cocamide
PEG-3 Cocamide
PEG-4 Cocamide
PEG-5 Cocamide
PEG-6 Cocamide
PEG-7 Cocamide
PEG-9 Cocamide MEA
PEG-11 Cocamide
PEG-20 Cocamide
PEG-20 Cocamide MEA

*Some of the ethanolamides have been reviewed (as indicated by *), and the Panel determined that it is appropriate to include them for completeness.
†Additional glycol ethers may be considered.

Report Tabled - Pentaerythrityl Tetraisostearate and Other Pentaerythrityl Tetraesters

The CIR Expert Panel tabled the report on pentaerythrityl tetraesters. The Panel noted high use concentrations in products that may involve aerosolization and requested clarification of the actual use concentration in spray products.

Pentaerythrityl cocoate was redefined in the International Cosmetic Ingredient Dictionary and Handbook as a monoester and has been removed from the report.

The remaining 16 ingredients included in this safety assessment are:

Pentaerythrityl Tetraisostearate
Pentaerythrityl Tetra C5-9 Acid Esters
Pentaerythrityl Tetra C5-10 Acid Esters
Pentaerythrityl Tetraacyrlate/ Tetracaprate
Pentaerythrityl Tetra laurate
Pentaerythrityl Tetramyristate
Pentaerythrityl Tetra stearate
Pentaerythrityl Tetrabehenate

CIR 35th Anniversary Celebration

In 1976, the then Cosmetic, Toiletry, and Fragrance Association (now the Personal Care Products Council), with the support of the Consumer Federation of America and the Food and Drug Administration, formed the Cosmetic Ingredient Review Program to thoroughly review and assess the safety of ingredients used in cosmetics in an open, unbiased, and expert manner, and to publish the results in the open, peer-reviewed scientific literature. The year is now 2011, and for its first 35 years, CIR has done just that.

Joining the current members of the CIR Expert Panel at a dinner celebration event were past Panel members and liaisons and their spouses including: Dr. John and Kitty Bailey, Dr. Jerry and Carol McEwen, and Dr. Arnold and Linda Schroeter. Members of the CIR
CIR Director, Alan Andersen, thanked each of the Panel members and liaisons, past and present, for their efforts over the past 35 years for their commitment to “doing the right thing and doing the thing right.” Panel members and liaisons and spouses included: Panel chair, Dr. Wilma Bergfeld and her husband John; Dr. Curt Klassen and his wife Cherry; Dr. Daniel Liebler and his wife Karen; Team leader, Dr. Donald Belsito and his wife Maria; Team leader, Dr. Jim Marks and his wife Joyce; Dr. Paul Snyder and his wife Erica; Rachel Weintraub and her husband Scott Reiter; Dr. Ron Hill and his wife Shelley; Dr. Ron Shank and his wife Kathy; and Dr. Tom Slaga and his wife Mary. Dr. Andersen presented each of the Panel members and liaisons a crystal decanter engraved with the recipient’s name or organization “on the occasion of the CIR 35th anniversary, September 26th, 2011” and offered a toast to CIR’s first 35 years and the beginning of the next 35 years!

Lezlee Westine expressed both the appreciation of the Personal Care Products Council for the work done by CIR and the great feeling of being a part of such a significant celebration. Peter Hutt reminded the group of the moment in time when the FDA Commissioner at the time answered the question posed by the industry trade association, “Do you (FDA) want to do this or do you want us to do it?” The answer was “us” and the CIR program was born!

As each of the Panel members and liaisons spoke about their experiences over the years, it was clear that former Panel chair, Dr. Karl Beyer, got it exactly right when he said of the Expert Panel, “the whole is greater than the sum of its parts.”

**Cosmetic Sprays and Aerosol’s presentation – Dr. Helga Rothe**

Dr. Helga Rothe, Senior Scientist at the Procter and Gamble Darmstadt Innovation Center in Germany, discussed particle-size distributions released from the use of cosmetic spray products, focusing especially on pump and propellant hair spray products. She reported that typically <1% of the airborne droplets released from pump sprays are in the range considered to be respirable (i.e., <10 μm). For propellant sprays, 1% to 5% of the droplets emitted may be within the respirable range, based on her experience.

She noted that the duration of exposure during hair spray use is only a few minutes. For example, the droplets released from a propellant hair spray are distributed within 1 to 2 m3 around the breathing zone during the first 2 minutes after spraying, which expands to a 10 m3 cloud (about the size of a bathroom) over the subsequent 18 minutes. Dr. Rothe explained that the European Union’s current threshold for protecting workers from pulmonary overload during occupational exposure to respirable inert dust particles is 1.5 mg/m3, 8-hour time-weighted average. Inhalation exposures to aerosols from cosmetic sprays will be much lower than this threshold, primarily because of the comparatively much shorter exposure duration associated with cosmetic spray use.

The CIR Expert Panel noted that, in practice, 95% to 99 % of the droplets released from cosmetic sprays have aerodynamic equivalent diameters in the 10 μm to 110 μm range. Thus, most aerosol droplets incidentally inhaled from these sprays are deposited in the nasopharyngeal region of the respiratory tract and are not respirable. However, some of the droplets are respirable. Such information will be included in each safety assessment for which the ingredient is or may be used in a pump or propellant spray. Information will continue to be sought from suppliers and formulators to specifically identify such spray uses.

The Panel will continue to review relevant inhalation toxicity data to determine the safety of cosmetic ingredients. If inhalation toxicity data are absent or provide an insufficient basis to support the safety of an ingredient used in products that may be aerosolized, the Panel will evaluate the sufficiency of other data that may be available on a case-by-case basis. Such data would include the potential for the ingredient to cause systemic toxicity, ocular or dermal irritation or sensitization, or other effects. In addition, the Panel will characterize the importance of the inhalation route for assessing the safety of the ingredient and evaluate data that may be available to estimate the potential respiratory doses of an ingredient in aerosolized products.

**2012 Ingredient Review Priorities**

This annual priority list determines the cosmetic ingredients that will be reviewed by the CIR Expert Panel in 2012. These ingredients are:
TALC

Chamomile Ingredients
MATRICARIA CHAMOMILLA FLOWER EXTRACT
ANTHEMIS NOBILIS FLOWER EXTRACT
CHAMOMILLA RECUTITA (MATRICARIA) FLOWER/LEAF EXTRACT

Standard α-Amino Acids
ARGININE

Amino Acid Alkyl Amides
LAUROYL LYSIN

Hydrolyzed Proteins
HYDROLYZED SOY PROTEIN
HYDROLYZED SILK

Dimethicone Crosspolymers
DIMETHICON/VINYL DIMETHICONE CROSSPOLYMER
DIMETHICONE CROSSPOLYMER

BORON NITRITE

Vitis vinifera Ingredients
VITIS VINIFERA (GRAPE) SEED EXTRACT

NITROCELLULOSE

Modified Terephthalate Polymers
POLYETHYLENE TEREPTHALATE

TROMETHAMINE

PALMITOYL OLIGOPEPTIDE

Fatty Acid-Amidopropyl Dimethylamines
STEARAMIDOPROPYL DIMETHYLAMINE

Methyl Glucose Polyethers and Esters
PEG-120 METHYL GLUCOSE DIOLEATE

6-HYDROXYINDOLE (HAIR DYE)

A list of related ingredients that are expected to be grouped in each review is available at http://www.cir-safety.org/2012.shtml. By making this list available to all interested parties, the CIR Expert Panel is calling for the submission of available unpublished data relevant to the safety of the ingredients and ingredient groups listed, including concentration of use data for all of these ingredients (including related ingredients that are expected to be In addition, the Panel announced that re-reviews of the following ingredient assessments are expected to be done in 2012.

In addition, the Panel announced that re-reviews of the following ingredient assessments are expected to be done in 2012:

Formic Acid

PEGylated Oils
PEG-30 Castor Oil
PEG-33 Castor Oil
PEG-35 Castor Oil
PEG-36 Castor Oil
PEG-40 Castor Oil
PEG-30 Hydrogenated Castor Oil
PEG-40 Hydrogenated Castor Oil

PPG-5 Lanolin Wax, and PPG-5 Lanolin Wax Glyceride

2-Amino-6-Chloro-4-Nitrophenol

Alkyl Esters
Cetyl Esters

m-Phenylendiamine and m-Phenylendiamine Sulfate
Memorandum

To: CIR Expert Panel Members and Liaisons
From: Alan Andersen, Director, CIR
Date: November 21, 2011
Subject: Re-Review Summaries

At the September 2011 meeting, the Panel determined to not re-open the safety assessment of 4-chlororesorcinol and glutaral.

The attached re-review summaries, are included for your review and approval.
4-Chlororesorcinol

CONCLUSION: In the 1996 safety assessment of 4-chlororesorcinol, the Cosmetic Ingredient Review (CIR) Expert Panel stated that this ingredient is safe as used in hair dye formulations. The Expert Panel reviewed newly available studies since that assessment along with updated frequency and concentration of use information. The Expert Panel determined not to reopen this safety assessment and confirmed that 4-chlororesorcinol is safe in the present practices of use and concentration in hair dye formulations.

DISCUSSION: The Panel reviewed new data that was published in the opinion released by the European Commission’s Scientific Committee on Consumer Safety (SCCS) in 2010, which determined that this ingredient was not a health risk, apart from sensitization, at a maximum concentration of 2.5%. The Panel noted that use of 4-chlororesorcinol in hair dyes has increased from 33 uses to 210 and that the current use concentration is up to 2%, which is higher than the 1% concentration previously reported on but below the SCCS limit.

In considering hair dye epidemiology data, the CIR Expert Panel concluded that the available epidemiology studies are insufficient to conclude there is a causal relationship between hair dye use and cancer or other toxicologic endpoints, based on lack of strength of the associations and inconsistency of findings. Use of direct hair dyes, while not the focus in all investigations, appears to have little evidence of any association with adverse events as reported in epidemiology studies. A detailed summary of the available hair dye epidemiology data is available at http://www.cir-safety.org/findings.shtml.

<table>
<thead>
<tr>
<th>Table 1. Historic and current uses and concentrations of 4-chlororesorcinol.</th>
<th>1,2,4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td># of Uses</td>
</tr>
<tr>
<td>4-Chlororesorcinol</td>
<td></td>
</tr>
<tr>
<td>Totals</td>
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</tr>
<tr>
<td>Duration of Use</td>
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<td>Leave-On</td>
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<tr>
<td>Rinse Off</td>
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<tr>
<td>Exposure Type</td>
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<td>Possible Ingestion</td>
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<tr>
<td>Inhalation</td>
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<tr>
<td>Mucous Membrane</td>
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<tr>
<td>Bath Products</td>
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</tr>
<tr>
<td>Baby Products</td>
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</tbody>
</table>

NA = Not Available; Totals = Rinse-off + Leave-on Product Uses.
Note: Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure type uses may not equal the sum total uses.

References


CONCLUSION: In the 1996 safety assessment of glutaral, the Cosmetic Ingredient Review (CIR) Expert Panel stated that this ingredient is safe for use at concentrations up to 0.5% in rinse-off products. There were insufficient data to determine the safety of glutaral in leave-on products and this ingredient should not be used in aerosolized products. The Expert Panel reviewed newly available studies since that assessment along with updated frequency and concentration of use information. The Expert Panel determined to not reopen this safety assessment and confirmed the original conclusion of glutaral.

DISCUSSION: Since the original conclusion, numerous studies have been published, including a 2-year NTP study on inhalation. While the number of uses for glutaral has decreased from 60 to 13, this ingredient is currently being used in an aerosol product and in leave-on products. The current concentration of use is $6 \times 10^{-6}\%$ in non-coloring hair products. The Panel received clarification that this concentration of glutaral is incidental and that glutaral is not added to the products for functional use. Additionally, while glutaral did not cause cancerous lesions in the 2-year NTP study, several studies have found that this ingredient does cause damage to the upper respiratory tract in animals.

### Table 1. Historic and current uses and concentrations of glutaral

<table>
<thead>
<tr>
<th>Exposure Type</th>
<th># of Uses</th>
<th>Conc. of Use (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye Area</td>
<td>2</td>
<td>NR</td>
</tr>
<tr>
<td>Incidental Ingestion</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Incidental Inhalation-Sprays</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Incidental Inhalation-Powders</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Dermal Contact</td>
<td>19</td>
<td>7</td>
</tr>
<tr>
<td>Deodorant (underarm)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Hair - Non-Coloring</td>
<td>41</td>
<td>6</td>
</tr>
<tr>
<td>Hair-Coloring</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Nail</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Mucous Membrane</td>
<td>NR</td>
<td>1</td>
</tr>
<tr>
<td>Baby Products</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td><strong>Duration of Use</strong></td>
<td><strong>60</strong></td>
<td><strong>13</strong></td>
</tr>
</tbody>
</table>

*Breakdown is not available.

Calculated concentration of incidental glutaral in the finished product. Glutaral is included at low concentrations in a raw material added to the final product. It is not functional in the final product. NR = Not Reported; Totals = Rinse-off + Leave-on Product Uses.

Note: Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure type uses may not equal the sum total uses.

References


